

THE CHEST & HEART ASSOCIATION OF BANGLADESH

EXECUTIVE COMMITTEE FOR 2007-2009

President	:	Prof. Mirza Mohammad Hiron
Vice-President	:	Prof. Md. Mostafizur Rahman Dr. AKM Mostafa Hussain Dr. Md. Rafiqul Islam
Secretary General	:	Dr. Md. Zahirul Islam Shakil
Treasurer	:	Dr. Biswas Akhtar Hossain
Joint Secretary	:	Dr. Md. Mizanur Rahman (Deceased) Dr. Md. Naimul Haque Shammi
Organising Secretary	:	Dr. Golam Sarwar LH Bhuiyan
Office Secretary	:	Dr. Md. Abdur Rouf
Members	:	Prof. Shafiqul Ahsan Dr. Md. Solaman Siddique Bhuiyan Dr. Md. Safiuddin Dr. Md. Zahidul Islam Dr. Mahmud Masum Attar Dr. SM Mustafa Zaman Dr. Mohammad Abdus Shakur Khan Dr. Md. Ziaul Karim Dr. Bashir Ahmed Dr. Md. Abu Raihan Dr. Narayan Chandra Datta

THE CHEST & HEART JOURNAL

(An official organ of the Chest & Heart
Association of Bangladesh)

Volume 33, Number 1, January 2009

EDITORIAL BOARD

Chairman : Prof. Shah Md. Keramat Ali

Editor : Prof. Shafiqul Ahsan

Assistant Editors : Dr. SM Mustafa Zaman
Dr. Md. Abdur Rouf
Dr. Golam Sarwar LH Bhuiyan

Members

Prof. Mirza Mohammad Hiron	Prof. Md. Mostafizur Rahman
Prof. Md. Atiqur Rahman	Prof. Golam Mohiuddin Akbor Chowdhury
Dr. Asif Mujtaba Mahmud	Dr. Solaman Siddique Bhuiyan
Dr. Wahiduzzaman Bhuiyan	Dr. AKM Mustafa Hossain
Dr. Md. Rafiqul Islam	Dr. Biswas Akhtar Hossain
Dr. Md. Khairul Hassan Jessy	Dr. Md. Mizanur Rahman
Dr. Md. Shahedur Rahman Khan	Dr. Md. Abdul Qayyum
Dr. Mohammad Abdus Shakur Khan	Dr. Mahmud Masum Attar
Dr. Basir Ahmed	Dr. Md. Naimul Haque Shammi
Dr. Narayan Chandra Datta	Dr. Mohammad Safiuddin
Dr. Md. Zahirul Islam Shakil	Dr. Rajashish Chakraborty
Dr. Ziaul Karim	Dr. Md. Zahidul Islam
Dr. Md. Abu Raihan	

Published by : Professor Shafiqul Ahsan, on behalf of Chest and Heart Association of Bangladesh

Printed at : Asian Colour Printing, 130, DIT Extension Road, Fakirerpool, Dhaka-1000, Bangladesh
Phone : 9357726, 8362258, E-mail: asianclr@yahoo.com

Address of Correspondence : The Editor, Chest and Heart Journal.
C/o. Library wing, Institute of Diseases of the Chest & Hospital.
Mohakhali, Dhaka-1212

THE CHEST & HEART ASSOCIATION OF BANGLADESH

ACADEMIC CELL

Chairman	:	Prof. Md. Mostafizur Rahman
Co-Chairman	:	Dr. Md. Zillur Rahman
Coordinator	:	Dr. Md. Mohiuddin Ahmad
Joint Coordinator	:	Dr. Kazi Saifuddin Bennoor Dr. Saifuddin Chowdhury
Members	:	Prof. AKM Shamsul Huq Prof. Jamshed Hayder Siddique Prof. Md. Hasibul Hossain Prof. Md. Rashidul Hasan Prof. Md. Ali Hossain Prof. Shamsul Arafeen Khan Prof. Rowshan Ali Dr. Md. Kamrul Alam Dr. Khaleda Begum Dr. Shah Mohammad Saifur Rahman Dr. Maksud Ahmed Dr. Shamim Ahmed Dr. Mahmud Rahim Dr. Md. Jahangir Rashid Dr. Md. Zahirul Islam Shakil

RESEARCH & INFORMATION CELL

Chairperson	:	Prof. KMHS Sirajul Haque
Co-Chairman	:	Dr. AKM Razzaque
Coordinator	:	Dr. Mohammad Abdus Shakur Khan
Joint Coordinator	:	Dr. Md. Abu Hasanat Dr. SM Abdullah Al Mamun
Members	:	Prof. Md. Atiqur Rahman Prof. Mahbub Anwar Prof. Sufia Begum Dr. AKM Akramul Haque Dr. Manabendra Kumar Nath Dr. Shamsul Alam Dr. Md. Delwar Hossain Dr. SAHM Mesbahul Islam Dr. Md. Zakir Hossain Sarker Dr. Adnan Yusuf Choudhury Dr. Md. Abdul Khaleque Dr. Md. Zahirul Islam Shakil

CONTENTS

Original Articles

- Role of Salmeterol in the Treatment of COPD Patients Receiving Ipratropium Bromide 1
Md Ilias, Shamim Ahmed, Md. Shahedur Rahman Khan, Mirza Mohammed Hiron, Md. Abdur Rouf, Md. Delwar Hossain, Shah Mesbahul Islam, Taslima Begum
- Immediate Outcome of Percutaneous Transvenous Mitral Commissurotomy 11
for Patients of Mitral Stenosis with Atrial Fibrillation
Md. Toufiqur Rahman, Syed Azizul Haque, Kh. Qamrul Islam, Abdul Wadud Chowdhury, Abul Khair, Ashraf Uddin Chowdhury, SM Mustafa Zaman
- Single Versus Combination Nebulized Bronchodilator Therapy, in the Treatment 17
of Acute episodes of Bronchial Asthma
Shah Md. Saifur Rahman, Md. Naimul Haque, Narayan Chandra Datta, Syed Rezaul Huq Barkat Ullah, Abu Raihan, K.H Jessy, Tapash Kumar Bosh, A.K.M Mustafa Hossain, Biswas Akhter Hossain, Mirza Mohammad Hiron
- Effects of Decortication on Lung Function in Chronic Empyema Thoracis 22
Md. Mofizur Rahman Mia, Shahedur Rahman Chowdhury, Shafiqul Ahsan GM Akbar Chowdhury, AKM Razzaque
- Reversal of Stage-I Hypertension by Behavioural Intervention: 29
18 Month Study in Urban Bangladesh
AKM Alamgir, Shah Mohammad Keramat Ali, KMHS Sirajul Haque
- Current Management in Day Care Transfusion Unit at Dhaka Medical College Hospital 37
IA Begum, J Biswas, MA Fayez, MS Dowllah S Begum
- Fluticasone and Montelukast Compared with Fluticasone and Salmeterol 41
in Protecting Against Asthma Exacerbation in Adults
A.K.M. Mustafa Hussain, Md. Naimul Huque, Narayan Chandra Datta, Biswas Akhter Hussain, Abu Raihan, Shah Muhammad Saifur Rahman, M.A. Rouf, Mirza Mohammad Hiron
- Pattern of Radiological Features of Sputum Smear Positive Pulmonary Tuberculosis 45
Md. Minhajul Islam
- Location and Histological Pattern of Lung Carcinoma In Relation to the Smoking Habit 48
Rokeya Sultana, Mirza Mohammad Hiron, AKM Mustafa Hussain, Syed Rezaul Haque Mostafizur Rahman, Abdur Rouf
- Down Syndrome with Congenital Heart Disease: Analysis of Cases Over Two Years 54
in A Non-Invasive Laboratory of A Tertiary Hospital
Lt. Colonel Nurun Nahar Fatema
- Review Article**
- Non-Invasive Ventilation and its Role in COPD 59
MN Haque, SAHMM Islam, BA Hossain, MR Hassan, MB Ullah, SR Huq
- Case Report**
- Tender Hepatomegaly As Presentation of Disseminated Tuberculosis - A Case Report 66
MU Jalal, KC Ganguly, K Hassan, SMS Rahman, M Ilias, AKM Hussain, MM Hiron

INSTRUCTION TO AUTHORS ABOUT UNIFORM MANUSCRIPT WRITING

The Chest and Heart Journal is published twice in a year in the months of January and July. The journal publishes original papers, reviews concerned with recent practice and case report of exceptional merits. Papers are accepted for publication with an understanding that they are subject to editorial revision. A covering letter signed by all authors must state that the data have not been published elsewhere in whole or in part and all authors agree their publication in Chest and Heart Journal. All submitted manuscripts are reviewed by the editors and rejected manuscripts will not be returned. Ethical aspects will be considered in the assessment of the paper. Three typed copies of the article and one copy in a 3.5" high density floppy diskette processed in word perfect 6.0 or MS Word 6.0 should be submitted to the editor.

Preparation of Manuscripts

Manuscripts should be typed on one side of good quality paper, with margins of at least 25mm and using double space throughout. Each component of the manuscript should begin on a new page in the sequence of title page, abstract, text, references, tables, and legend for illustrations. The title page should include the title of the paper, name of the author(s), name of the department(s) to which work should be attributed. The text should be presented in the form of Introduction, Materials and Methods, Results, and Discussion. The text should not exceed 2500 words and a word count should be supplied.

Abstracts/Summary

Provide on a separate page an abstract of not more than 250 words. This abstract should consist of four paragraphs, labeled Background, Methods, Results and Conclusions. They should briefly describe the problem being addressed in the study, how the study was performed, the salient results, and what the authors conclude from the results.

Table

Each table should be typed in on separate sheet. Table should have brief title for each, should be numbered consecutively using Roman numbers and be cited in the consecutive order, internal horizontal and vertical rules should not be used.

Results should be presented in logical sequence in the text, tables or illustration. Do not repeat in the text all data in the tables or illustrations; emphasize or summarize only important observations.

Drug Names

Generic names should generally be used. When proprietary brands are used in research, include the brand name in parentheses in the Methods section.

Illustrations

Figure should be professionally designed symbols, lettering, and numbering should be clear and large. The back of each figure should include the sequence number and the proper orientation (e.g. "top"). Photographs and photomicrographs should be supplied as glossy black and white prints unmounted. Legend for each illustration should be submitted in separate sheets. All photographs, graphs and diagrams should be referred to as figures numbered consecutively in the text in Roman numerals.

Discussion

Emphasize the new and important aspects of the study and the conclusions that follow from them. The detail data or other material given in the Introduction or the Results section should not be repeated. The implications of the findings and their limitations, including implication for future research should be included in the Discussion section. The observations should be compared and related to other relevant studies, new hypothesis is appreciated, and however they should be clearly labeled as such. Recommendations may be included only when appropriate.

References

References should be numbered consecutively in the order in which they are first mentioned in the text. Identify references in text, tables, and legend by Roman numerals in parenthesis. Use the styles of the example below, which are based on the formats used by the US National Library of Medicine (NLM) in the Index Medicus.

Avoid using abstracts as references. References to paper accepted but not yet published should be designated as “in press” or “forthcoming”; authors should obtain written permission to cite such papers as well as verification that they have been accepted for publication. Information from manuscripts submitted but not accepted should be cited as “unpublished observations” with written permission from the source. Avoid using a “personal communication” unless it provides essential information not available from a public source. For scientific articles, authors should obtain written permission and confirmation of accuracy from the source of a personal communication.

The references must be verified by the authors(s) against the original documents.

1. Articles in Journal

- a) List all six authors when six or less;
Connors JP, Roper CL, Ferguson TB. Transbronchial Catheterisation of Pulmonary Abscess. *Ann Thorac Surg* 1975; 19 : 254-7.
- b) When seven or more, list the first three and then add et al;
Karalus NC, Cursons RT, Leng RA, et al. Community acquired pneumonia: aetiology and prognostic Index evaluation. *Thorax* 1991; 46 : 413-12.
- c) No author given;
Cancer in South Africa (editorial). *S Afr Med J* 1994; 84-15.
- d) Organization as author
The Cardiac Society of Australia and New Zealand. Clinical exercise stress training. Safety and performance guideline. *Med J Aust* 1996; 164 : 282-4.

2. Books and Other Manuscripts

- a) Personal author
Tierney LM, -McPhee SJ, Papakadis MA. *Current Medical Diagnosis and Treatment. Lange Medical books/McGraw Hill* 2000.
- b) Editor(s), compiler(s) as author
Baum GL, Wolinsky E, editor. *Text Book of Pulmonary diseases. 5th ed. New York: Little Brown Co. 1994.*
- c) Organization as author and publisher
World Health Organization, *Ethical Criteria for Medical Drug Promotion. Geneva: World Health Organization; 1988.*
- d) Chapter in a book
Macnee W. Chronic bronchitis and emphysema. Seaton A, Seaton D, editors. *Crofton and Douglas's Respiratory Diseases. 5th ed. UK. The Blackwell Science; 2000; p.616-95.*
- e) Dissertation
Kaplan SJ. *Post-hospital home health care: the elderly's access and utilization (dissertation). St. Louis (MO). Washington Univ; 1995.*

3. Other published material

- a) Newspaper article
Lee G. Hospitalizations tied to ozone pollution: study estimates 50,000 admissions annually. *The Washington Post* 1996, June 21; Sect. A : 3(col. 5).
- b) Dictionary and similar references
Student's medical dictionary. 26th ed. Baltimore: Williams & Wilkins; 1995. Apraxia; p.119-20.

4. Unpublished Material

a) In press

Leshner AI. Molecular mechanisms of cocaine addiction. N Engl J Med In Press 1997.

5. Electronic Material

a) Journal articles in electronic format

Morse SS. Factors in the emergence of infectious diseases. Emerg Infect Dis Serial online I 1995 Jan-Mar I cited 1996 June 5 I; 1(1): 24 screens I

Available from: URL: <http://www.cdc.gov/ncidod/EID/eid.htm>

Nomenclature and Abbreviation

1. Abbreviations and symbols must be standard and SI units should be used thoughtout.
2. Terms such as electrocardiogram, ultrasonogram etc. should when mentioned first, be written in full followed by accepted abbreviations (ECG, USG etc.)

Permissions

A written statement must accompany materials taken from other sources from both author and publisher giving permission to the Journal for reproduction. Obtain permission in writing from at least on a author of papers still in press, unpublished data, and personal communications.

Review and Action

Manuscripts are examined by the editorial staff and are usually sent to reviewers, but we reserve the right of final selection.

Proof

Two marked copies of the proofs may be sent to the principal author, which should be read carefully for error. One corrected copy must be returned to the editor within the next three days. Major alteration in the text can not be accepted.

Editorial Mail

Manuscripts and other communication for the editors should be addressed to

The Editor
Chest and Heart Journal
C/o. Library
Institute of Diseases of the Chest & Hospital
Mohakhali, Dhaka-1212

Rates of Advertisement in CHEST AND HEART JOURNAL

Page facing inside back cover	Tk. 20,000/-
Page facing inside front cover	Tk. 20,000/-
Ordinary full page	Tk. 15,000/-

Technical details :

Language	English
Size of the Journal	8.50" x 11.25"

Extra :

- i) 30% on each additional colour
- ii) Block making

Terms and Conditions :

1. Advertisement order with blocks or materials should reach the Secretary General, Chest and Heart Association of Bangladesh and Editor, Chest and Heart Journal
2. Payment must be made within two weeks from the date of publication of the Journal.

N. B. If the advertisement is made through an advertising agent, the commission should be borne by the firm concerned.

ORIGINAL ARTICLE

Immediate Outcome of Percutaneous Transvenous Mitral Commissurotomy for Patients of Mitral Stenosis with Atrial Fibrillation

Md. Toufiqur Rahman¹, Syed Azizul Haque², Kh. Qamrul Islam³,
Abdul Wadud Chowdhury⁴, Abul Khair⁵, Ashraf Uddin Chowdhury⁶, SM Mustafa Zaman⁷

Abstract

Objectives: *The purpose of this study was to address the effect of atrial fibrillation (AF) on the immediate outcome of patients undergoing Percutaneous Transvenous Mitral Commissurotomy (PTMC).*

Background: *There is controversy as to whether the presence of AF has a direct negative effect on the outcome after PTMC.*

Methods: *The immediate procedural and in-hospital clinical outcome after PTMC of 88 patients with AF were prospectively collected and compared with those of 96 patients in normal sinus rhythm (NSR).*

Results: *Patients with AF were older (51 ± 12 vs. 38 ± 13 years; $p < 0.0001$) and presented more frequently with New York Heart Association (NYHA) class III-IV (79.8% vs. 59.9%; $p < 0.0001$), echocardiographic score >8 (39.8% vs. 24.9%; $p < 0.0001$), calcified valves under fluoroscopy (25.2% vs. 20.1%, $p < 0.0001$) and with history of previous surgical commissurotomy (22.2% vs. 10.5%; $p = 0.0002$). In patients with AF, PTMC resulted in inferior outcomes, as reflected in a smaller post-PTMC mitral valve area (1.7 ± 0.6 vs. 2 ± 0.4 cm²; $p < 0.0001$).*

Conclusion: *Patients with AF have a worse immediate outcome after PTMC. However, the presence of AF by itself does not unfavorably influence the outcome, but is a marker for clinical and morphologic features associated with inferior results after PTMC.*

Key Words: *Immediate outcome, PTMC, Atrial fibrillation.*

[Chest & Heart Journal 2009; 33(1) : 11-16]

Introduction

Although Rheumatic heart disease (RHD) is increasingly rare in developed countries, it remains the most common cardiac disorders in developing countries like Bangladesh. Of the

cardiac malfunction that can result from RHD, mitral stenosis (MS) is perhaps the most common. Percutaneous Transvenous Mitral Commissurotomy (PTMC) has been established as an alternative to surgical mitral commissurotomy in

1. Asst. Professor, Department of Cardiology, National Institute of Cardiovascular Diseases, Dhaka.
 2. Professor, Department of Cardiology, Dinajpur Medical College & Hospital.
 3. Associate Professor, Department of Cardiology, National Institute of Cardiovascular Diseases.
 4. Associate Professor, Department of Cardiology, Dhaka Medical College & Hospital.
 5. Assistant Professor, Department of Cardiology, National Institute of Cardiovascular Diseases.
 6. Assistant Professor, Department of Cardiology, National Institute of Cardiovascular Diseases.
 7. Assistant Professor, Department of Cardiology, Bangabandhu Sheikh Mujib Medical University, Dhaka
- Correspondence to:** Dr. Md. Toufiqur Rahman, FCPS, MD. Asst. Professor, Cardiology, Room No.323, South Block, National institute of Cardiovascular Diseases, Dhaka., E-mail: drtoufiq1971@yahoo.com

the treatment of patients with symptomatic mitral stenosis¹⁻⁷. Several studies have demonstrated that this technique provides sustained clinical and hemodynamic improvement in a selected group of patients with mitral stenosis. Certain clinical and morphologic factors such as age^{5,6} history of previous surgical commissurotomy^{5,6,9} presence of calcification under fluoroscopy^{6,8,11} echocardiographic score^{6,10,12} New York Heart Association (NYHA) class IV at presentation^{6,8,10} and the presence of severe tricuspid regurgitation¹⁵, have been identified as predictors of immediate and long-term outcome after PTMC. The development of atrial fibrillation (AF) is common and important sequelae in patients with mitral stenosis, and it is associated with hemodynamic and clinical decompensation. Previous surgical studies have demonstrated that the presence of AF is associated with suboptimal immediate and long-term outcome after surgical mitral commissurotomy¹⁶⁻²⁰. However, there is controversy as to whether AF is an important independent predictor of the immediate and long-term outcome of patients undergoing PTMC. Thus, the purpose of this study was to address this important clinical issue by evaluating the effect of AF on the immediate outcome of PTMC in patients undergoing the procedure.

Methods

Study population. The study group included 184 consecutive patients who underwent PTMC at the National Institute of cardiovascular Diseases (NICVD), Dhaka and Al-Helal Heart Institute, Mirpur between May 2003 and August 2007. Of these 184 patients, 88 (48.1%) had AF at the time of the procedure and 96 (51.9%) had normal sinus rhythm (NSR). All patients were screened clinically and by transthoracic echocardiography. Patients with AF and those with previous embolic events had undergone anticoagulation with warfarin for at least three months before consideration for PTMC. Transesophageal echocardiography was performed in patients with a suboptimal transthoracic study, in those with a history of a previous embolic event and in those with a possible left atrial thrombus by the transthoracic study. Patients with left atrial thrombus were treated with warfarin for at least two to three months, and PTMC was performed only if resolution of the left atrial thrombus was demonstrated by repeat transesophageal echocardiography.

PTMC procedure. All patients underwent PTMC using the transseptal antegrade technique after informed consent was obtained. The Inoue technique was used with these patients. The maximum volume of the Inoue balloon used was determined by the equation: maximum balloon volume (mm) = (patient's height (cm)/10) + 10. Left ventriculography was performed in all patients before and after PTMC to assess the severity of mitral regurgitation.

Data collection and definitions. All data were prospectively collected. Demographic and clinical variables included age, gender, body surface area, New York Heart Association (NYHA) functional class at presentation, presence of AF and previous surgical commissurotomy. Laboratory variables included the echocardiographic score, pre- and post-PTMC severity of mitral regurgitation using contrast left ventriculography and the presence of fluoroscopically visible mitral valve calcification, which was graded from 0 to 4. Procedural-related variables included mean left atrial pressure, mean mitral valve gradient and Aortic pressure before and after PTMC.

Prospectively collected procedure related complications included death, mitral valve replacement (MVR), pericardial tamponade, thromboembolism, third-degree atrioventricular block, post-PTMC mitral regurgitation $\geq 2+$. Procedure-related death was defined as in-hospital death that was directly related to the PTMC procedure. Successful outcome of PTMC was defined as a post-PTMC mitral valve area ≥ 1.5 cm², without $>2+$ increase in the severity of mitral regurgitation and post-PTMC mitral regurgitation $<3+$.

Statistical analysis. Continuous variables are expressed as mean \pm standard deviation (SD), and categorical variables as percent. Student *t* test and chi-square analysis were carried out for comparison of continuous and categorical variables, respectively. *p* Values ≤ 0.05 were considered significant. Demographic, clinical, echocardiographic, procedural and angiographic variables were tested to determine significant ($p < 0.05$) univariate correlates of immediate success in both the overall and in the AF groups.

Results:

Table-I
Baseline Demographic Characteristics

Parameters	Group-I (AF) N = 88	Group-II (NSR) N=96	P Value
Age (years)	51 ± 12	38 ± 13	< 0.0001
Sex			
Male	18 (20.2 %)	16 (16.1 %)	NS
Female	70 (80.3 %)	80 (84.4 %)	NS

Preprocedural clinical and morphologic variables.

Baseline demographic characteristics of the two groups of patients were shown in Table 1. Patients in AF were older (51 ± 12 vs. 38 ± 13 years, p < 0.0001). Female were more than male in both groups.

Table-II
Baseline Clinical and Echocardiographic Characteristics

Parameters	Group-I (AF) N = 88	Group-II (NSR) N=96	P Value
RHD status			
MS	48 (55.26%)	58 (60.13%)	NS
MS with MR < Grade -II	40 (44.74 %)	38 (39.87 %)	NS
NYHA Status			
Class 1-II	18 (20.2%)	38 (40.1%)	NS
Class-III-IV	70 (79.8%)	58 (59.9%)	< 0.0001
Wilkins Echo score			
≤8	53 (60.2%)	72 (75.1%)	< 0.0001
≥8	35 (39.8 %)	24 (24.9%)	< 0.0001
Fluoroscopic Calcium > 2+ Prior	31 (25.2%)	19 (20.1%)	< 0.0001
Commissurotomy	19 (22.2%)	10 (10.5%)	0.0002
Mitral Regurgitation 1+	37 (42.1%)	36 (37.2%)	0.003
Mitral Regurgitation 2+	08 (9.2%)	04 (4.1%)	0.0002

Baseline clinical and echocardiographic characteristics of the two groups of patients were shown in Table II. Patients in AF were presented more frequently with NYHA functional class III-IV (79.8% vs. 59.9%, p < 0.0001), history of previous surgical commissurotomy (22.2% vs. 10.5%, p = 0.0002), 2+ grade of mitral calcification by fluoroscopy (35.2% vs. 20.1%, p < 0.0001),

echocardiographic score >8 (39.8% vs. 24.9%, p < 0.0001) and pre-PTMC mitral regurgitation ≥1+ (42.1% vs. 32.2%, p = 0.0006).

Table-III
Hemodynamic Characteristics before PTMC

Parameters	Group-I (AF) N = 88	Group-II (NSR) N=96	P Value
MVA (cm ²)	0.71 ± 0.11	0.79 ± 0.12	0.0002
Transmitral gradient (mmHg)	27 ± 02	23 ± 02	NS
LA size (mm)	54 ± 08	50 ± 11	NS
LA Pressure (mmHg)	51 ± 09	48 ± 08	NS
Aortic Pressure (mmHg)	88 ± 12	92 ± 10	NS

Hemodynamic findings before PTMC were shown in Table III . Before PTMC, patients in AF had lower pre-PTMC mitral valve area (0.72 ± 0.11 vs. 0.79 ± 0.12 cm², p = 0.0002). There were no significant differences of transmitral gradient, left atrial size, left atrial pressure and aortic pressure between two groups.

Table-IV
Hemodynamic Characteristics after PTMC

Parameters	Group-I (AF) N = 88	Group-II (NSR) N=96	P Value
MVA (cm ²)	1.7 ± 0.6	2.0 ± 0.4	< 0.0001
Transmitral gradient (mmHg)	07 ± 03	06 ± 02	NS
LA size (mm)	48 ± 03	46 ± 04	NS
LA Pressure (mm Hg)	17 ± 6	15 ± 6	< 0.0001
Aortic Pressure (mmHg)	97 ± 07	99 ± 06	NS

Hemodynamic findings after PTMC were shown in Table IV. After PTMC, patients in AF had significantly lower post-PTMC mitral valve area (1.7 ± 0.6 cm² vs. 2.0 ± 0.4 cm², p < 0.0001). In addition, mean left atrial (17 ± 6 vs. 15 ± 6 mm Hg, p < 0.0001) pressures were significantly higher after PTMC in the AF group. There were no significant differences of transmitral gradient, left atrial size and aortic pressure between two groups.

Table-V
Complications and In hospital events

Characteristics	Group-I (AF) N = 88	Group-II (NSR) N=96	P Value
Procedural success	80 (90.9 %)	94 (97.9 %)	< 0.0001
Procedural death	0	0	NS
In hospital death	2 (02.2 %)	1 (01.1%)	NS
MR grade—Post PTMC			
2 +	05 (05 .7 %)	04 (04.2 %)	NS
3 +	05 (05.7%)	02 (02.1 %)	NS
Left to right shunt (ASD)	10 (11.4 %)	08 (08.4 %)	NS
AV block	0	0	NS
Local vascular complications like pain, hemorrhage, hematoma	20 (22.8 %)	16 (16.8 %)	NS
Thromboembolism	01 (01. 1 %)	0	NS
Pericardial temponade (Haemopericardium)	01 (01.1 %)	01 (01.1 %)	NS

The immediate procedural results and in-hospital outcomes are shown in Table V.

Patients in the AF group have a lower procedural success (90.9% vs. 97.9%, $p < 0.0001$). Univariate predictors of procedural success in the AF group included age, male gender, history of previous commissurotomy, NYHA functional status at presentation; fluoroscopic mitral valve calcification, echocardiographic score, pre-PTMC mitral valve area and pre- PTMC mitral regurgitation . Multiple stepwise logistic regression analysis identified pre-PTMC mitral valve area ($p \leq 0.0001$), echocardiographic score ≤ 8 ($p = 0.001$), male gender ($p = 0.038$) and absence of previous surgical commissurotomy ($p = 0.048$) as independent predictors of procedural success in patients in AF.

There was no procedural death in both groups. There are 2 (02.2%) in hospital death in AF group and 1(01.1%) in NSR group. 1 patient in AF group died from massive CVD after PTMC. In AF group 1 patient died from renal failure and electrolyte imbalance .In NSR group 1 patient died from multisystem organ failure due to sepsis unrelated to PTMC.

There were no differences between the AF and NSR group in the incidence of 2+ (05.7% vs. 04.2% , $p=NS$) or 3+ (05.7% vs. 02.1%, $p=NS$) post PTMC mitral regurgitation as assessed by left ventriculography.

There was no A-V block in both groups during or after PTMC.

Pericardial temponade occurred in 1 patient in AF group and 1 patient in NSR group. Those two patients were successfully treated with pericardiocentesis in the catheterization laboratory and PTMC was completed successfully.

Thromboembolic events occurred in 01 (01.1%) patient in AF group.

Left to right shunt (ASD) occurred in 10 (11.4%) patients in AF group and 08(05.4%) in NSR group.

Local vascular complications like pain, haemorrhage, haematoma occurred in 20(22.8%) patients in AF group and 16(16.8%) patients in NSR group.

Discussion

The present study demonstrates that patients with rheumatic mitral stenosis in AF have a worse immediate outcome after PTMC. However, the presence of AF by itself does not unfavorably influence the outcome, but is a marker for clinical and morphologic features associated with inferior results after PTMC.

Although the presence of AF is not an independent predictor of procedural success, patients in AF have an inferior immediate hemodynamic outcome of PTMC as reflected in a lower procedural success rate (90.9% vs. 97.9%, $p < 0.0001$) and a smaller post-PTMC mitral valve area ($1.7 \pm 0.6 \text{ cm}^2$ vs. $2 \pm 0.4 \text{ cm}^2$, $p < 0.0001$). However, there were not significant differences in the post-PTMC incidence

of severe mitral regurgitation, or left to right shunting between the two groups of patients. A higher incidence of clinical and morphologic characteristics associated with suboptimal results after PTMC in this patient account for these results. Although the presence of AF was associated with higher in-hospital mortality, other procedural complications such as in-hospital MVR, pericardial tamponade and thromboembolic events were similar in the two groups of patients.

Previous studies on the influence of AF on the immediate success after PTMC have been controversial. Previous report showed that the presence of AF was an independent predictor of suboptimal result after PTMC in a smaller group of patients¹³. Hung et al.²⁶ reported that AF was a univariate predictor of suboptimal immediate result but not an independent predictor by multivariate analysis.

Iung et al.²⁷ identified sinus rhythm as univariate predictor of good functional results five years after a successful procedure, but the multivariate analysis failed to demonstrate rhythm as an independent predictor of long-term success. Pan et al. identified the presence of AF as an independent predictor of late success. Conversely, in the larger series from the NHLBI registry of percutaneous balloon mitral commissurotomy, AF was not an independent predictor of procedural success or long-term outcome at 4 years of follow-up²⁸. Other reports also did not reveal any association between AF and suboptimal immediate or long-term outcome after percutaneous balloon valvotomy^{4,5,15}. The inconsistency of the results of these studies is more likely explained by the size of the patient population included in each study as well as different baseline clinical and morphologic characteristics of the patients.

Conclusion

The present study demonstrated that the presence of AF is associated with worse outcome after PTMC. Analysis of preprocedural and procedural characteristics revealed that this association is most likely explained by the presence of multiple factors in the AF group that adversely affect the immediate outcome of PTMC. Therefore, the presence of AF should not be the only determinant in the decision process regarding treatment options

in a patient with rheumatic mitral stenosis because its presence does not necessarily predict adverse outcome. An echocardiographic score ≤ 8 primarily identifies a subgroup of patients in AF in whom percutaneous balloon valvotomy is very likely to be successful and provide good results.

References

1. Inoue K, Owaki T, Nakamura T, Miyamoto N. Clinical application of intravenous mitral commissurotomy by a new balloon catheter. *J Thorac Cardiovas Surg.* 1984;87:394–402.
2. Rahman MT, Haque SA, Islam KQ, Chowdhury AW, Chowdhury AU, Khair MA; Immediate Outcome and Safety of Percutaneous Transvenous Mitral Commissurotomy In Patients with Restenosis After Closed Mitral Commissurotomy. *Bangladesh Heart journal.* 2008; 23(1):44-47
3. Palacios IF, Block PC, Brandi S, et al. Percutaneous balloon valvotomy for patients with severe mitral stenosis. *Circulation.* 1987;75: 778–784.
4. Nobuyoshi M, Hamasaki N, Kimura T, et al. Indications, complications and short-term clinical outcome of percutaneous transvenous mitral commissurotomy. *Circulation.* 1989;80:782–792.
5. Haque SA, Chowdhury AU, Rahman MT, Islam KQ. Immediate outcome of percutaneous transvenous mitral commissurotomy (PTMC). *Bangladesh J Medicine.* 2004;15: 45-48.
6. Palacios IF. Percutaneous mitral balloon valvotomy for patients with mitral stenosis. *Curr Opin Cardiol.* 1994;9:164–175.
7. Arora R, Kalra GS, Ramachandra GS, et al. Percutaneous transatrial mitral commissurotomy: immediate and intermediate results. *J Am Coll Cardiol.* 1994;23:1327–1332.
8. Islam KQ, Rahman MT, Haque SA. Percutaneous Transvenous Mitral commissurotomy In Juvenile Rheumatic mitral stenosis, Immediate and In – Hospital Results. *Chest and heart Journal.* 2007; 31(2): 94-99

9. Jang IK, Block PC, Newell JB, Tuczu EM, Palacios IF. Percutaneous mitral balloon valvotomy for recurrent mitral stenosis after surgical commissurotomy. *Am J Cardiol.* 1995;75:601–605.
10. Davidson CJ, Bashore TM, Mickel M, Davis K. Balloon mitral commissurotomy after previous surgical commissurotomy. *Circulation.* 1992;86:91–99.
11. Tuzcu EM, Block PC, Griffin B, Dinsmore R, Newell JB, Palacios IF. Percutaneous mitral balloon valvotomy in patients with calcific mitral stenosis: immediate and long-term outcome. *J Am Coll Cardiol.* 1994;23:1604–1609.
12. Palacios IF. Farewell to surgical mitral commissurotomy for many patients. *Circulation.* 1998;97:223–226.
13. Abascal VM, Wilkins G, O’Shea JP, et al. Prediction of successful outcome in 130 patients undergoing percutaneous balloon mitral valvotomy. *Circulation.* 1990;82:448–456.
14. Dean LS, Mickel M, Bonan R, et al. Four-year follow-up of patients undergoing percutaneous balloon mitral commissurotomy. A report from the national Heart, Lung, and Blood Institute Balloon Valvuloplasty Registry. *J Am Coll Cardiol.* 1996;28:1452–1457.
15. Desideri A, Vanderperren O, Serra A, et al. Long-term (9 to 33 months) echocardiographic follow-up after successful percutaneous mitral commissurotomy. *Am J Cardiol.* 1992; 69: 1602–1606.
16. Sellors DM, Bedford DE, Sommerville W. Valvotomy in the treatment of mitral stenosis. *Br Med J.* 1953;2:1059–1067
17. Ellis LB, Benson H, Harken DE. The effect of age and other factors on the early and late results following closed mitral valvuloplasty. *Am Heart J.* 1968;75:743–751.
18. Smith WM, Neutze JM, Barrat-Boyes BG, Lowe JB. Open mitral valvotomy: effect of preoperative factors on result. *J Thorac Cardiovasc Surg.* 1981;82:738–751.
19. Commerford PJ, Hastie T, Beck W. Closed mitral valvotomy: actuarial analysis of results in 654 patients over 12 years and analysis of preoperative predictors of long-term survival. *Ann Thorac Surg.* 1982;33:473–479.
20. Ellis LB, Harken DE, Black H. A clinical study of 1,000 consecutive cases of mitral stenosis two to nine years after mitral valvuloplasty. *Circulation.* 1959; 19:803–820.
21. Roth RB, Block PC, Palacios IF. Predictors of increase mitral regurgitation after percutaneous mitral balloon valvotomy. *Cathet Cardiovasc Diagn.* 1990; 20:17–21.
22. Orange SE, Kawanishi DT, Lopez BM, Curry SM, Rahimtoola SH. Actuarial outcome after catheter balloon commissurotomy in patients with mitral stenosis. *Circulation.* 1997; 95:382–389.
23. Keren G, Etzion T, Sherez J, et al. Atrial fibrillation and atrial enlargement in patients with mitral stenosis. *Am Heart J.* 1987; 114:1146–1154.
24. Thiedemann KU, Ferrans VJ. Left atrial ultrastructure in mitral valvular disease. *Am J Pathol.* 1977; 89:575–604.
25. Unverferth DV, Fertel EH, Unverferth BJ, Leiver CV. Atrial fibrillation in mitral stenosis, hemodynamic and metabolic factors. *Int J Cardiol.* 1984;5:143–149.
26. Hung JS, Chern MS, Wu JJ, et al. Short and long-term results of catheter balloon percutaneous transvenous mitral commissurotomy. *Am J Cardiol.* 1991;67:854–862.
27. Iung B, Cormier B, Ducimere P, et al. Functional results 5 years after successful percutaneous mitral commissurotomy in a series of 528 patients and analysis of predictive factors. *J Am Coll Cardiol.* 1996;27:407–414
28. Complications and mortality of percutaneous balloon mitral commissurotomy. A report from the National Heart, Lung, and Blood Institute Balloon Valvuloplasty Registry. *Circulation.* 1992; 85:2014–2024.

ORIGINAL ARTICLE

Role of Salmeterol in the Treatment of COPD Patients Receiving Ipratropium Bromide

Md Ilias¹, Shamim Ahmed², Md. Shahedur Rahman Khan³, Mirza Mohammed Hiron⁴,
Md. Abdur Rouf¹, Md. Delwar Hossain³, Shah Mesbahul Islam³, Taslima Begum⁵

Abstract:

Chronic obstructive pulmonary disease is a leading cause of morbidity and mortality worldwide and results in a economic and social burden that is both substantial and increasing.. COPD is currently the fourth leading cause of death worldwide. The WHO predicts that COPD by 2020 will be the 5th most prevalent disease and the 3rd most common cause of death. It is also common clinical problem in Bangladesh Although country wide prevalence study in Bangladesh is yet to be available, there is small scale study based on hospital population shows the prevalence among the patients of OPD is 0.7% and inpatient about 5.9%. Symptomatic bronchodilator therapy is a cornerstone of COPD management and an objective assessment of this treatment is recommended in all patients. In COPD cholinergic vagus tone is thought to be the only reversible component of airway obstruction. The anti- cholinergic agent ipratropium is an effective and safe drug. anti- cholinergic usually used in COPD as regular basis. In addition inhaled corticosteroid has additive effect. b_2 agonist release bronchial smooth muscle and cause symptomatic improvement in COPD. Long acting b_2 agonist salmeterol has been shown to increase ciliary beat frequency and to accelerate mucociliary clearance which is impaired in COPD.

Short acting b_2 agonist can be used as need basis or in severe cases as regular dose three to four times daily. But limited information is available of the effect of long acting b_2 agonist salmeterol in COPD.

More recent therapies for COPD include salmeterol a long acting inhaled b_2 agonist and anticholinergic such as ipratropium bromide which have resulted in large body of published data assessing the efficacy from numerous clinical trials. However its positioning in the current treatment in COPD remains to be defined. Salmeterol is long acting b_2 agonist having bronchodilator effect as well as anti inflammatory effect. Anticholinergic drug is the first line drug in COPD. When salmeterol is given with ipratropium bromide will it get synergistic effect.

Salmeterol is available, easily administered and having less side effect in long term use. So the study will help physician to take decision about the long term use of salmeterol in COPD patients. Therefore the present study is designed to evaluate the role of salmeterol as an add on therapy to the current first line drug ipratropium.

[Chest & Heart Journal 2009; 33(1) : 1-10]

1. Medical Officer, NIDCH
2. Academic Registrar, Respiratory Medicine, NIDCH
3. Assistant Professor of Respiratory Medicine, NIDCH
4. Professor of Respiratory Medicine, NIDCH
5. Assistant Professor, Gynae and Obs department, SSMC and Mitford Hospital Dhaka.

Correspondence to: Dr. Md. Ilias, MBBS, MD (Chest), Medical Officer, NIDCH, Mohakhali, Dhaka

Introduction

Chronic obstructive pulmonary disease is a leading cause of morbidity and mortality worldwide and results in a economic and social burden that is both substantial and increasing. Many people suffer from this disease for years and die prematurely from its complications. COPD is currently the fourth leading cause of death worldwide¹. The WHO predicts that COPD, by 2020, will be the 5th most prevalent disease and the 3rd most common cause of death. However, the prevalence and morbidity data greatly underestimate the total burden of COPD because of the disease is usually not diagnosed until it is clinically apparent and moderately advanced².

It is also common clinical problem in Bangladesh. It is one of the common conditions seen by physicians. It can be very disabling for the patient and frustrating for the physician. Although country wide prevalence study in Bangladesh is yet to be available, there is small scale study based on hospital population shows the prevalence among the patients of OPD is 0.7% and inpatient about 5.9%. However, the problem is increasing in this country like other parts of the world due to urbanization, industrialization and change of profession of people from agriculture and fresh air based rural communities to industry and smoking based urban communities.

Symptomatic bronchodilator therapy is a cornerstone of COPD management and an objective assessment of this treatment is recommended in all patients. In COPD cholinergic vagus tone is thought to be the only reversible component of airway obstruction. The anti-cholinergic agent ipratropium is an effective and safe drug. Anti-cholinergic usually used in COPD as regular basis. In addition inhaled corticosteroid has additive effect. β_2 agonist release bronchial smooth muscle and cause symptomatic improvement in COPD. Long acting β_2 agonist salmeterol has been shown to increase ciliary beat frequency and to accelerate mucociliary clearance which is impaired in COPD³.

Short acting β_2 agonist can be used as need basis or in severe cases as regular dose three to four times daily. But limited information is available of the effect of long acting β_2 agonist salmeterol in

COPD. However recently some have been recommended salmeterol as first line agent for stable COPD⁴.

Canadian provincial drug plan manager have noted a substantial increase in the use of salmeterol in recent years, an observation supported by data from International Medical services Canada, which collects information on Canadian patterns of drug prescribing and estimates use between 1997 and 200%⁵.

With increasing understanding of the pathophysiology of COPD, a number of pharmacological and surgical approaches to management of the disease have been developed. International management guidelines recommended that the goals of treatment should be to prevent and control symptoms, prevent and reduce the severity of acute exacerbations, improve lung functions and improve health status.

More recent therapies for COPD include salmeterol a long acting inhaled β_2 agonist and anticholinergic such as ipratropium bromide which have resulted in large body of published data assessing the efficacy from numerous clinical trials⁶. However its positioning in the current treatment in COPD remains to be defined. Therefore the present study is designed to evaluate the role of salmeterol as an add on therapy to the current first line drug ipratropium.

COPD is a large public health problem. In a setting of diminished resources and in the face of infinite challenges, studies are needed to unfold the problem of treating airflow limitation. Keeping all this attributes in mind, the study was planned in a setting of NIDCH which is playing pivotal role in handling such common clinical problem of public interest.

Objectives:

- To explore better therapy in patients with stable COPD.
- To compare the effect of salmeterol or placebo to concurrent anticholinergic therapy.
- To assess the effects of salmeterol in lung function
- To observe the effect of salmeterol in improvement of quality of life and exacerbation in patients with moderately severe COPD.

Methodology:

It was a prospective type of study carried out during the period from July 2005 to December 2006 in the out patient department (OPD) of National Institute of Diseases of the chest and Hospital (NIDCH), Mohakhali, Dhaka.. A total number of 80 (39 in group A and 41 in group B) participants having the diagnosis of COPD underwent long term follow up for the study

Inclusion criteria:

- Clinical diagnosis of COPD, as defined by GOLD
- Age > 40 years.
- Respiratory symptoms (Cough, shortness of breath and sputum production) for greater than 5 years.
- History of cigarette smoking > 10 pack years.
- Clinically stable airway obstruction.
- A forced expiratory volume in one second FEV₁ of d" 80% to e"50% of predicted normal values and ratio of FEV₁ to FVC of d"70%

Exclusion criteria:

If the patient had history of asthma, allergic rhinitis or atopy

- A significant disease other than COPD.
- A recent history of myocardial infarction (d" 1 year), heart failure or cardiac arrhythmia requiring drug treatment.
- If the patient require regular day time supplemental oxygen or were on doses exceeding the equivalent of 10mg prednisolone daily Patients with known hypersensitivity to anticholinergic drug Known symptomatic prostatic hypertrophy
- Narrow angle glaucoma
- during the month prior to entering study

A total number of 100 patients were selected for the study. Ultimately 80 patients (39 in group A and 41 in group B) had completed the study and were used for the statistical analysis. A standard proforma and questionnaire was designed and filled up for each patient. Changes in symptomatology and spirometric parameters were recorded in specific proforma.

In the first phase of the study a standard questionnaire was designed with a view to select patients who would be included as study population.

The questionnaire was analyzed to find out the patients who meet inclusion and exclusion criteria.

Written informed consent was obtained from all patients before study procedure were taken. After a run in period of two weeks on 40 µgm four times daily ipratropium, they were randomized into two groups. The two groups A and B were identified first. In two pieces of paper A and B were marked and one piece of paper was drawn by the first patient. It was B. Then the first patient was put in group B, the second patient in group A and so on. Group A was given ipratropium 40mgm q.i.d.+ salmeterol Matched placebo and group B was given ipratropium 40mgm q.i.d.+salmeterol 50mgm twice daily.. All drugs were inhaled from the pMDI. Patients were given salbutamol to use as rescue medication. The study had a run in period of two weeks and a treatment period of 8 week. Each patient was evaluated at the beginning of treatment period, at 2nd, 5th and 8th week excluding the initial two weeks. Before entry and completion of the study patients were undergone a medical examination, lab testing and 12 lead ECG. At each schedule visit detail of clinical status, adverse events, exacerbation and withdrawal were recorded. The outcome parameters were (1) Spirometry (FEV₁ and FVC) (2) Six minute walk test (3) SF-36 health related quality of life questionnaire score (HRQoL) (4) Base line dyspnoea index (5) Patients self assessment (6) Supplemental use of salbutamol. The Spirometry was performed meeting the criteria of ATS. Salbutamol was stopped for at least 12 hours before pulmonary function test.

During the run and treatment period patients maintained a daily symptom record and concomitant use of salbutmol

Results

A total of 100 patients entered in the study. Initially 50 patients were in group A and 50 patients in group B. But a total of 20 patients were excluded from the study because they were not available at the final stage of the study . Ultimately data of 80 patients (39 in group A and 41 in group B) were used for statistical analysis. Patients in group A were treated with inhaler ipratropium 40 µgm four times daily + salmeterol matched placebo twice daily and patients who were treated with inhaler ipratropium 40 µgm four times daily + inhaler salmeterol 50 µgm twice daily were considered as group B for the study.

Table-I
Age distribution of the study patients

Parameters	GroupA (n=39)		GroupB (n=41)		Total (n=80)		P value
	No	%	No	%	No	%	
41-50	08	20.0	09	22.5	17	21.25	.677
51-60	16	42.5	19	47.5	35	45.0	
61-70	13	32.5	12	27.5	25	30.0	
71 & above	02	5.0	01	2.5	03	7.5	
Mean±SD (yrs)	56.82±8.75		55.28±8.34				

NB: P value reached from unpaired student's t test

Table-II
Sex distribution of the study patients

Parameters	GroupA (n=39)		GroupB (n=41)		Total (n=80)		P value
	No	%	No	%	No	%	
Male	38	97.5	39	95.5	77	96.30	.559
Female	01	2.5	02	4.5	03	3.70	

NB: P value reached from Chi square test

Table-III
Distribution of the study patients by occupation

Parameters	GroupA (n=39)		GroupB (n=41)		Total (n=80)		P value
	No	%	No	%	No	%	
Farmer	15	40.0	15	37.5	30	38.75	.787
Teacher	08	20.0	08	20.0	16	20.0	
Service holder	06	15	07	17.5	13	16.25	
Business man	06	15	06	15	12	15	
Retired person	03	7.5	03	5.0	05	6.25	
House wife	01	2.5	02	5.0	03	3.75	

NB: P value reached from Chi square test

Table-IV
Distribution of the study patients by level of education.

Level of education	Group A(n=39)		Group B (n=41)		Total (n=80)		P value
	No	%	No	%	No	%	
Illiterate	06	15.0	08	20.0	14	17.5	501.
Primary	9	25.0	12	27.5	21	26.25	
Secondary	08	20.0	07	17.5	15	18.75	
Higher Secondary	16	40.0	14	35.0	30	37.5	
above							

NB: P value reached from Chi square test

Table-V
Nutritional status of the study patients

Parameters	Group A(n=39)		Group B (n=41)		Total (n=80)		P value
	No	%	No	%	No	%	
Ht in Cm							.589
<150	06	17.5	06	15	12	16.25	
150-159	18	45.0	19	47.5	37	46.25	
160-169	11	27.5	14	32.5	25	30.0	
170&above	04	10.0	02	5.0	06	7.5	
Mean±SD	158±8.32		158.1±7.62				
Wt in Kg							.699
<45	07	17.5	06	15	13	16.25	
45-49	13	32.5	17	42.5	30	37.5	
50-54	15	40.0	13	30.10	28	35.0	
55 & above	04	10.0	05	12.5	09	11.25	
Mean ±SD	49.58±5.45		49.35±5.27				
BMI							.414
<18.5	11	27.5	09	22.5	20	25.0	
18.5-24.9	22	57.5	25	60.10	47	58.75	
25&above	06	15.0	07	17.5	13	16.25	
Mean ±SD	19.83±1.27		19.77±1.05				

NB: P value reached from unpaired student's t test

Table-VI
Smoking habits in study patients

Smoking habit	Group A(n=39)		Group B (n=41)		Total (n=80)		P value
	No	%	No	%	No	%	
Current smoker	31	79.5	29	70.7	60	75.0	
10-20 pack years	10	25.0	09	21.9	19	22.5	
>20 pack years	21	55.0	20	50.0	41	52.5	.335
Ex-smoker	08	20.0	12	30.0	20	25.0	
10-20 pack years	02	5.0	04	10.0	06	7.5	
>20 pack year	06	15.0	08	20.0	14	17.5	

NB : P value reached from chi-square test

Table-VII
Major Symptoms at the start of the trial in patients

Parameters	Group A(n=39)		Group B (n=41)		Total (n=80)		P value
	No	%	No	%	No	%	
Dyspnoea	39	100.0	41	100.0	80	100.0	—
Cough	39	100.0	41	100.0	80	100.0	—
Sputum	33	82.5	32	77.5	65	80.0	.759
No	6	17.5	09	22.5	15	20.0	
Scanty & mucoid	21	52.5	19	47.5	40	50.0	
copious & purulent	12	30.0	12	30.0	24	30.0	
Wheeze	21	52.5	19	47.5	40	50.0	.657
Chest tightness	11	27.5	13	32.5	24	30.0	.628

NB: P value reached from Chi square test

Table-VIII*Analysis of duration of cough & dyspnoea*

Parameters	Group A (n =39)	Group B (n =41)	P value
Dyspnoea			.976
Range (yrs)	3.-18	3-21	
Mean±SD Cough	10.03±4.06	10.25±4.14	.995
Range (yrs)	3-18	3-17	
Mean±SD	10.73±3.99	10.55±4.01	

NB: P value reached from unpaired student's t test

Table-IX*Effects of treatment on FEV₁*

	FEV ₁ (L)			
	Group A (n=39)		Group B (n=41)	
	Mean±SD	P value	Mean±SD	P value
Baseline	1.60±0.36		1.73±0.34	
1st follow up	1.60±0.36	0.983 ^{ns}	1.90±0.35	0.018*
2nd follow up	1.60±0.36	0.973 ^{ns}	1.95±0.33	0.003**
3rd follow up	1.74±0.59	0.154 ^{ns}	1.99±0.32	0.000***

Group A : Ipratropium+Placebo

Group B : Ipratropium+Salmeterol

ANOVA (multiple comparison with baseline)

ns = Not significant

* = Significant at P<0.05

** = Significant at P<0.01

*** = Significant at P<0.001

FEV₁, FVC and FEV₁/FVC ratio were measured at baseline after getting two weeks of ipratropium. The group A was given inhaler placebo and group B was given inhaler salmeterol along with ipratropium to both group. The mean baseline FEV₁ in group A was 1.60±0.36 and in group B 1.73±0.34. In subsequent visit the difference of FEV₁ with baseline in group A was not significant statistically in any follow up visit (p>0.05). However difference of changes of mean FEV₁ after getting salmeterol in group B increased from baseline in every follow up and last follow up FEV₁ was 1.99±0.32 which was statistically significant (p<0.001)

Table-X*Effects of treatment on FVC*

	FVC (L)			
	Group A (n=39)		Group B (n=41)	
	Mean±SD	P value	Mean±SD	P value
Baseline	2.61±0.65		2.84±0.48	
1st follow up	2.72±0.52	0.388 ^{ns}	3.02±0.44	0.040*
2nd follow up	2.73±0.52	0.369 ^{ns}	3.11±0.36	0.003**
3rd follow up	2.74±0.52	0.311 ^{ns}	3.16±0.32	0.000***

The mean pre treatment FVC in group A at baseline was 2.61±0.65. The mean FVC in last follow up in group A was 2.74±0.53. The difference of mean between baseline and follow up visit was not statistically significant. (p>0.05). However in group B mean baseline FVC was 2.84±0.48 and the mean FVC in last follow up was 3.16±0.32. The difference of changes was statistically significant (p<0.001)

Table-XI*Effects of treatment on base line dyspnoea index*

	Dyspnoea index			
	Group A (n=39)		Group B (n=41)	
	Mean±SD	P value	Mean±SD	P value
Baseline	4.97±0.81		5.49±0.51	
1st follow up	4.97±0.81	1.000 ^{ns}	6.20±0.40	0.000***
2nd follow up	5.08±0.87	0.568 ^{ns}	7.59±0.50	0.000***
3rd follow up	5.31±0.66	0.065 ^{ns}	7.78±0.61	0.000***

The mean base line dyspnoea index (BDI) score at baseline in group A was 4.97±0.81. None of the subsequent follow up showed changes in mean difference which was statistically significant (P>0.05).

But in group B the mean BDI score at baseline was 5.49±0.51. In subsequent follow up visit the mean BDI score gradually increased and at 3rd follow up it was 7.78±0.61. The changes of difference of mean was statistically significant (p<0.001)

Table-XII*Effects of treatment on 6 minute walking test*

	6 minute walking test (M)			
	Group A (n=39)		Group B (n=41)	
	Mean±SD	P value	Mean±SD	P value
Baseline	287.67±31.65		261.10±35.13	
1st follow up	290.59±31.14	0.682 ^{ns}	275.37±14.16	0.047*
2nd follow up	292.28±30.76	0.517 ^{ns}	281.24±37.74	0.005**
3rd follow up	293.95±32.02	0.378 ^{ns}	288.78±36.02	0.000***

Regarding 6 minute walk test, in group A the mean distance walked at base line was 287.67±31.65 meter. The mean distance of following visits showed no statistically significant difference from baseline (p<0.05).

On the other hand in group B the baseline mean was 261.10 ± 35.13 . On first visit the mean was 275 ± 14.16 , the difference was statistically significant ($p < 0.05$), which increased in subsequent visits. In 3rd follow up the mean was 288 ± 78 . The difference of changes was also statistically significant ($p < 0.001$).

Table-XIII
Effects of treatment on HRQoL score

	HRQoL				P value
	Group A (n=39)		Group B (n=41)		
	Mean±SD	P value	Mean±SD	P value	
Baseline	60.31±3.87		59.63±4.46		
1st follow up	60.77±4.09	0.600 ^{ns}	61.54±3.21	0.034 [*]	
2nd follow up	61.38±3.64	0.222 ^{ns}	62.17±4.01	0.005 ^{**}	
3rd follow up	61.79±3.89	0.092 ^{ns}	68.61±4.29	0.000 ^{***}	

The mean health related quality of life (HRQoL) score in group A at baseline was 60.31 ± 3.78 . Subsequent follow up showed HRQoL score in group A, no significant difference from the baseline ($p > 0.05$). In group B the baseline HRQoL score was 59.63 ± 4.46 . In first follow up the mean was 61.54 ± 3.21 , the difference was significant from baseline ($p < 0.05$). In the 3rd follow up the mean was 68 ± 4.29 , the difference was also statistically significant from baseline ($p < 0.001$).

Table-IX
Patient's self assessment at follow up

Assessment	Group A (n=39)		Group B (n=41)		P value
	No.	(%)	No.	(%)	
	1st follow up				
No improvement	39	(100.0)	24	(58.5)	
Improved	0	17	(41.5)		
2nd follow up					0.000 ^{***}
No improvement	39	(100.0)	4	(9.8)	
Improved	0		37	(90.2)	
3rd follow up					0.000 ^{***}
No improvement	35	(89.7)	0		
Improved	4	(10.3)	41	(100.0)	
Chi square test					

*** = Significant at $P < 0.001$

It was a subjective assessment by the patients. Among the studied patients in group A in the 1st and 2nd follow up patients self assessment regarding improvement as negative in 39 patients (100%). In the 3rd follow up only 4 patients (10.3%) reported improvement. On the other have in group

B in 1st visit 17 patients (41.5%) reported improvement. But in 2nd and 3rd visit 37 patients (90.2%) and 41 patients (100%) reported improvement. Analysis showed statistically significant difference of improvement between two groups ($p < 0.001$).

Table-XV
Report of use of salbutamol

Assessment	Group A (n=39)		Group B (n=41)		P value
	No.	(%)	No.	(%)	
	1st follow up				
Used	39	(100.0)	37	(90.2)	
Not used	0		4	(9.8)	
2nd follow up					0.000 ^{***}
Used	39	(100.0)	13	(31.7)	
Not used	0		28	(68.3)	
3rd follow up					0.000 ^{***}
Used	30	(76.9)	4	(9.8)	
Not used	9	(23.1)	37	(90.2)	

Chi square test

* = Significant at $P < 0.05$

*** = Significant at $P < 0.001$

Regarding the use of salbutamol as per need during testament period in group A in 1st and 2nd visits all 39 patient (100%) received salbutamol. But in 3rd visit 76.9% reported to take salbutamol. Again in group B in 1st visit 37 patients (90.2%) took salbutamol but in 3rd visit only 4 patients (9.8%) took salbutamol as per need. The analysis revealed statistically significant difference ($P < 0.001$) between two groups in terms of use of salbutamol as per need.

Discussion

It was a prospective type of study and was performed to show the effect of salmeterol on existing anticholinergic ipratropium in chronic stable COPD. The study was carried out in the out patient department of National Institute of Diseases of the Chest and Hospital (NIDCH), Mohakhali, Dhaka during the period from July 2008 to December 2008.

The case ultimately enrolled in the study represents those of mild to moderate (stage 1 and stage 2) COPD patients who were stable and free from important co morbid condition. A total of 100 patients were selected for the study. They were randomized in two groups (50 in each group). But 20 patient were not available till last

follow up and were excluded from analysis of data. So ultimately 80 patients (39 in group A and 41 in group B) underwent long term follow up for the study. Patients of group a were treated with ipratropium 40 mgm q.i.d.+ salmeterol matched placebo and patients of group B were treated with ipratropium 40 mgm q.i.d +salmeterol 50 mgm b.i.d.

The socio demographic data of the study population were evaluated. The mean age difference (group A was 56.82±8.75 years and group B was 55.28±8.34 years) was not statistically significant. O' Donnell et. al. (2004) in a similar study showed mean age of patients in both group was 64±2 years. Mean age in our patients was a bit lower which may be due to comparatively low life expectancy of our population.

The highest percentage was male in both group. No statistically significant sex of difference was found between to group. High male preponderance in our study may be due to increased smoking habit among male. Smoking and environment pollution including occupational exposures are principal predisposing factors for COPD (Gold updated 2005) . Small number of female in this study is probably due to few female smoke in this country and lesser health seeking behavior of female. But in the western world , as male female difference in cigarette consumption continues to narrow, existing sex difference in the occurrence of COPD can be expected to disappear in near future⁸.

Both group was homogenous in respect of occupation level of education socioeconomic status and nutrition.

All the patients studied in both group was current or ex-smokers with majority history of smoking more than 20 pack years. Most of the patients were current smoker in both group. Current smokers comprise 49% in the study population, in a study conducted by Hanania et al.⁹. The man pack year of smoking in his study was very high.

It is clear that COPD does not have a single cause and multiple factors must act in concert for the disordered to become clinically evident. Cigarette smoking is the principal identified risk factor in the causation of COPD, yet only minority of persons who smoke develop COPD² while an occasional life long non smoker may develop severe disease.

Host factors are largely important in this respect. Occupational dust and chemicals, outdoor and indoor pollution and infection are also emerging risk factors of COPD⁷. For most occupational exposures , the risk of developing COPD appears to be more pronounced in those workers who smoke cigarette. In general, the magnitude of occupational effects is substantially less important than the smoking effect and occupation alone rarely lead to the development of clinically apparent COPD¹⁰.

Cough and dyspnoea were the predominant systems in both the group. All the patients in both the groups presented with these symptoms. Dyspnoea and cough are two universal feature of COPD. It was also observed in our study.

On compilation of the data, outcome parameters were evaluated. Outcome parameters were compared with baseline in both the groups. After a run in period of two weeks baseline parameters were taken.

These were forced expiratory volume in one second (FEV₁), forced vital capacity(FVC) distance walked in six minutes (Six minute walk test), base line dyspnoea index (BDI), health related quality of life (HRQoL) score. On subsequent follow up visit patients self assessment and reports of supplemental use of sulbutamol was taken. Both groups were followed up at 2nd, 5th and 8th week of treatment period.

The baseline FEV₁, and FVC group B improved significantly after 8 weeks of treatment. But no significant improvement in group A. FEV₁ and FVC consistently increase after treatment with salmeterol reflecting improved lung emptying during forced expiratory maneuver. In COPD, expiratory flow limitation, a pivotal pathophysiological abnormality is traditionally measured by FEV₁ . In similar study stockely et al (2006a), showed gradual improvement in FEV₁ and FVC. In our study lung function (FEV₁ and FVC) showed gradual improvement. The improvement was well maintained and there was no evidence of tolerance. A meta analysis of nine randomized controlled trials concluded that salmeterol added to other therapies significantly increase pre bronchodilator FEV₁ with no evidence of tolerance or loss of activity over 12 months⁹.

One of the most important symptom in COPD is dyspnoea or the perception of breathlessness. In our study dyspnoea was assessed by baseline dyspnoea index (BDI). There is significant improvement of BDI score in group B from baseline but no significant improvement in patients of group A. The improvement of dyspnoea may be due to in part to the reduced resistive work of breathing due to even modest bronchodilator. Similar improvement in BDI score was found Mahler (Mahler et al.1999) in his study. He described improved dyspnoea rating using BDI that was 5.9 to 7.2. So our study is consistent with study. Dyspnoea intensity also decreased at a given exercise after salmeterol compared to placebo (O'donnell et al.¹⁰).

Assessment of functional exercise capacity has gained importance in the evaluation of patients of COPD. Timed walking tests are widely used to evaluate functional exercise performance as they are likely to measure the ability to undertake the activities of day to day life¹¹. In our study six minute walk distance improved significantly in group B patients. Gupta et al.¹² found similar result in his study where he showed salmeterol increase six minute walk distance significantly. But in a study Husereau et al.⁵ showed six minutes walk distance does not always improve significantly. For this test well motivation and encouragement is necessary to walk faster. Furthermore some patients with COPD are limited in their exercise capacity by leg discomfort and general fatigue rather than by breathlessness. Therefore bronchodilator therapy sometime may not alter timed walking test.

Health status is a broad term that encompasses the patients overall health with particular emphasis on the impact of impaired health on his or her quality of life. Measure of health status can be either generic (i.e applicable across a range of disease) or disease specific. In our study we used generic health measure by SF-36. We found no significant difference of HRQoL score from baseline to last follow up in group A but in group B, HRQoL score is increased from baseline to last follow up.

Stockley et al. (2006b) found a consistent, statistically significant and clinically meaningful

improvement in health status with salmeterol compared with usual therapy. The finding was similar with our study. The gain in quality of life achieved in patients taking salmeterol 50 mg twice daily were clearly in excess of the estimated threshold for clinical significance¹³. But in one study Tashkin et al. found no significant improvement of overall health related quality of life compared with placebo although combination of salmeterol and ipratropium provide clinically and statistically significant improvement in health related quality of life.

Patients self assessment was subjective assessment by the patients. It was mainly dependent on symptoms like shortness of breath, chest tightness and cough. In group B all patients reported improvement but in group A only 4 patients reported improvement in last follow up.

Regarding patients self assessment Gupta et al.¹² also observed significant difference in changes in cough and dyspnoea in salmeterol group in his study. But interestingly Mahler et al.¹³ observed night time symptoms improvement rather than day time symptoms. This might be due to more exposure in dusty and polluted environment at day time. Regarding supplemental use of salbutamol as per need during treatment period, significant reduction of use of salbutamol in patients treated with salmeterol as compared to placebo group was observed in our study. In a review Husereau et al.⁵ in five of six trials, salmeterol was associated with less salbutamol use than was placebo treatment. So our result was consistent with this study.

Current evidence supports the recommendation of the Global Initiative for chronic obstructive lung diseases (GOLD) guideline of at least one of the two classes of long acting inhaled bronchodilators as in initial maintenance therapy for symptomatic COPD. The present study showed that salmeterol has important and significant advantage in combination with inhaled ipratropium. Besides the parameter studied, salmeterol reduces frequency of exacerbation significantly¹³. Salmeterol has longer duration of action and sustain improvement in lung function. It allows twice daily dosing which is convenient for patient with COPD and may enhance compliance with the treatment.

So from our study it can be decided that salmeterol 50mgm twice daily with along with ipratropim 40mgm four times daily can be used as first line therapy in mild to moderate chronic stable COPD

Conclusion:

Salmeterol in an effective treatment for patients with COPD. The addition of salmeterol significantly improved lung function and dyspnoea, increased exercise capacity and resulted in an enhanced quality of life. On the basis of evidence gathered so far and the findings of the present study, we suggest that salmeterol with anticholinergic drug ipratropium would be a useful therapeutic strategy in mild to moderate chronic stable COPD.

References:

1. Asthma Association, Bangladesh. National Guideline-Asthma-Bronchiolitis-COPD (ABC) 2005, 3rd Edition ; 147-53.
2. Celli BR, Macnee W, Agusti A, Berg B. Standard for the diagnosis and treatment of patients with COPD: a summary for the ATS/ERS position paper. *Eur Respir J*, 2004; 23: 932-946
3. Bennett WD, Almond MA, Zeman KL, Johnson JG, Donohue JF. Effects of salmeterol on mucociliary and cough clearance in chronic bronchitis. *Pulm Pharmacol Ther*, 2006; 19(2): 96-100
4. Cazzola M, Donner CF. Long acting beta 2 agonist in the management of stable chronic obstructive pulmonary disease. *Drugs*, 2000; 60: 307-320
5. Biernacki W, Flenly DC, Muir AL, Macnee W 1988. Pulmonary hypertension and right ventricular function in patients with COPD. *Chest*, 94: 1196-75.
6. Stockley RA, Whitehead PJ, Williams MK. Improved outcomes in patients with chronic obstructive pulmonary disease treated with salmeterol compared with placebo/usual therapy: results of a meta analysis. *Respir Res*, 2006; 7(1): 147.
7. Boyd, G Morice AH, Pounsford JC, Siebert M, Peslis N. An evaluation of salmeterol in the treatment of chronic obstructive pulmonary disease. *Eur Respir J*, 1997; 10: 815-821.
8. Jessy KH 1998. Comparisn of daily versus alternate day therapy with corticosteroids in the treatment of chronic obstructive pulmonary disease, NIDCH.
9. Hanania NA, Kalberg C, Yates J., Emmett A, Hostman D, and Knobil K 2005. The bronchodilator response to salmeterol is maintained with regular long term use in patients with COPD. *Pulm Pharmacol Ther*, 18(1): 19-22
10. O'Donnel DE, Voduc N, Fitzpatric M, Webb KA. Effect of salmeterol on ventilatory response to exercise in chronic obstructive pulmonary disease. *Eur Respir J*, 2004; 24: 86-94.
11. Troosters T, Gosselink R, Decramer M. Six minute walking distance in healthy elderly subjects. *Eur Respir J*, 1994; 14: 270-274.
12. Gupta AK, Chhabra SK. An evaluation of salmeterol in the treatment of chronic obstructive pulmonary disease. *Indian J Chest Dis Allied Sci*, July, 2002;44(3): 165-72
13. Mahler DA, Donohue JF, Barbee RA, Goldman MD, Gross NIJ. Efficacy of salmeterol xinafoate in the treatment of COPD. *Chest*, 1999; 115: 957-965
14. Taskhin DP and Cooper CB 2004. The role of long acting bronchodilators in the management of stable COPD. *Chest* , 125: 249-259
15. Fanta CH 1997. Clinical aspects of COPD. The ACCP Pulmonary Board Review, 7-15.

ORIGINAL ARTICLE

Single Versus Combination Nebulized Bronchodilator Therapy, in the Treatment of Acute episodes of Bronchial Asthma

Shah Md. Saifur Rahman¹, Md. Naimul Haque², Narayan Chandra Datta², Syed Rezaul Haq², Barkat Ullah², Abu Raihan¹, K.H Jessy², Tapash Kumar Bosh¹, A.K.M Mustafa Hossain³, Biswas Akhter Hossain⁴, Mirza Mohammad Hiron⁵

Abstract

The effectiveness of nebulized anticholinergic and sympathomimetic regimens was evaluated in a prospective study of 79 patients with acute airways obstruction. Patients were assigned to one of three treatment regimens according to a randomized schedule: (1) 1 mg of Ipratropium bromide, (2) 0.5 mg of salbutamol (3) 1 mg of Ipratropium plus 0.5 mg of salbutamol. In 79 patients with acute exacerbation of asthma (mean one-second forced expiratory volume, 1.18 ± 0.64 liters), all three regimens produced significant improvement in one-second forced expiratory volume ($p < 0.001$). The greatest improvement followed treatment with the Ipratropium salbutamol combination (0.53 ± 0.51 liters at 90 minutes) and was significantly greater than that following either Ipratropium alone ($p < 0.001$) or salbutamol alone ($p < 0.05$). So, it is concluded that, in patients with acute asthma, combination therapy with sympathomimetic and anticholinergic agents is more efficacious than either one alone.

[Chest & Heart Journal 2009; 33(1) : 17-21]

Introduction

The optimal bronchodilator regimen for the treatment of acute airways obstruction, maximizes bronchodilator efficacy while minimizing unwanted side effects. Increasing attention is being given to combination drug regimens¹⁻³. Anticholinergic agents which act through different receptor and biochemical pathways from either sympathomimetic or methylxanthine agents, may be well suited for use in combination bronchodilator regimens^{4,5}. In the treatment of stable asthma, anticholinergic agents have been shown to increase bronchodilator responsiveness

with no significant increase in side effects when added to a regimen of sympathomimetic agents and methylxanthines^{6,7}. The role of anticholinergic drugs in the treatment of acute asthma, either alone or combination, has not yet been evaluated fully.

Among available anticholinergic agents, ipratropium bromide, a quaternary derivative of atropine, may be best suited to combination bronchodilator regimens, because it is poorly absorbed from airway mucosal surfaces in aerosol form, thereby offering bronchodilatation without unwanted systemic antimuscarinic effects^{4,5,6}.

1. Registrar Medicine, NIDCH, Dhaka.
2. Assistant Professor, Respiratory Medicine, NIDCH, Dhaka.
3. Associate Professor, NIDCH, Dhaka.
4. Medical Superintendent, NIDCH, Dhaka.
5. Director-Cum-Professor, Respiratory Medicine, NIDCH, Dhaka.

Correspondence to: Shah Md. Saifur Rahman, Registrar Medicine, NIDCH, Dhaka.

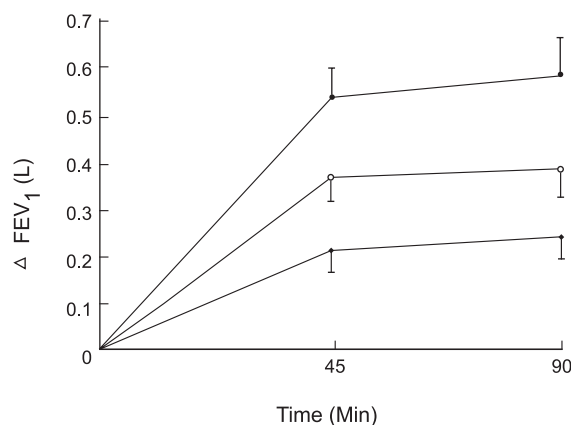


Fig.-1. for 79 patients with asthma, mean increases in one-second forced expiratory volume above baseline after inhalation of ipratropium (triangles), salbutamol (open circles), or the combination (solid circles). Bars represent ± 1 standard error.

We have evaluated the effectiveness of three nebulized bronchodilator regimens in a large number of patients with asthma who presented with acute airways obstruction. We wanted to determine whether administration of a beta agonist and an anticholinergic agent together was superior to use of either drug alone.

Patients and Methods

A total number of 79 patient in Emergency Department of National Asthma Center in Mohakhali, Dhaka were studied. An identical protocol was adhered and data were accumulated for subsequent analysis. Review of results was performed to ensure that no regimen was hazardous.

Patients

Consecutive patients, older than 18 years of age, who came to the emergency room for treatment of acute asthma were asked to participate. Patients were considered for the study if they were able to perform a forced expiratory maneuver and if their forced expiratory volume in one second was less than 70 percent of predicted. Exclusion criteria were complicating medical illnesses such as pneumonia, pulmonary edema, acute myocardial infarction, or frequent ventricular ectopic beats. Pregnant women and nursing mothers were not studied. Patients were also excluded if they had received a nebulized bronchodilator solution in the previous six hours or if they required treatment protocol written in formed consent was obtained from each patient.

Treatment Regimens

Patients were assigned to one of three treatment regimens in Group 1- 1 mg of ipratropium, Group

2- 0.5 mg of salbutamol, Group 3- 1 mg of ipratropium and 0.5 mg of salbutamol randomized schedule. Unit-dose vials containing these drugs were coded but identical in appearance. In each vial, the drugs were dissolved in 2 ml of isotonic saline. The solution was administered via a nebulizer driven by Electricity through a face masks. Administration was continued until no solution was visible in the nebulizer chamber.

Treatment with intravenous aminophylline or intravenous corticosteroids was given at the discretion of the attending physicians. Use of these drugs was recorded to allow for separate analysis of patients thus treated; all other drugs were prescribed. Patients were evaluated and treated in the emergency room by medical officers under the supervision of the investigators and by emergency room staff physicians.

Measurements.

Immediately before, and 45 and 90 minutes after the start of nebulizer treatment, spirometric measurements were obtained using a portable spirometer and respiratory rate, heart rate, and blood pressure were recorded. Forced vital capacity, one-second forced expiratory volume, maximal mid-expiratory flow rate, and peak expiratory flow rate were derived from the best of three forced expiratory maneuvers; best was defined as the curve with the highest sum of one-second forced expiratory volume and forced vital capacity. Predicted normal values were those of Knudson et al¹⁴.

Data Analysis.

Patients were classified according to the criteria of the American Thoracic Society¹⁵. Repeated-measures analysis of variance was used to compare the drug regimens for post-treatment improvement in pulmonary function parameters, expressed as improvement above baseline. When appropriate, paired or unpaired t tests were used to compare the difference between means.

Results

A total 86 patients were initially evaluated and received treatment with one of the three drug regimens. Two patients with asthma, randomly assigned to receive ipratropium alone, showed clinical deterioration during the 90-minute study period and were withdrawn from the study to receive supplemental sympathomimetic therapy. Data from 5 patients with asthma in the ipratropium group could not be analyzed for technical reasons. Thus, pulmonary function data from 79 patients were analyzed;

Table-I
Pulmonary Function Data before and at 45 and 90 Minutes after Treatment

		FVC (liters)	FEV ₁ (Liters/second)	MMEFR (Liters/second)	PEFR (Liters/sminute)
Patients with asthma Ipratropium (n=23)	Pre	2.36±1.10	1.21±0.64	0.60±0.51	125.67±72.90
	45	2.62±1.16	1.42±0.78	0.73±0.66	156.22±95.27
	90	2.69±1.16	1.45±0.76	0.74±0.67	155.25±87.34
Salbutamol (n=26)	Pre	2.13±0.99	1.09±0.62	0.53±0.37	108.08±76.87
	45	2.61±1.04	1.46±0.80	0.84±0.87	160.46±105.06
	90	2.64±1.07	1.47±0.83	0.84±1.03	159.25±106.01
Ipratropium+ Salbutamol (n=30)	pre	2.34±1.14	1.22±0.66	0.63±0.50	134.16±86.56
	45	3.06±1.23	1.75±0.88	1.07±1.12	203.18±124.49
	90	3.13±1.28	1.79±0.90	1.05±0.88	209.65±121.26

Table-II
Cardiovascular Data and Respiratory Rate before and 90 Minutes after Treatment

	Ipratropium		Ipratropium		Ipratropium	
	Baseline	90 Minutes	Baseline	90 Minutes	Baseline	90 Minutes
Heart rate (beats/minute)	94.1±18.5	90.4±17.4	91.7±15.5	89.2±15.0	95.3±16.5	90.4±15.6
Systolic blood pressure (mm Hg)	138.3±20.6	131.5±17.8	134.7±25.1	125.4±17.8	134.2±23.9	128.6±21.7
Diastolic pressure (mm Hg)	88.0±13.5	84.6±11.7	85.8±13.0	79.7±12.3	85.4±13.7	81.2±10.8
Respiratory rate (breaths/minute)	23.8±5.9	21.9±5.9	24.9±6.8	21.8±5.2	23.4±6.4	20.6±5.4

Patients with asthma

The mean (\pm SD) age of the asthmatic patients was 44.6 ± 18.1 years. Mean pre-treatment one-second forced expiratory volume was 1.18 ± 0.64 liters; this was 39 percent of the predicted value. There were no significant differences among treatment groups in pretreatment one-second forced expiratory volume or other baseline pulmonary function measurements. All three regimes produced significant improvement in one-second forced expiratory volume at 45 minutes after treatment (for each, $p < 0.001$), with only minutes after treatment (for each, $p < 0.001$), with only minimal further improvement at 90 minutes (Figure 1). Salbutamol administration produced greater improvement than did Ipratropium ($p < 0.05$), but the increment in one-second forced expiratory volume after the combined regimen was significantly greater than that produced

by either Ipratropium alone ($p < 0.001$) or Salbutamol alone ($p < 0.05$).

Post-treatment improvement in one-second forced expiratory volume (40.0 percent) was paralleled by improvements in forced vital capacity (change from baseline 31.2 percent), peak expiratory flow rate (57.3 percent), and maximal mid-expiratory flowrate (52.3 percent) and a similar pattern and levels of statistical significance among treatment regimens were achieved (Table I). Again, the greatest improvement occurred at 90 minutes in the patients receiving the ipratropium-salbutamol combination.

We wished to know whether the greater bronchodilator effect of combination versus single-agent therapy was a function of the degree of airways obstruction on presentation. We therefore examined separately the drug effects in

two groups of patients with asthma: those with a one-second forced expiratory volume of 1.0 liter or less on presentation and those with a one-second forced expiratory volume of more than 1.0 liter. By 90 minutes, for the low one-second forced expiratory volume group, the three regimens produced mean increases of 0.21 ± 0.23 liters (ipratropium), 0.26 ± 0.28 liters (salbutamol), and 0.51 ± 0.41 liters (ipratropium plus salbutamol). In the group with the higher one-second forced expiratory volume, the mean increases were 0.26 ± 0.42 liters, 0.51 ± 0.51 liters, 0.62 ± 0.59 liters, respectively. In both groups at 45 and 90 minutes, the difference among treatment regimens was statistically significant ($p < 0.005$). Although the greater bronchodilator effect of combination versus single-agent therapy was present in both groups of patients, the added benefits of combination therapy were more marked in patients with greater degrees of airflow obstruction on presentation.

Concomitant Therapy

Intravenous aminophylline was administered to 30.2 percent of all patients during the 90 minute study period. There were no significant differences in the percent of patients within each group receiving aminophylline (ipratropium group, 27.9 percent; salbutamol group, 32.4 percent; and combination therapy group, 30.3 percent). Intravenous hydrocortisone was administered to 11 percent of patients, and 2 percent received some other steroid preparation. As with aminophylline therapy, there were no significant differences among treatment groups in the proportion receiving corticosteroids (14.7 percent, 7.4 percent, and 16.6 percent for the ipratropium, salbutamol, and combination groups, respectively).

Cardiovascular Changes and Side Effects

No treatment regimen was associated with an increase in mean heart rate, blood pressure, or respiratory rate; all mean values decreased minimally over the 90-minute study period, irrespective of treatment group (Table II). The three most commonly reported side effects elicited by specific questioning were tremor (10.9 percent), dry mouth (12.4 percent), and bad taste (8.4 percent). Tremor was more commonly reported by patients receiving salbutamol alone (13.2 percent) or salbutamol plus ipratropium (16.7

percent) than by patients receiving ipratropium alone (2.9 percent). Only 7.4 percent of patients receiving ipratropium alone complained of a dry mouth, whereas 19.1 percent of those receiving salbutamol alone and 10.6 percent receiving the combination regimen reported this side effect. Other minor side effects such as eye irritation, sweating, and dizziness each occurred with an incidence of less than 3 percent. No patient withdrew from the study as a result of any side effect.

Discussion

Our data show that a nebulized combination of sympathomimetic and anticholinergic drugs provided greater bronchodilatation than either agent administered alone in patients with acute, severe asthma. Moreover, the improved bronchodilatation was achieved without additional side effects or cardiovascular changes.

In patients with stable asthma, single-dose studies have shown that the combination of ipratropium and salbutamol had significantly greater bronchodilator effect than either agent used alone [16,17]. Similar observations have been reported for the combination of inhaled ipratropium and oral theophylline in patients with stable asthma [18]. Bronchodilatation is also increased when inhaled ipratropium is added to the oral regimen of salbutamol and theophylline [7]. This additive effect is sustained in maintenance combination therapy for patients with chronic asthma [6]. In contrast, evaluation of these drugs in patients with acute severe asthma has, in general, consisted of a protocol of sequential drug administration in small numbers of patients [9-11]. Although those studies have concluded that there is no difference between ipratropium bromide and sympathomimetic therapy, this conclusion ignores the potential for a large type II error. To avoid this pitfall, we enrolled enough patients with asthma to detect, at the $\alpha = 0.05$ significance level, a difference in one-second forced expiratory volume improvement between regimens of at least 200 ml, with 80 percent probability ($\beta = 0.2$). In fact, we detected a significant difference of 141 ml at 90 minutes between ipratropium and salbutamol, and of 194 ml between the combination and salbutamol alone.

The question is whether these statistically significant added increases in one-second forced expiratory volume are also clinically important. Patients with acute severe asthma frequently show poor bronchodilator responsiveness; the men presenting one-second forced expiratory volume of less than 40 percent of predicted value (91.18liters) in the patients described here in suggests that many of them had life-threatening asthma^{19,20}. The response to salbutamol represents a 38.9 percent short-term improvement, whereas that achieved by combination therapy was 55.6 percent. In this setting, the additive therapeutic effect is certainly clinically valuable. Like Rossing et al [3], we found that added benefits of combination bronchodilator therapy were greatest in patients whose need was greatest, those whose one-second forced expiratory volume was less than 1 liter at presentation.

Conclusion

Our results indicate that ipratropium cannot be recommended for monotherapy in patients with acute severe asthma. Although salbutamol was superior to ipratropium, the combination of these drugs produced additive bronchodilatation and was the most effective regimen tested in these patients with acute exacerbations of bronchoconstriction.

References

1. Wolfe JD, Tashkin DP, Calvarese B, Simmons M: Bronchodilator effects of terbutaline and aminophylline alone and in combination in asthmatic patients. *N Engl J Med* 1978;298:363-367.
2. Shenfield GM: Combination bronchodilator therapy. *Drugs* 1982;24:414-439.
3. Rossing TH, Fanta CH, McFadden ER: A controlled trial of the use of single versus combined-drug therapy in the treatment of acute episodes of asthma. *Am Rev Respir Dis* 1981;123:190-194.
4. Pakes GE, Brogden RN, Heel RC, Speight TM, Avery GS: Ipratropium bromide: a review of its pharmacologic properties and therapeutic efficacy in asthma and chronic bronchitis. *Drugs* 1980;20:237-266.
5. Gross NJ, Skorodin MS: Anticholinergic, antimuscarinic bronchodilators. *AM Rev Respir Dis* 1984; 129:856-870.
6. Rebuck AS, Gent M, Chapman KR: Anticholinergic and sympathomimetic combination therapy of asthma. *J Allergy Clin Immunol* 1983;71:317-323.
7. Lefcoe NM, Toogeed JH, Blennerhassett G, Baskerville J, Paterson NAM: The addition of an aerosol anticholinergic to an oral beta agonist plus theophylline in asthma and bronchitis. *Chest* 1982;82:300-305.
8. Chapman KR, Smith DL, Rebuck AS, Leenen FHH: Hemodynamic effects of inhaled ipratropium bromide; alone and combined with an inhaled B-2 agonist. *Am Rev Respir Dis* 1985;132:845-847.
9. Ward MJ, Fentem PH, Smith WHR, Davies D: Ipratropium bromide in acute asthma. *Br Med J* 1981;282:598-600.
10. Ward MJ, MacFarlane JT, Davies D: Treatment of acute severe asthma with intravenous aminophylline and nebulized ipratropium bromide after salbutamol (abstr). *Thorax* 1982;27:785.
11. Leahy BC, Gomm SA, Alien SC: Comparison of nebulized salbutamol with nebulized ipratropium bromide in acute asthma. *Br J Dis Chest* 1983;77:159-163.
12. Lightbody IM, Ingram CG, Legge JS, Johnston RN: Ipratropium bromide, salbutamol and prednisolone in bronchial asthma and chronic bronchitis. *Br J Dis Chest* 1978;72:181-186.
13. Knudson RJ, Slatin RC, Lebowitz MD, et al: The maximum expiratory flow-volume curve. Normal standards, variability and effects of age. *Am Rev Respir Dis* 1976;113:587-600.
14. American Thoracic Society: Definitions and classifications of chronic bronchitis, asthma and pulmonary emphysema. *Am Rev Respir Dis* 1962;85:762-768.
15. Elwood RK, Abboud RT: The short-term bronchodilator effects of fenoterol and Ipratropium in asthma. *J Allergy Clin Immunol* 1982;69:467-473.
16. Ruffin RE, McIntyre E, Crockett AJ, Zielonka K, Alpers JH: Combination bronchodilator therapy in asthma, *J Allergy Clin Immunol* 1982;69:60-65.
17. Sybert A, Weiss EB: Status asthmaticus. In: Weiss EB, Segal MS, Stein M, eds. *Bronchial asthma: Mechanisms and therapeutics*, 2nd ed. Boston: Little, Brown, 1985;808-842.
18. Rebuck AS, Read J: Assessment and management of severe asthma. *Am J Med* 1971;51:788-798.

ORIGINAL ARTICLE

Effects of Decortication on Lung Function in Chronic Empyema Thoracis

Md. Mofizur Rahman Mia¹, Shahedur Rahman Chowdhury², Shafiqul Ahsan³
GM Akbar Chowdhury⁴, AKM Razzaque⁵

Abstract

Objective: The purpose of the study is to evaluate the lung function before and after lung decortication in chronic empyema thoracis. Methods: Fifty-nine patients with the diagnosis chronic empyema thoracis were evaluated in a prospective manner by spirometry before and five months after decortication. Results: Histopathology of 28 (47.5%) was granulomatous lesion consistent with tuberculosis and the rest 31 (52.5%) were non-specific inflammatory lesion. Preoperative mean value of FVC was $1.85 \pm 0.41(L)$, %FVC was $47.85 \pm 7.51\%$, FEV_1 was $1.78 \pm 0.40(L)$, and % FEV_1 was $52.18 \pm 8.88\%$. The rate of change of FVC was 39.6%, %FVC was 49.5%, FEV_1 was 41.9% and % FEV_1 was 46.8% during preoperative to final follow up after 5 months of decortication. Conclusions: In patients with chronic empyema thoracis, all spirometric parameters reduced severely. After decortication, parameters significantly improved but not reach predicted values. There was no influence of sex, side and etiology of the diseases (tubercular or nontubercular).

[Chest & Heart Journal 2009; 33(1) : 22-28]

Introduction:

Empyema from the Greek, is defined simply as "pus in a natural body cavity". American Thoracic Society (ATS) divides the formation of an empyema into three stages that represent a continuous spectrum. Within 3-4 weeks the third or organization stage begins with massive ingrowth of fibroblasts and formation of collagen fibers over both visceral and parietal surface. The pus is very thick, and the lung, which at this stage is virtually functionless, is imprisoned within a thick fibrin peel. Empyema is established by pus obtained on thoracentesis, glucose concentration less than 60 mg/ dl, LDH greater than three times the upper

limit of normal, and pH less than 7.0. This process leads to a gradual decline in aeration, with resultant atelectasis and reduced pulmonary function severely.

Medical management of empyema is a misnomer. Medical management or conservative non-interventional therapy is rarely effective and often contraindicated for management of empyema. Thoracentesis and culture sensitivity based antibiotic therapy are appropriate and gradually successful for stage I parapneumonic effusions but not stage II or stage III empyema. Treatments of stage II consist of fibrinolysis via chest tube or thoracoscopic (VATS) debridement, but they are

1. Assistant Professor, Department of Thoracic Surgery, NIDCH, Dhaka.
2. Registrar, Department of Thoracic Surgery, NIDCH
3. Professor of Thoracic Surgery, NIDCH
4. Professor, Department of Thoracic Surgery, NIDCH
5. Associate Professor of Thoracic Surgery, NIDCH.

Correspondence to: Dr. Md. Mofizur Rahman Mia, Assistant Professor, Department of Thoracic Surgery, NIDCH, Dhaka.

not effective in chronic empyema thoracis, which requires formal decortication by thoracotomy.

Decortication, a term derived from Latin, literally means stripping off the “bark” from the lung. It is a surgical procedure that consists of removing a restricting membrane from the lung. Re-expansion of the lung with obliteration of the space is almost always achieved if the underlying parenchyma is normal. This result is always permanent and is accompanied by subjective improvement particularly if decortication takes place early in the process of empyema.

Among functional studies in-patient with chronic empyema thoracis, spirometry are the most common and useful lung function test. Its clinical utility is well accepted; it is the least expensive and most widely available method. The primary spirometric indices are FVC, FEV₁, %FEV₁ and %FVC. Clinical utility of other spirometric measures are less well established.

Materials and methods:

This non-randomized prospective clinical study was conducted in the department of thoracic surgery in NIDCH, from July 2005 to January 2008. Initially 70 (seventy) patients of clinically suspected chronic empyema thoracis who underwent decortication during the study period were included. Exclusion criteria were clinical suggestions and X-ray chest demonstrating parenchymal damage, patients with co-morbid diseases (e.g. chronic liver diseases, renal failure, recent myocardial infarction.), patients planned for decortication but resectional surgery was needed and age of the patients below 6 years as they cannot follow the instruction for performing spirometry.

All patients received a diagnostic work up, which included chest radiography (CXR), sputum for Acid-fast bacilli (AFB), sputum for culture and sensitivity (C/S), CT scan and rigid bronchoscopy in selected patients. All patients also had undergone spirometry preoperatively and post operatively for assessing pulmonary function. Preoperative spirometry was performed within one week prior to operation. Each time the following parameters were measured; FVC, % FVC (the percentage of

the predicted normal values), FEV₁, % FEV₁ (the percentage of the predicted normal values).

All patients were prepared for the operative procedure. Physiotherapy was introduced in every patient for adequate preparation and an expected favorable outcome. Blood transfusion, nutritional supplement and correction of other deficiencies were done as required. Patients with pulmonary tuberculosis whether they were sputum positive or negative had to continue antitubercular drugs for at least 4 to 6 weeks preoperatively and carried on postoperatively. Only on the day of operation these drugs were stopped. In 1st postoperative day drugs were again started. Tube thoracostomy was performed if the patient had symptoms caused by large amount of pleural fluid or fever and also to reduce the toxicity of the patient. Complete lung decortication was performed through standard postero-lateral thoracotomy with or without rib resection. The parietal wall of the empyema sac was detached from the chest wall by extra pleural dissection.

Postoperative evaluations were performed at least two times: 1st after one month and finally after five months of decortication. In every follow up patients were evaluated clinically, with the help of chest X-ray and spirometry. All of them came for the 1st follow up but 11 (eleven) of them did not come at final follow up. Finally the 59 (fifty nine) patients were used for the analyses. Tuberculous empyema was confirmed by AFB staining or by the presence of typical caseous necrosis. Data were analyzed using SPSS version 11.5. Unpaired t-test, chi-square test and Fisher's exact test were used to find the significant difference of different statistics. For each analytic test the level of significance was set at 0.05 and $p < 0.05$ was considered significant.

Observation and results:

Of the 59 patients, 48 patients were male and 11 were female and male female ratio was 4.1:1. The mean age of the study subject was 29.9 ± 11.1 . The mean age of the male patients was 30.7 ± 10.9 years and that of female patients was 26.5 ± 11.8 years (Table I).

Table-I
Age and sex distribution of the study patients (n=59)

Age in Years	Male		Female		Total		P Value
	n	%	n	%	n	%	
<20 yrs	6	12.5	4	36.4	10	16.9	
20 – 29 yrs	19	39.6	3	27.3	22	37.3	
30 – 39 yrs	11	22.9	2	18.2	13	22.0	
40 – 49 yrs	9	18.8	2	18.2	11	18.6	
≥50 yrs	3	6.3	0	0.0	3	5.1	
Total	48	100.0	11	100.0	59	100.0	
Mean ± SD)	30.7 ± 10.9		26.5 ± 11.8		29.9 ± 11.1		0.254

Insignificant (p > 0.05) with unpaired t-test, Z=8.79, p<0.001

Chest pain (83.1%), fever (81.4%), dyspnoea (72.9%), weight loss (54.2%), cough (54.2%) and general malaise (54.2%) etc. were the characteristic presentation in the study population (Table -II)

Table-II
Clinical presentation of the patients (n=59)

	n	%
Chest pain	49	83.1
Fever	48	81.4
Dyspnoea	43	72.9
Weight loss	35	59.3
Cough	32	54.2
General malaise	20	33.9

Table-III showed 28 (47.5%) were granulomatous lesion consistent with tuberculosis and the rest 31 (52.5%) was non- specific inflammatory lesion.

Table-III
Histopathological findings of specimen of the study patients

Histopathological finding	n	%
Granulomatous lesion consistent with tuberculosis	28	47.5
Non- specific inflammatory lesion	31	52.5
Total	59	100

Table IV showed preoperative mean value of FVC was 1.85 ± 0.41(L), %FVC was 47.85 ± 7.51%, FEV₁ was 1.78 ± 0.40(L), and % FEV₁ was 52.18 ± 8.88%,

Table IV
Preoperative spirometric values (n=59)

Spirometric parameters	Mean ±SD
FVC	1.85 ± 0.41
%FVC	47.85 ± 7.51
FEV ₁	1.78 ± 0.40
%FEV ₁	52.18 ± 8.88

Table V and figure (1- 4) shows the rate of change of FVC was 39.6%, %FVC was 49.5%, FEV₁ was 41.9% and %FEV₁ was 46.8% during preoperative to final follow up after 5 months of decortication.

The rate of change in male and female were 37.2% and 50.3% in FVC, 48.0% and 55.7% in %FVC, 40.2% and 49.4% in FEV₁, 44.9% and 55.0% in %FEV₁ respectively (Table VI).

The rate of change in 28 tubercular and 31 non-tubercular patients were 34.6% and 44.2% in FVC, 45.8% and 52.8% in %FVC, 39.7% and 43.9% in FEV₁, 44.6% and 48.7% in %FEV₁ respectively (Table VII).

The rate of change in right and left were 43.5% and 36.6% in FVC, 53.4% and 46.4% in %FVC, 44.3% and 36.1% in FEV₁, 49.2% and 41.8% in %FEV₁ respectively. Analysis revealed no statistically significant (p>0.05) rate of change between right and left affected side of the patients in unpaired t-test (table VIII).

Table-V*Changes of spirometric parameters after decortication (n=59)*Spirometric parameters Preoperative 1st follow up after 1 month Final follow up after 5 months P value

	Mean±SD	Mean±SD	Mean±SD	Pre V _s 1 st	Pre V _s Final
FVC (L)	1.85±0.41	1.92±0.40	2.56±0.43	0.023	0.001
% [†]		3.5	39.6		0.001
%FVC	47.85±7.51	50.41±7.02	70.59±7.20	0.003	0.001
% [†]		6.4	49.5		0.001
FEV ₁ (L)	1.78±0.40	1.82±0.37	2.49±0.44	0.090	0.001
% [†]		3.1	41.9		0.001
%FEV ₁	52.18±8.88	53.60±9.82	75.25±8.00	0.232	0.001
% [†]		3.9	46.8		0.001

†Rate of change

Insignificant (p > 0.05) with paired t-test

Significant (p < 0.05) with paired t-test

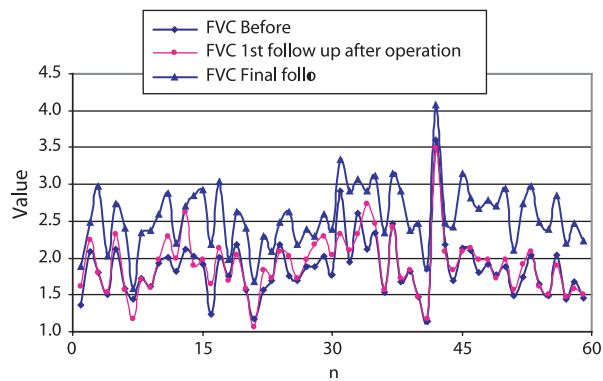
**Fig.-4:** %FEV₁ for all patients before operation, 1st follow up and final follow up after decortication

Table-VI
Change of spirometric parameters after 5 months of decortication separately for male and female (n=59).

Spirom-etric Parameters	Male (n=48)		Female(n=11)		P value
	Preoperative mean±SD	Final follow up after 5 months mean±SD	Preoperative mean±SD	Final follow up after 5 months mean±SD	
FVC	1.94± 0.39	2.64± 0.39	1.47± 0.21	2.19± 0.41	
%†		37.2		50.3	0.013
%FVC	48.13 ± 8.16	70.22± 6.72	46.60± 3.43	72.21± 9.22	
%†		48.0		55.7	0.196
FEV ₁	1.87± 0.38	2.58± 0.40	1.42± 0.26	2.12± 0.45	
%†		40.2		49.4	0.159
%FEV ₁	52.69± 9.65	74.84± 7.63	49.95± 3.58	77.05± 9.65	
%†		44.9		55.0	0.158

†Rate of change, Insignificant (p > 0.05) with unpaired t-test,
 Significant (p < 0.05) with unpaired t-test

Table-VII
Changes of spirometric parameters after 5 months of decortication separately for tubercular and non-tubercular patients (n=59)

Spirometric Parameters	Tubercular (n=28)		Non-Tubercular(n=31)		P value
	Preoperative mean±SD	Final follow up after 5 months mean±SD	Preoperative mean±SD	Final follow up after 5 months mean±SD	
FVC	1.96 ± 0.45	2.61± 0.45	1.76± 0.35	2.52± 0.42	
%†		34.6		44.2	0.021
%FVC	48.36± 8.86	69.44± 7.98	47.38± 6.16	71.64± 6.37	
%†		45.8		52.8	0.128
FEV ₁	1.84± 0.42	2.53± 0.39	1.73± 0.38	2.46± 0.48	
%†		39.7		43.9	0.408
%FEV ₁	52.59± 10.45	74.24± 7.86	51.82± 7.34	76.16± 8.15	
%†		44.6		48.7	0.470

†Rate of change, Insignificant (p > 0.05) with unpaired t-test,
 Significant (p < 0.05) with unpaired t-test

Table-VIII
Changes of spirometric parameters after 5 months of decortication according to the side (n=59)

Spirometric Parameter	Right(n=33)		Left (n=26)		P value
	Preoperative mean±SD	Final follow up after 5 months mean± SD	Preoperative mean± SD	Final follow up after 5 months mean± SD	
FVC	1.84± 0.30	2.60± 0.32	1.88± 0.48	1.90± 2.53	
%†		43.5		36.6	0.106
%FVC	47.01± 5.43	71.44± 6.53	48.50± 8.84	69.92± 7.72	
%†		53.4		46.4	0.128
FEV ₁	1.74± 0.32	2.57± 0.36	1.81± 0.45	2.43± 0.49	
%†		44.3		36.1	0.153
%FEV ₁	50.37± 6.95	75.98± 8.37	53.61± 10.03	74.68± 7.78	
%†		49.2		41.8	0.853

†Rate of change
 Insignificant (p > 0.05) with Unpaired t-test

Discussion:

Empyema is classified into 3 stages: the initial or exudative stage, which progress to the fibrinopurulent stage and it culminates in the organized stage. During the third stage, organization begins as the fibroblasts in the fibrin layer begin the deposition of fibrous tissue. As the organization progresses, a peel of fibrous tissue forms between the visceral and parietal pleura, the lung becomes encased. This process leads to a gradual decline in aeration, with resultant atelectasis and reduced pulmonary function, perhaps leading to the total destruction of the lung and to the chest deformity.

Empyema thoracis is one of the debilitating diseases in our country, which makes the suffering population cripple and making continuous burden to our society. Among the surgical procedures decortication is relatively safe and rewarding in empyema thoracis and it causes marked improvement in overall functions. The patient's capacity for performing everyday duties was better after decortication. Regarding etiology of empyema thoracis, in a study by Ahasan et al. at NIDCH showed 63% cases were tubercular and rest 37% non-tubercular. Another study by Rahman et al. showed 48% cases of empyema were tubercular and rest 52% non-tubercular. Similar finding also found in a study by Banga et al. at All India Institute of Medical Sciences (AIIMS), New Delhi, they found 42% patients tubercular and rest 58% non-tubercular. In this series histopathology of decorticated specimen showed granulomatous lesion consistent with tuberculosis in 47.5% cases and nonspecific inflammatory lesion in 52.5% cases, which is consistence with other study.

When the dominant etiologic factor in chronic empyema thoracis was tuberculosis, this factor carries a high risk of morbidity and fatal outcome may result. Many authors showed that the spirometric parameters did not improved after decortication. Toomes et al. and Petro et al. showed that measured spirometric parameters did not improved significantly after an operation. However, results of this study showed that spirometric parameters improved significantly after decortication. Postoperative pulmonary function test performed in this study five months after discharge from the hospital. Because of

prolonged lung collapse, postoperative pain, anesthetic effects, restriction due to chest wall resection, prolonged bed rest and infective sputum spectoration, atelectasis and respiratory failure developed adverse pulmonary effects.

There is no single spirometric parameters that explains the physiology of chronic empyema thoracis. Preoperative mean value of FVC was $1.85 \pm 0.41(L)$, %FVC was $47.85 \pm 7.51\%$, FEV₁ was $1.78 \pm 0.40(L)$, and % FEV₁ was $52.18 \pm 8.88\%$. Result showed in all patients, the preoperative mean FVC, %FVC, FEV₁ and %FEV₁ were reduced bellow normal limit.

Swoboda et al. showed that the mean rate of change was +22.3% in FEV₁ and +30% in FVC. Rzyman et al. showed that the mean FEV₁ and FVC increased 15 and 20% respectively. In this two studies, the preoperative mean values amount of change for the spirometric parameters were similar with our data. Samson et al. showed 79 (77%) had a good to excellent result, with prompt pulmonary re-expansion and satisfactory improvement in pulmonary function; and 21 (20%) had a fair to poor result, LeMense et al. also showed decortication had an excellent success rate of 95%.

Conclusion:

Though to validate the observations and draw any conclusion, a large number of patients should be included in the study and both short and long term follow up are necessary. Considering all facts and figures found in the study following conclusion can be drawn:

1. In patients with chronic empyema thoracis, preoperative values of FVC, FEV₁, % FVC and % FEV₁ are severely reduced.
2. After decortication, FVC, FEV₁, %FVC and % FEV₁ significantly improved but not reach predicted values.
3. Sex, side of the diseases (right or left) and etiology of the diseases (tubercular or nontubercular) has no influence on functional recovery.

Reference:

1. Ahsan S, Rahman MZ, Islam N, Islam AKMS and Khan MNA, et al. Chlorhexidine Wash: A treatment of Empyema Thoracis, Chest & Heart Bull, vol. 1996; 20: 53-56

2. Antony VB. 2004, Pathophysiology and diagnosis of pleural diseases, In Baum's Textbook of Pulmonary Diseases, Lippincott Williams & Wilkins (Edits), 530 Walnut Street, Philadelphia, New York, pp. 1357-1367
3. Banga A, Khilnani GC, Sharma SK, Dey AB, Wig N and Banga N et al., A study of empyema thoracis and role of intrapleural streptokinase in its managements, BMC Infectious diseases, 2004; 4: 19.
4. Choi SS, Kim DJ, Kim KD and Chung KY, et al. Change in pulmonary function following empyema and decortication in tuberculous and non- tuberculous chronic empyema thoracis, Yonsei Med J, 2004; 45(4): 643-648.
5. Deslauriers J, Paris F & Tarrazona V, Fibrothorax and decortication. 2002; In: Thoracic Surgery, 2nd edition. Pearson FG, Cooper JD, Deslauriers J, Ginsberg R, Hiebert CA et al. (Edtrs), Churchill Livingstone, New York, pp. 1265-1280.
6. Iioka S, Sawamura K, Mori T, Iuchi K and Nakamura K. et al. Surgical treatment of chronic empyema. A new one-stage operation, J Thorac Cardiovasc Surg, 1985; 90: 179-185
7. Iliac N, Petricevie A & Tocilj J. Pulmonary function after dcortication of the lung, Lijec Vjesn, 1995; 117: 271-273
8. Jaffe A. & Cohen G. Thoracic empyema, Archives of Disease in Childhood, 2003; 88: 839-841
9. Khan MNA, Islam AKMS, Ahsan S, Karim MS, Sabur SAMA et al., 1995; Surgical management of pulmonary tuberculosis in Bangladesh, Chest and Heart Bulletin, 1995; 19(1): 1-9.
10. Lee RB. 2005, Empyema thoracic, In: Sabiston & Spencer Surgery of the Chest, 7th edition. Sellke FW, Nido PJ, & Swanson SJ (Editrs), Elsevier Saunders, Philadelphia, USA, pp. 431-434
11. LeMense GP, Strange C & Sahn SA, Empyema thoracis. Therapeutic management and outcome, *Chest*, 1995; 107: 1532-1537
12. Light RW. Parapneumonic effusion and empyema, The Proceedings of American Thoracic Society, 2006; 3: 75-80
13. Nieminen MM, Antila P, Markula J & Karvonen J. Effect of decortication in fibrothorax on pulmonary function, *Respiration*, vol. 1985; 48: 94-96.
14. Paris F, Deslauriers J, Calvo V, 2002, Empyema and bronchopleural fistula, in: Thoracic Surgery, 2nd edition. Pearson FG, Cooper JD, Deslauriers J, Ginsberg R, Hiebert CA et al. (Edtrs), Churchill Livingstone, New York, pp. 1265-1280
15. Rahman MZ, Ahsan S, Islam AKMS & Khan BR, Analysis of thousand cases of adult empyema thoracis, *Chest and Heart Bull*, 1996; 20(2): 69-80
16. Rzyman W, Skokowski J, Romanowicz G, Lass P & Dziadziuszko R. Decortication in chronic pleural empyema - effect on lung function, *European J Cardiothorac Surg*, 2002; 21: 502-507
17. Ris HB & Krueger T. Video-assisted thoracoscopic surgery and open decortication for pleural empyema, *Multimedia Manual of Cardio-thorac Surg*, 2006; 1-18
18. Seaton D. Empyema, 2000, In: Crofton and Douglas's Respiratory Diseases, Seaton A, Seaton D & Leitch AG, Blackwell Science, UK, pp. 445-459.
19. Swoboda L, Laule K, Blattmann H & Hasse J. Decortication in chronic pleural empyema. Investigation of lung function based on perfusion scintigraphy, *Thoac. Cardiovasc. Surgeon*, 1990; 38(6): 359-361.
20. Thomas T, Gopinath N, Betts RH & Ghosh AK. Decortication in pulmonary tuberculosis, *Indian Journal of Tuberculosis*, 1954; 62-68.
21. Toomes h, Vogt-Moykopf I & Ahrendt J., Decortication of the lung *Thorac Cardiovasc Surg*, 1983; 31: 338-341
22. Watson TJ 2005, Empyema thoracis, In: Sabiston & Spencer Surgery of the Chest, 7th edition. Sellke FW, Nido PJ, & Swanson SJ (Editrs), Elsevier Saunders, Philadelphia, USA, pp. 431-434.

ORIGINAL ARTICLE

Fluticasone and Montelukast Compared with Fluticasone and Salmeterol in Protecting Against Asthma Exacerbation in Adults

A.K.M. Mustafa Hussain¹, Md. Naimul Huque², Narayan Chandra Datta², Biswas Akhter Hussain³, Abu Raihan⁴, Shah Muhammad Saifur Rahman⁴, M.A. Rouf², Mirza Mohammad Hiron⁵

Abstract

The study was designed to assess the effect of salmeterol versus montelukast added to inhaled fluticasone propionate on asthma exacerbation in patients whose symptoms are inadequately controlled with fluticasone alone. A 52 week, double blind trial during which patients whose symptoms remained uncontrolled by inhaled corticosteroids were randomized to add Salmeterol or montelukast. Patients (15-72 years; n=86) had a clinical history of chronic asthma for ≥ 1 year, a baseline forced expiratory volume in one second (FEV_1) value 50-90% predicted, and a β agonist improvement of $\geq 12\%$ in FEV_1 .

The primary end point was the percentage of patients with at least one asthma exacerbation. 20.1% of the patients in the group receiving fluticasone & montelukast had an asthma exacerbation compared with 19.1% in the group receiving fluticasone & Salmeterol; the difference was 1% (95% confidence interval -3.1% to 5.0%). With a risk ratio (fluticasone-montelukast/fluticasone-salmeterol) of 1.05 (0.86 to 1.29), treatment with fluticasone & montelukast was shown to be non-inferior to treatment with fluticasone & salmeterol. Fluticasone & Salmeterol significantly increased FEV_1 before a β agonist was used and morning peak expiratory flow compared with fluticasone & montelukast ($P \leq 0.001$), whereas FEV_1 after a β agonist was used and improvements in asthma specific quality of life and nocturnal awakenings were similar between the groups. Fluticasone & montelukast significantly ($P=0.011$) reduced peripheral blood eosinophil counts compared with fluticasone & Salmeterol. Both treatments were generally well tolerated. The addition of montelukast in patients whose symptoms remain uncontrolled by inhaled Fluticasone could provide equivalent clinical control to Salmeterol.

[Chest & Heart Journal 2009; 33(1) : 41-44]

Introduction

Anti-inflammatory treatment with inhaled corticosteroids improves lung function, decreases symptoms, reduces asthma exacerbations, and has been the cornerstone of treatment for more than two decades.¹ Current guideline recommends

inhaled corticosteroids as first line treatments for patients with persistent asthma.^{1,2}

However, many patients remain symptomatic despite inhaled corticosteroid treatment, and inflammation of the airways may persist during treatment with inhaled and even oral

1. Associate professor of respiratory Medicine, NIDCH

2. Assistant professor of respiratory Medicine, NIDCH

3. Medical Superintendent, NIDCH

4. Registrar, NIDCH

5. Professor of Respiratory Medicine cum Director, NIDCH

Correspondence to: Dr. A.K.M. Mustafa Hussain, Associate professor of respiratory Medicine, NIDCH

corticosteroids.³

Increasing the dose of inhaled corticosteroids is one therapeutic option. However, at higher doses side effects become a concern due to a narrow therapeutic index, and responses are variable,⁴ implying that such doses may not necessarily treat asthma more effectively. Adding an inhaled long acting β agonist to an inhaled corticosteroid is more effective in improving lung function and reducing symptoms^{5 6} and asthma exacerbations.⁷ Combination treatments is therefore recommended in current guidelines to achieve additional control.^{1 2} An alternative approach is to add a leukotriene receptor antagonist to an inhaled corticosteroid.⁸ Cysteinyl leukotrienes released by eosinophils and mast cells mediate pro-inflammatory events in asthma.⁹

The addition of a long acting β agonist or a leukotriene receptor antagonist to inhaled corticosteroids has been shown to prevent exacerbations and improve quality of life,^{13 14} but few data are available to compare the benefits of these alternative strategies. We report a randomized controlled trial of adding Salmeterol or montelukast to an inhaled corticosteroid for patients who remained symptomatic while using an inhaled corticosteroid alone, which assessed the rate of asthma exacerbations over a one year period.

Methods

This study was a randomized, double blind, parallel group conducted at NIDCH, Mohakhali, and Dhaka of 52 weeks duration including a 4 week run-in period when patients received non-blinded inhaled dry powder fluticasone 100 μ g twice daily. During the last two weeks of this period, single blind placebo montelukast were added. A 48 week period

of double blind treatment followed, during which in addition to fluticasone 100 μ g twice daily, patients received either montelukast 10mg once daily (in the evening) or salmeterol 50 μ g twice daily. Allocation numbers were sequentially assigned at each study and were associated with treatment groups by use of a computer generated allocation schedule. The blinded, clinical supplies were labeled with allocation numbers and patient instructions. The study was conducted between January 2008 and December 2009. Patients gave written informed consent.

Statistical analysis

We used an analysis of covariance model with effects for treatment. And we used the baseline value as a covariate analyzed differences in treatment for blood eosinophil count, asthma specific quality of life, nocturnal awakening, peak expiratory flow, and FEV₁ as a change from baseline. We used generalized linear models, similar to models used for analyzing the percentage of patients with asthma exacerbations, to analyze differences between treatments for use of resources. We included all randomized patients in the safety analyses. We assessed the safety by statistical & clinical review of adverse experiences.

Results

We screened 268 patients and 186 were entered into the study. Of these, 93 participants were randomized to the fluticasone-montelukast group and 93 to the Fluticasone-Salmeterol group (table 1). Discontinuance of patients was similar between both treatment groups. We found no differences between the two groups for baseline characteristics (table 2), including history of nocturnal asthma or previous use of inhaled corticosteroids (dosage and type; data not shown).

Table-I
Participants in the randomized, double blind, parallel group of 52 weeks.
Values are numbers (%) of patients

	Fluticasone-Montelukast (n=93)	Fluticasone-Salmeterol (n=93)
Completed the study	77 (83.3)	79 (85.2)
Discontinued the study	15 (16.7)	13 (14.8)
Clinical adverse experience	5 (5.1)	5 (4.7)
Laboratory adverse experience	0(0)	1(0.3)
Lack of efficacy	1 (0.5)	1 (0.9)
Protocol deviation	2 (2.0)	2 (2.0)
Lost to follow up	2 (1.6)	2 (1.6)
Patient moved	2 (0.9)	1 (0.7)
Withdrew consent	3 (2.9)	3 (3.0)
Site terminated	2 (1.1)	1 (0.5)

Table-II*Patients' demographics and baseline characteristics. Data are means (SD) unless otherwise indicated*

	Fluticasone-Montelukast (n=93)	Fluticasone-Salmeterol (n=93)
No (%) of female participants	51 (54.6)	52 (55.2)
Age (yrs)	41.2(13.6)	41.0 (13.7)
Age range (yrs)	5 (5.1)	5 (4.7)
Use of β agonist (puffs/day)	3.3 (2.5)	3.3 (2.2)
FEV ₁ before β agonist (l)	2.4 (0.8)	2.5(0.8)
FEV ₁ % predicted	71.3 (13.2)	72.7 (13.9)
FEV ₁ % reversibility after a β agonist was used	18.4(12.3)	18.8 (13.0)
Peak expiratory flow in the morning (l/min)	384(50)	389(106)
No of nocturnal awakenings (days/week)	2.6(2.4)	2.5(2.4)

Table-III*Numbers (percentages) with 95% confidence intervals of all patients in the treatment group with at least one asthma exacerbation and components during the 48 week period of double blind treatment*

	Fluticasone- Montelukast group(n=93)	Salmeterol- Fluticasone (n=93)	Comparison between treatment groups: risk ratio
Asthma exacerbation	8(20.1; 17.3 to 23.1)	17(19.1; 16.3 to 22.1)	1.05 (0.86 to 1.29)
Admission to hospital	5(0.7; 0.2 to 1.6)	7(0.9; 0.4 to 1.9)	0.71(0.21 to 2.22)
Unscheduled visit to medical specialist	10(11.0; 8.8 to 13.4)	10(10.8; 8.6 to 13.2)	1.02(0.76 to 1.36)
Visit to emergency dept.	3 (2.8; 1.7 to 4.3)	3 (2.8; 1.8 to 4.3)	0.99(0.55 to 1.81)
Use of oral, IM, IV, or rectal corticosteroid	14(15.8; 13.3 to 18.6)	13 (14.4; 12.0 to 17.1)	1.10(0.86 to 1.40)

Discussion

Adding Montelukast to the treatment of patients who continue to experience symptoms while receiving inhaled fluticasone is at least as effective as adding Salmeterol to treatment in these patients. Furthermore, the difference in the proportion of patients with asthma exacerbations between the two treatment groups in our study was small, (1%, 95% confidence interval -3.1 to 5.0), indicative of a difference that is not clinically important. Both drugs significantly decreased the frequency of nocturnal awakening, a variable exacerbation of the underlying asthma condition that is associated with an increased influx of inflammatory cells, particularly lymphocytes, macrophages, and eosinophils, into the small & peripheral airways. It is therefore reasonable to speculate that the protective effect seen with montelukast is due to its anti-inflammatory action in the small airways. Measurement of patient-oriented assessments such as quality of life provides information on the impact of disease in patients with asthma. Both Salmeterol & montelukast provided as add-on treatment to fluticasone were

beneficial in improving the quality of life score, indicating improvement in the global assessment of disease control.

Lung function improved in both treatment groups. While the change in FEV₁ before a bronchodilator was used significantly better with add-on Salmeterol, FEV₁ after a bronchodilator had been used did not differ between the two groups, resulting in comparatively significant loss of reversibility of FEV₁ in the fluticasone-salmeterol group over the yr. This observation calls for a longer prospective trial looking at the effect of long term treatment with salmeterol & montelukast on the development of lung function over time.

Conclusion

Current guidelines for the treatment of patients with moderate to persistent asthma recommend the use of an inhaled corticosteroid and, if needed, along acting inhaled β agonist. The results of this study imply that the addition of montelukast in patients whose symptoms remain uncontrolled with inhaled fluticasone could be as effective as adding salmeterol in protecting against asthma

exacerbations. They therefore imply that the use of leukotriene receptor antagonists such as montelukast is an additional therapeutic option for these patients.

References

1. National institutes of Health, National Heart, Lung & Blood Institute. Asthma management & prevention. Global initiative for asthma. A practical guide for public health officials & health care professionals. Based on the global strategy for asthma management and prevention NHLBI/WHO workshop report. Bethesda, MD: NIH, 1995.
2. British asthma guidelines coordinating committee. British guidelines on asthma management: 1995 review & position statement. *Thorax* 1997;52;SI-24
3. EI-radhi AS, Hogg CL, Bungre JK, Bush A, Corrigan CJ. *Arch Dis Child* 2000;83:158-62
4. Barnes PJ. Efficacy of inhaled corticosteroids in asthma. *J Allergy Clin Immunol* 1998;102:531-8
5. Greening A, Wind P, North field M, Shaw G. Added Salmeterol versus higher-dose corticosteroid in asthma patients with symptoms on existing inhaled corticosteroids. *Lancet* 1994; 344:219-24
6. Woolcock A, Lundback B, Ringdal N, Jacques L. Comparison of addition of Salmeterol to inhaled steroids with doubling of the dose of inhaled steroids. *Am J Respir Care med* 1996;153:1481-8
7. Pauwels RA, Lofdahl C-G,, Postma DS, Tattersfield AE, O'Byrne P, Barnes PJ, et al., Effect of inhaled formoterol & budesonide on exacerbations of asthma. *N Eng J Med* 1997;337:1405-11
8. Laviolette M, Malmstorm K, Lu S, Chervinsky P, Pomet JC, Peszek I, et al. Montelukast added to inhaled beclomethasone in treatment of asthma. *Am J Resp Crit care Med* 1999;160:1862-8
9. Drazen JM, Isreal E, O'Byrne PM. Treatments of asthma with drugs modifying the leukotriene pathway. *N Eng J Med* 1999;340:197-206
10. Pizzicini E, Leff JA, Reiss TF, Hendele L, Boulet LP, Wei LX, et al. Montelukast reduces airway eosinophilic inflammation in asthma. A randomized controlled trial. *Eur resp J* 1999;14:12-8
11. Reiss TF, Sorkness CA, Stricker W, Botto A, Busse WW, Kundu S, Zhang J. Effect of montelukast (MK-0476): a potent cysteinyl leukotriene receptor antagonist, on bronchodilation in asthmatic subjects related with or without inhaled corticosteroid. *Thorax* 1997;52:45-8
12. Villaran C, O'Neill SJ, Helbling A, van Noored JA, Lee TH, Chuchalin AG, et al. Montelukast versus Salmeterol in asthma patients & exercise induced bronchoconstriction. Montelukast/Salmeterol Exercise Study group. *J Allergy Clin Immunol* 1999;104:547-53

ORIGINAL ARTICLE

Current Management in Day Care Transfusion Unit at Dhaka Medical College Hospital

IA Begum¹, J Biswas², MA Fayez³, MS Dowllah⁴ S Begum⁵

Abstract:

Transfusion of blood and components in DCTU is essential for the management of anaemic patients. Transfusion in a DCTU is also an alternative to hospital admission as well as cost effective benefit for patients. Total 520 units of blood and blood components covering this period and rational use of blood gave benefit to the patients for their treatment and cost Out of 520 units transfusion WB 286 units ie. 55%, packed cell 209 units ie. 40.19%, FFP 18 units (3.46%), and platelets 03 (.57%) were used. Out of 520 patients 306(58.85%) came from outside Dhaka city and 214(41.15%) from Dhaka city . So DCTU gave less hospital stay for those patients and also the rational use of components of blood gave benefit for treatment.

[Chest & Heart Journal 2009; 33(1) : 37-40]

Introduction

The clinical transfusion of blood and components of blood is essential and helpful for all patients those who suffer from haematological disorders, haemoglobinopathies and who received chemotherapy. Transfusion in a DCTU is also an alternative to hospital admission. In early 1990 the authorities of the Institute of Post graduate Medical and Research (IPGM&R) Dacca, Bangladesh established the DCTU within the department of Blood transfusion. In DMCH the day care transfusion center was established in 2005 with a single bed aiming to provide transfusions to those patients who needed transfusion before or after chemotherapy or radiotherapy or those required transfusion at regular interval like Thalassaemia, HbE disease, Sickle cell anaemia, Haemophilia etc or any other diseases those required transfusion of blood or components of blood but not required hospital admission In Bangladesh one bed is allotted for 3151 people ²

and is troublesome for a patient or their relatives in admission for transfusion in DMCH. A transfusion is a relatively simple medical procedure that doctors use to make up for a loss of blood or any part of blood such as red cells platelets etc. Transfusion is given through an intravenous line; a tiny tube that is inserted in a vein with a small needle The whole procedure usually takes about 2 to 4 hours depending on amount of blood or component of blood needed ³ Usually one unit of blood or component of blood transfusion requires 2-3 hours or less if FFP or PRP or PL is transfused. After the completion of transfusion patient is discharged. So the patient needs no hospitalization for for transfusion and this system is now established in different Medical College Hospital and as popular as it is a cost effective and reduce the hazards of availability of bed for admission.

In this study analysis of prospective data about transfusion of unit of blood and blood components

1. Assistant Professor of Transfusion Medicine, National Institute of Diseases of Chest and Hospital.
2. Professor and Chair person of Transfusion Medicine, Bangabandhu Sheikh Mujib Medical University.
3. Assistant Professor Radiology and Imaging East West Medical College Hospital, Turag, Dhaka.
4. Ex. Surgical Specialist, Combined Military Hospital, Dhaka.
5. Professor of Transfusion Medicine, National Institute of Diseases of Chest and Hospital.

Correspondence to: Dr. Ismat Ara, Assistant Professor, NIDCH, Mohakhali, Dhaka.

in different diseases and adverse transfusion reactions during and after transfusion from July 2007 to December 2009 of about 520 patients were performed.

The aim of this study may help to established in setting up and smooth I-1,111111110 of day care transfusion unit with all equipment facility to manage the patient properly as well as emergency care. This will also increase the rational use of blood and blood components.

Materials and Methods

In this study the total number of patients was 520. Study period from July 2007 to Decmber 2008. Blood and Blood components were transfused for all referred patients. Before transfusion therapy a prescribed data like Name, Age, Sex and Clinical diagnosis were recorded Before transfusion pre-transfusion status of the patient were also recorded and the required components were selected carefully for transfusion of each patient. Patients were monitored by doctors during and after transfusion. The types of blood and blood components transfused were whole blood, packed red cells, PRP, FFP and platelets. No medication was usually required before transfusion. Usually multi transfused patients and who had experience mild transfusion reaction received anti-histamin tablet as pec-medication to avoid mild reaction like itching, urticaria. Some patients also received washed red cell.

Results

A total of 520 patients 204 (39.23%) were male, 316(60.77%) were 6 female. Patients resided Outside Dhaka city were 306(58.85%) and at Dhaka city ? 14(4l .15%).Reported patients had cancer of different solid organs 381(73.27%) and other diseases.

Thalassaemia 09(1.73%). Aplastic anaemia 15(2.88%), Sickle cell anaemia 1(.19%), Lymphoma 16(.077%), Chronic Rheumatic disease 10(1.92%), Menorrhagia 27(5.19%), Hb H disease 5(.96%). Leukaemia 4(.77%). Combined deficiency 4(.77%), Haemophilia 14(2.69%), Anaemia of other diseases 34(6.54%)

Most of the patient received fresh whole blood and some received different components are listed below:

Table-I

Distribution of blood component

Component	Number of Unit	Percentage
Whole blood	286 units	55.00
Packed Red cell	209 units	40.19
FFP	18 units	03.46
Platelets	03 units	00.57

Blood grouping of those patients were recorded:

Table-II

Distribution of blood Group)

Blood group	Distribution blood Group	Percentage
Gr.A	134	25.77
Gr. B	145	27.88
Gr.O	202	35.85
Gr.AB	39	7.5

Rh D positive 98.08% and Rh D negative 1.92% Charts are given below:

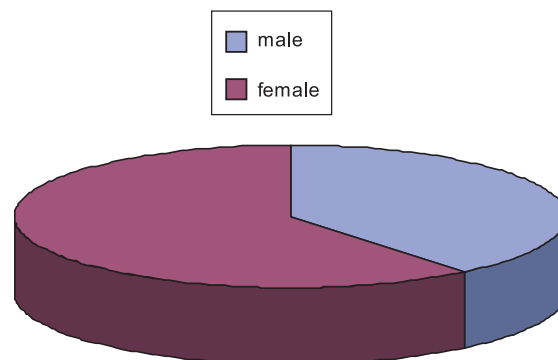


Fig.-1: Sex Distribution

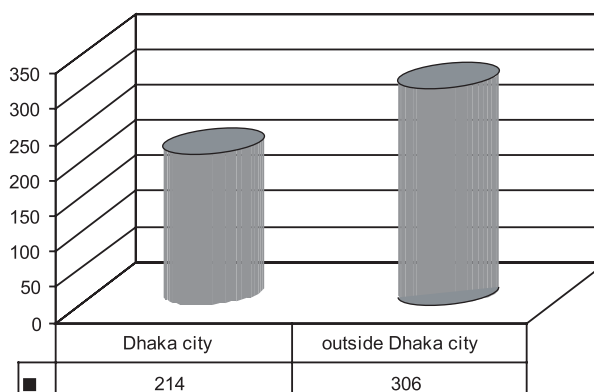


Fig.-2 : Distribution of Residence of patient

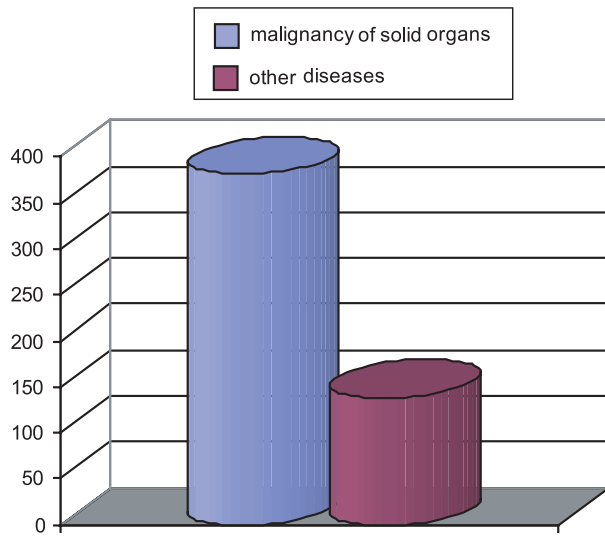


Fig.-3: Distribution of Malignancy of solid organ and other diseases

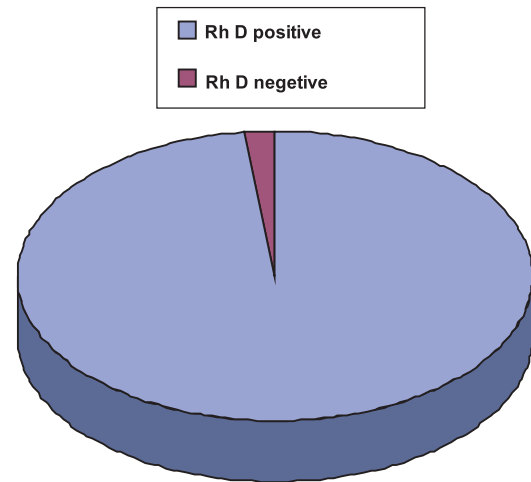


Fig.-6: Distribution of Rh blood group

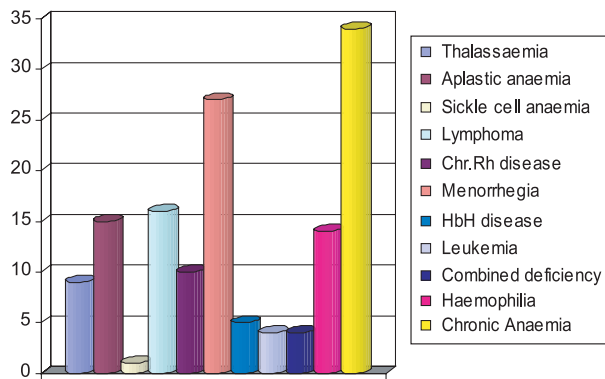


Fig.-4: Distribution of different diseases

■ Gr.A	134
■ Gr.B	145
■ Gr.O	202
■ Gr.AB	39

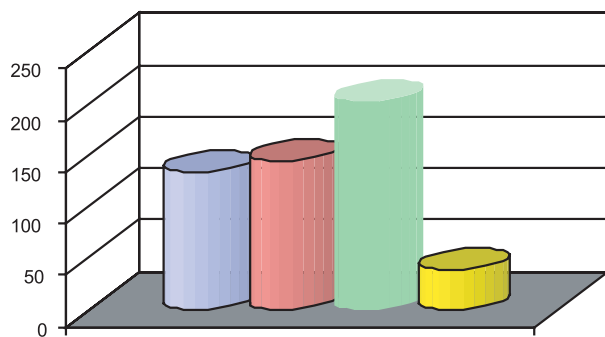


Fig.-5: Distribution of blood group

Discussion

Among the patients of solid organ malignancies and other diseases like Thalassaemia, Aplastic anaemia, DUB (Dysfunctional uterine bleeding) and any other haematological or gynecological diseases require repeated transfusion of blood and blood components. The demand of transfusion is increasing day by day. Some patients like Thalassaemia requires transfusion at regular interval but other does not⁵. This study is based mainly on reviewing of clinical record and analyzing the practical management of those patients with blood and components of blood. Clinical parameter of transfusion was haemoglobin level, the WBC count (total and differential) Platelet count for the required component of transfusion. Out of total 520 patients, most of them had cancer of solid organs, 381 in number (73.27%) required whole blood or components of blood before chemotherapy as well as after chemotherapy or radiotherapy. After chemotherapy some required leucocytes and other required platelets; because of leucopenia or thrombocytopenia⁴. Those patients having Aplastic anaemia 15 in number (2.88%), Chronic Rh diseases 10(1.92%), Thalassaemia 9(1.73%), Lymphoma 16(3.07%), Haemophilia 14(2.69%), Leukemia 4(.71%), Menorrhagia 27(5.19%), Hb H disease 5(.96%). Anaemia of other diseases 34(6.54%). Total transfusion was 520 units covering this period , tried to transfuse the required components and give importance in rational use of blood components. Out of 520 units transfusion of whole

blood (W.B.)286 units ie.55% and other like packed cell 209 units (40.19%), FFP 18 units (3.46%) and the lowest use was platelet 03(.57%).In DCTU most patients 306(58.85%)were residing outside Dhaka city and they had no donor to transfuse fresh blood or required components. In those cases stored blood or packed cell and sometimes FFP were used. Out of 520 patients 214 (41.15%) came to DCTU for transfusion from different corners of Dhaka city. They also

had the same problem of donors. So, transfusion of whole blood was more than that of component.

Majority of the patients attending in DCTU were of lower socio-economic group 410(78.85%) and 100(19.23%) of middle class and only 10(1.92%) were of solvent group. Basing on socio-economic condition, characteristics and quality of livelihood indicated that lower economic class was satisfied in transfusion at DCTU. The other patients having better capacity demanded more facilities and improved services at DCTU.

From this study the cancer patients of solid organs received whole blood instead of components because of unavailability of donors. If donor panel was registered in DCTU or nationally rational use of blood components could be performed. Adverse socio-economic condition is a problem for blood transfusion center. 410(78.95%) patients were in lower socio-economic group who cannot effort facilities and can not arrange blood donors.

The patients reported to DCTU is more from peripheral regions. So, more DCTU is required to set up in the peripheral levels, ie. Hospitals and clinics to reduce pressure on Dhaka city.

Awareness of the patient is most important for reducing complications, reporting to DCTU at regular intervals.

Conclusion

DCTU provides life saving support and also treated by transfusing whole blood and blood components.

It is an alternative to hospital admission by which reduces the sufferings of patients with cost effective. DCTU promotes serious patients to provide hospital beds .

So DCTU should be provided with better facilities including trained stuffs , equipments . Govt. and non Govt. organizations should extent their hands to improve Day Care Transfusion Centre in all hospitals and clinics.

Acknowledgement

The authors thank all patients, blood donors and the technical stuff of the Department of Transfusion Medicine, Dhaka Medical College Hospital for their assistance.

Reference

1. K.M.G.Haque, K.M. Kabir, M. Sultan, Dhaka, Bangladesh. Current Management Station of Transfusion Dependent Thalassaemia Patient in Bangladesh: Experience of a Day Care Transfusion Unit. *Transfusion Today*. 1995; 23: 4-5.
2. N Shil, J Biswas, A Islam, A Khatun, Day Care Transfusion Therapy - One year experience in a Day Care Transfusion Unit of Transfusion Medicine Department in a Tertiary Care Hospital. *Bangladesh Journal of Medicine*, 2005; 16 (2): 83-86.
3. MA Kashem, KM Huda, MA Islam. Disease pattern of Blood Recipients in a Day Care Transfusion Center, A prospective study in a Day Care Transfusion Center of Blood Transfusion Department ,Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh . *Sir Salimullah Medical College Journal*. 2002; 8(2): 83-85.
4. Piromelli S. Management of Cooley's Anaemia.In : *Bailliere's Clinical Haematology. International Practice and Research . The Haemoglobinopathies*. Higgs DR Weatherall DJ eds, *Bailliere Tyndall Masch* , 1993; 6(1): 287-325.
5. Remonnay R, Devaux Y, Carrer M. A cost-benefit analysis of out patient blood transfusion in patient with Cancer. *Inter national Society of Technology Assessment in Health Care Mectiny 19th : 2003 Abstract no .82*.

ORIGINAL ARTICLE

Pattern of Radiological Features of Sputum Smear Positive Pulmonary Tuberculosis

Md. Minhajul Islam

Abstract:

This is a retrospective study to see the pattern of radiological features of sputum smear positive cases of pulmonary tuberculosis. A total of 163 patients X-ray were evaluated. Different combinations of shadows were seen. Bilateral involvements were 86 and right lung involvements were 50 and left lung 26. One sputum +ve case shows normal CXR. Patchy opacities shown 73% and cavitory lesion was 37.60%. Right lung involvement is 31% and left lung involvement is 16%.

[Chest & Heart Journal 2009; 33(1) : 45-47]

Introduction:

The value of Chest X-ray in the investigation of a patient with respiratory disease needs no emphasis¹. The posterior anterior (PA) is the standard view taken with the x-ray tube between 5 and 6 ft. (1.5 – 2 m) from the subject and with the film against the front of the chest.

For radiographic description, the lung fields are subdivided into zones, e.g. upper zone, midzone and lower zone. The portion of lung above the horizontal line through the lower border of the 2nd ribs at their junction with the costal cartilages is called upper zone. The portion of lung between the lower border of the upper zone and a horizontal line through the lower border of the 4th ribs at their junction with costal cartilages is called midzone. The portion of lung below midzone is called lower zone.

TB can cause many abnormalities : The common appearances are: 2

- 1) Patchy or nodular shadowing in the upper zones (often bilateral)
- 2) Cavitation
- 3) Calcification

Some other possibilities:

- 1) Hilar or mediastinal lymphadenopathy
- 2) Segmental or lobar collapse
- 3) Dense round or oval shadows
- 4) Diffuse fine nodular shadows
- 5) Plural effusion

Materials and methods:

This retrospective study was carried in the chest disease clinic, Kurigram. X-rays of the sputum +ve cases were evaluated. Total no of X-rays evaluated were 163. Only new and fresh cases were evaluated in the study. Three consecutive sputum samples should have to be positive. Relapse, defaulter, failure and retreatment cases were excluded from the study. TB with concomitant other illness e.g. Ca of lung, ILD, Asthma, COPD etc were excluded from the study. Sputum negative cases were excluded from our study as per our protocol.

Results of our study were shown in the following tables:

Table-I
Shows sex distribution

Male	Female	Total
124	39	163

Table-II
Shows age distribution

Ages	Nos
0-14	2
15-24	32
25-34	29
35-44	34
45-54	33
55-64	23
65 and above	10
Total	163

Table-III
Sowing unilateral or bilateral involvement

Unilateral	76	46.63%
Bilateral	86	52.78%
Total	163	

Table-IV
Showing cavitary lesion

1. CXR with cavity	45	27.60%
2. CXR without cavity	117	71.78%
3. CXR normal	01	
Total	163	

Table-V

1. Right lung	32
2. Left Lung	12
3. Bilateral	01
Total	45

Table-VI

Single	36
Two or more	09
Total	45

Table – VII

1. Patchy opacities only	63
2. Patchy opaciies with cavities	35
3. Nodular opacities	12
4. Nodular opacities with cavities	03
5. Patchy opacities with dense homogenous opacities	05
6. Patchy oipacities withnodular opacities	06
7. Collapse consolidation	03
8. Calcified opacities	02
9. Simpoles cavity	04
10. Patchy opacities ith consolidation with cavities	02
11. Patchy opaeties with fibrosis	05
12. Fibrosis with collapse	06
13. Collapse with cavity	01
14. Non-homogenous opacities	07
15. Patchy opacities with fibrosus band	01
16. Patchy opacities with plural effusion	02
17. Miliary shadows on both lungs	01
18. Hydropneumothorax	01
19. Egg shell opacities	01
20. Ground glass appearance	01
21. Normal CXR	01
Total	163

Table-VIII
Showing distribution of radiological features according to involvement of zones

	Right lung	Left lung	Bilateral Involvement	Total
1. All zones	10	06	52	67
2. Upper and mid-zones	21	11	23	55
3. Mid and lower zones	06	02	03	11
4. Upper and lower zones	01	00	00	01
5. Only upper zone	05	03	02	10
6. Only and mid zone	03	04	06	13
7. Only lower zone	04	00	00	04
Total	50	26	86	162

NB. One CXR is normal

Discussion:

No chest x-ray pattern is absolutely typical of pulmonary tuberculosis. The chest X-ray findings associated the pulmonary tuberculosis are non specific. The vast majority of patients (over 90%) with cavitary pulmonary tubnerculosis are sputum positive³. A normal chest X-ray for practical perposes excludses tuberculosis. Though very rarely tuberculosis causes tuberculous bronchitis which can not be seen on an X-ray⁴. In our study

we have one such cases which is sputum positive with normal C-XR.

There is a virtually endless spectrum of possible combinations of shadows. For instance, it is common for chronic fibrotic tuberculosis to be complicated by acute spread of the disease. In our study, different type of combinations of shadows shown in table-VII.

Male are predominant and majority of patients are within 15 to 55, as shown in Table I & II in age and sex distribution. This is same as in other studies in Bangladesh.

Regarding distribution in different zones, unilateral involvement is 46.63% and bilateral involvement is 52.76% . Patchy opacities alone is seen in 39% but patchy opacities along with other

pattern of radiological shadows is seen in 73% cases. Cavitary lesion 27.60% nodular opacities 12.88%. Right lung involvement is 31% and Left lung involvement is 16%. All zones of both lung involvement is 32%.

References:

1. Douglas Seaton. Pulmonary tuberculosis. In Crofton and Douglas's Respiratory Diseases, 5th Ed., Blackwell Science Ltd. 1: p- 507-527.
2. Peter DO Davics. Respiratory tuberculosis, In Medicine international, 1995; 31: 325-332.
3. TB- A Clinical manual for South East Asia. WHO / TB / 96,200 (SEA).
4. Clofton J, Horne N, Miller F. Pulmonary tuberculosis in adults. In clinical tuberculosis. 1st Edition. CBS Publishers & Distributor, 1996, 97.

ORIGINAL ARTICLE

Reversal of Stage-I Hypertension by Behavioural Intervention: 18 Month Study in Urban Bangladesh

AKM Alamgir¹, Shah Mohammad Keramat Ali², KMHS Sirajul Haque³

Abstract

Background: This quasi-experimental community trial was conducted at the urban Mohammadpur area of Dhaka, Bangladesh to evaluate reversal of blood pressure from stage-I hypertension after reduction of excess bodyweight, reduction of extra salt intake, increment of physical activity and cessation of smoking.

Materials and Methods: This home-to-home follow-up study was conducted from August 2005 to February 2009 among 4,930 respondents, out of 7,474 adults (response rate 65.96%), of age 18 years or above with intervention period of 18 months. Cluster randomized sampling was done to collect 282 cases with stage-I hypertension (196 male, 86 female) without any complications or co-morbidity. Global standard tools were used to evaluate outcome. Follow-up was done after 6, 12 and 18 month of intervention.

Results: Mean age of respondents was 36.82 ± 11.37 year. Drop-out from study was 25.5% at the end of 18 months. Mean change of systolic BP were -4.3 ± 6.5 , -6.6 ± 5.7 and -9.1 ± 5.7 mmHg after 6m, 12m and 18m respectively. Mean change of diastolic BP were -3.6 ± 4.8 , -6.2 ± 4.5 and -8.4 ± 4.6 mmHg after 6m, 12m and 18m respectively. Percent reduction of BP was -7.0% for systolic and -9.9% for diastolic after 18m intervention. Blood pressure of 7.8% cases became normal while BP of 48.9% cases reversed to pre-hypertension. Quality of life, evaluated by GHQ-28, improved from 38 at baseline to 25 for objective and from 8.2 to 2.4 for subjective rating on a scale from zero to ten after 18months.

Conclusion: Mean blood pressure reduction was $-9.1/-8.4$ mmHg. Reversal of hypertension was possible in 56.7% cases by behavioural risk reduction. Subjective and objective scores for wellbeing were improved. This study outcome is recommended to be used by physicians while treating stage-I hypertension.

Key word: Reversal of Hypertension, Behavioural Risk Intervention, Salt reduction

[Chest & Heart Journal 2009; 33(1) : 29-36]

Introduction

Raised blood pressure shortens life, increases hospitalization rate, results occupancy of more hospital beds, increases treatment cost and ultimately become social burden during most

productive and contributing peak mid life years. Cardiovascular disease (CVD) epidemic is a global health care challenge responsible for about 60% of worldwide deaths and 47% of the global burden of diseases each year. In South East Asia Region

1. Professor & Head, Dept. of Community Medicine, Dhaka National Medical College
2. Professor, Clinical Nutrition, Institute of Nutrition and Food Science, University of Dhaka, Bangladesh
3. Professor and Chairman, Dept. of Cardiology & Dean, Faculty of Medicine, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh

Correspondence to: Prof. AKM Alamgir, Dept. of Community Medicine, Dhaka National Medical College, 53/1, Johnson Road, Dhaka-1100, Bangladesh, E-mail: drakmalamgir@hotmail.com

(SEAR) non-communicable diseases are emerging as major public health problems accounting for 51% of all deaths and 44% of the disease burden.^{1,2} Traditionally Bangladeshi peoples were agrarians with fresh fish, fruits and vegetables eating food habit and leading physically active life style. But economic transition, under-planned urbanization, disproportionate industrialization, rural to semi-urban migration, formation of urban slum and rapid globalization brought about lifestyle changes among this population. People over here started to be in more sedentary jobs. Traditional local diets rich in fibres, low fat content and complex carbohydrates are being replaced by cheap energy-dense food with a high content of saturated fats or trans-fatty acids and refined carbohydrates with high glycaemic index. This change along with no physical activity contributes continuously increasing prevalence and problems of high blood pressure in Bangladeshi society.³⁻¹²

With such background, this study was conducted to evaluate impact of behavioural and life style modification on essential hypertension and also to quantify the amount of reduction of blood pressure in a urban community of Bangladesh. Different behavioural intervention studies found positive benefits by reversal or reduction of blood pressure level through lifestyle modification.¹³⁻¹⁵

Materials and Methods

This quasi-experimental before-after community intervention prospective trial was conducted on 282 respondents with uncomplicated primary stage-I hypertension with age 18 years and above during the period June 2006 - February 2009 at Mohammadpur area of Dhaka City in Bangladesh. Sampling technique was Cluster Randomized Sampling.¹⁶ Intervention period was 18 months for each case. Total population of the area was 7,474 according to national voter list.¹⁷ In total 4,930 adults (response rate of 65.96%) were interviewed to find out cases with stage-I hypertension. Their blood pressure was measured. Case selection was done by pre-fixed inclusion and exclusion criteria. Screening was done for any evidence of end organ damage or any co-morbidity. Informed consent was taken from respondents using MONICA tool. Data collection tools comprised of a questionnaire, check list, informed consent form, GHQ-28 & PHQ-9 questionnaire, equipments for anthropometric measurement or clinical examination like- 3M Littmann Classic II SE (USA) Stethoscope, ALPK2 Mercurial Sphygmomanometer, Height-length Measuring

stadiometer, Omron Digital Weighing Scale [Model HN-280], Fukuda C 100 ECG machine and Glucometer etc.

One-to-one counseling was given to the respondents with stage-I hypertension for quitting extra salt intake, cessation of tobacco consumption, and reduction of excess body weight through change of dietary habit and increment of physical activities. Counseling sessions were of 3-tier level - home based individual, centre-based individual and center based peer-group interactive shared group-sessions. Physical activity profile was checked and was expressed in terms of Metabolic Equivalent (METs). Measurement precision was up to 100g for weight, 0.2 cm for height and 2mmHg for BP. Measurement tools were standardized and validated regularly as per WHO protocol. Measurement procedures were according to WHO STEPS recommendation.¹⁸⁻²⁰ Behaviour was evaluated using global protocols.²¹⁻²³ Physical activity was evaluated following standard scales.²⁴⁻²⁶ Permission was taken from the Ethical Review Committee of Bangladesh Medical Research Council.

Any non-compliant or complicated case was immediately referred to cardiologist or nearby specialized cardiology centres. Study or intervention end-points meant drop-out, migration of study subject or falling in the exclusion criteria. No incidence of death happened during study period. Questionnaire was checked for completeness, consistency, mutually exclusiveness, exhaustion, reliability and validity. Evaluation was a factorial design to monitor and test statistically the outcome of interest i.e. change of blood pressure, reduction of salt intake, weight reduction, increment of the duration of physical activity, cessation of tobacco consumption and qualitative changes of life. Analysis was done using SPSS for windows.

Result

Normal blood pressure was found among 45.6%, pre-hypertension among 34.3% and hypertension (JNC-7 criteria) among 20.1% respondents. In total 52.8% respondents were not aware about their raised blood pressure level. This study started to follow 282 respondents. Drop-out from intervention was 25.5% after 18 months follow-up. Attrition of male members was found to be more than female members in every stage.

Mean systolic blood pressure of the cases with stage-I hypertension was 137.9 ± 11.7 mmHg and became 127.1 ± 9.5 mmHg after 18month intervention (Table-1). Mean diastolic blood pressure was 91.2 ± 4.8 mmHg at baseline but became 82.3 ± 4.6 after 18m intervention.

Table-I
Mean Blood Pressure during Intervention

	Systolic		Diastolic	
	Baseline	After 18 m	Baseline	After 18 m
Sample	282	210	282	210
Mean BP (mmHg)	137.9±11.7	127.1 ± 9.5	91.2 ± 4.8	82.3 ± 4.6
Percent Reduction		7.0%		9.9%
Paired t-test value	t=22.9 df	209 p<0.001	t=26.5 df	209 p<0.001

Mean change of sBP was -9.1±5.7 mmHg and dBP -8.4±4.6mmHg after 18 months intervention. Mean change of blood pressure at the end of the study is - 9.1/-8.4 mmHg (Fig-1).

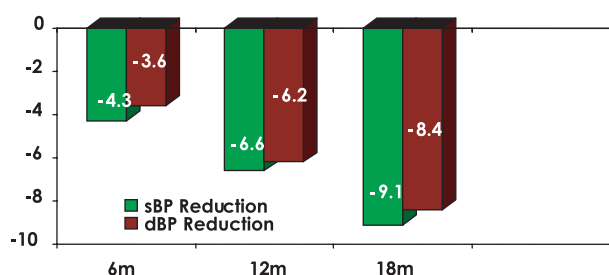


Fig-1: Change of BP after Intervention

Systolic blood pressure reduced 3.1%, 4.9% and 7.0% after 6m, 12m and 18m intervention respectively while the percentage reduction value for dBP was 3.9%, 7.1% & 9.9% respectively (Fig-2).

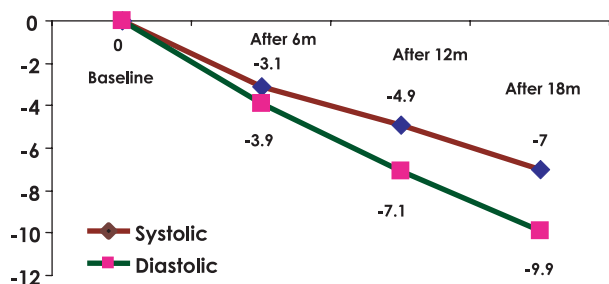


Fig-2: Percent Reduction of BP during Intervention

Blood pressure level of 48.9% respondents with stage-I hypertension reduced to pre-hypertension and 7.8% to normal level while 17.7% remained in stage-I but their mean blood pressure was reduced than their own baseline level. BP of 14.9% increased to stage-II from stage-I and 10.7% developed comorbidity or pregnancy during study (Fig-3).

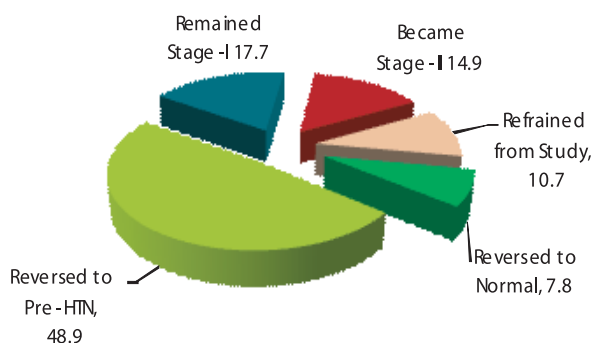


Fig-3: Reversal of stage-I HTN

Salt intake behaviour was significantly reduced during the intervention period. At baseline level 124 respondents (44%) used extra salt while eating. After 18m of intervention salt intake was found among 05(1.8%) respondents. Change of salt intake significantly relates to change of both sBP (F= 9.688; p=0.000; adjusted r²=0.077) and dBP (F=6.544; p=0.002; r²=0.050).

Mean baseline bodyweight of the respondents with uncomplicated stage-I hypertension was 63.2 ± 8.1 kg. After 18 months intervention mean value became 61.1 ± 7.8 Kg. The mean change of weight was - 1.8 ± 1.8 Kg after 18 month (Table-2).

Table-II
Body Weight Change among Respondents at Different Period

Description	Baseline	After 6 m	After 12 m	After 18 m
Number of participants	282	258(24 drop-outs)	224(58 drop-outs)	210(72 drop-outs)
Mean weight (Kg)	63.2 ± 8.1	62.6 ± 8.1	61.5 ± 7.7	61.1 ± 7.8
Mean Change (Kg)		- 0.8 ± 2.0	- 1.4 ± 1.8	- 1.8 ± 1.8
Percent Change (Kg)		-1.3	-2.2	-2.9

Percent reduction of body weight was calculated comparing with the baseline mean weight. Mean weight reduction of the respondents were -1.3%, -2.2% and -2.9% after 6, 12 and 18 month respectively (Fig-4).

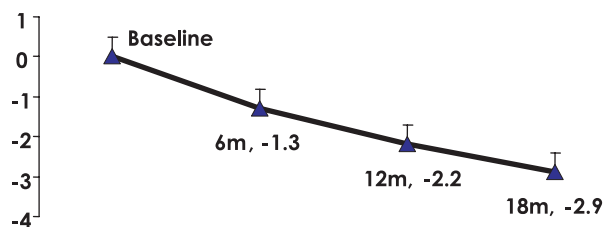


Fig-4: *Percent reduction of body weight*

Mean value of heavy physical activity by respondents was found to be 9.8 ± 22.1 minutes at beginning and 36.8 ± 35.2 minutes after 18 month. Mean value of moderate physical activity was measured to be 230.8 ± 224.4 , and 518.0 ± 275.7 minutes at beginning and after 18 months respectively. Mean value of light activity was calculated to be 492.4 ± 380.2 and 1512.7 ± 438.3 minute at baseline study and after 18 month respectively. After 18m intervention, mean increase in light, moderate and heavy physical activity were 993.5 ± 318.2 minutes/week, 289.8 ± 171.5 minutes/week and 27.7 ± 24.4 minutes/week respectively. Total increment of physical activity was 4658.9 ± 1395.1 minutes/week in 18 month. Tests of ANOVA between change of METs and change of BP showed more influence of METs change on diastolic BP than on systolic BP (For sBP $F= 3.531$ $p= 0.062$ while for dBP $F= 4.389$ $p=0.037$).

At the beginning, 22.7% respondents with uncomplicated stage-I hypertension were found to have smoking habit with an average consumption of 8.7 ± 24.2 sticks per week. Number of smokers after 18 month intervention became 10.6% taking 2.1 ± 7.8 sticks per week. Paired-sample t-test between baseline and 18 month indicated significant difference from baseline smoking habit ($t=5.480$ $df 209$ $p< 0.001$).

Multiple regression analysis was done for testing individual role of change of physical activity (expressed in METs), body weight, salt intake and smoking habit, after removing the effect of other confounding variables like age, sex, level of

education, yearly expenditure, owner of house, height and intake of beef.

Salt intake was found to be the best predictor for systolic BP reduction, (Beta =0.273, $t= 4.148$, $p=0.000$) followed by increment of physical activity (Beta =0.179, $t= 2.702$, $p=0.007$) (Table-3). Role of reduction of weight in 18 months is critical to decide (Beta =0.126, $t= 1.860$, $p=0.064$) while no significant role was found for reduction of smoking tobacco (Beta =0.009, $t= 0.124$, $p=0.902$) for systolic BP. Again salt reduction was found to be the best predictor to reduce dBP (Beta =0.173, $t= 2.462$, $p=0.015$) followed by METs increment (Beta =0.138, $t= 1.982$, $p=0.049$). Weight reduction was also found to have significant role (Beta =0.144, $t= 2.038$, $p=0.043$) but smoking contributing no significant impact (Beta =0.025, $t= 0.340$, $p=0.735$).

Table-III
Predictor Co-efficient and Significance for BP at 18m

Systolic Blood Pressure Predictors				
No.	Description	Beta	t	p
1.	Salt reduction	0.273	4.148	0.000
2.	METs increment	0.179	2.702	0.007
3.	Weight Reduction	0.126	1.860	0.064
4.	Smoking Reduction	0.009	0.124	0.902
Diastolic Blood Pressure Predictors				
No.	Description	Beta	t	p
1.	Salt reduction	0.173	2.462	0.015
2.	Weight Reduction	0.144	2.038	0.043
3.	METs increment	0.138	1.982	0.049
4.	Smoking Reduction	0.025	0.340	0.735

Behavioural models emphasized sympathetic, empathetic and supportive relationship with respondents, non-confrontational approach, explaining reliably benefits of behavioural change and counseling respondents to choose consciously adaptable behavioural changes for reducing blood pressure. Perceived change of the respondents about their individualized feeling of wellbeing was assessed with rating scale from '0' to '10' as highest. Mean reduction was from 8.2 at baseline to 2.4 at the end of 18 months (Fig-5).

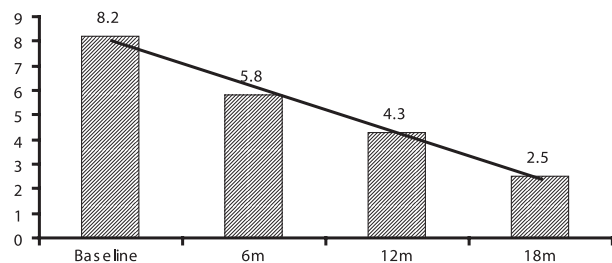


Fig-5: Subjective Rating about Wellbeing

Average GHQ-28 consistent score reduced from 38 on average at baseline to 35 at the end of 6 month, 28 at the end of 12 month and 25 at the end of 18 months intervention (Fig-6). Stressful mental condition and tension were reduced after intervention. Respondents felt well and compatible with health and got improved in their decision making ability after counseling.

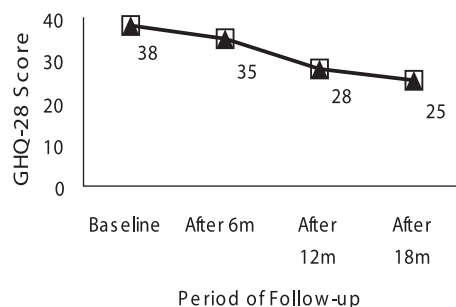


Fig-6: Objective Feeling of Welbeing

Discussion

Prevalence of pre-hypertension (JNC-7 criteria) was found to be 34.3% and prevalence of hypertension was found to be 20.1% at this urban community study. Measurement tools, procedures and protocols adopted in this study were very consistent and valid. This prevalence rate reflected a similar finding by Ali et al⁵ (1987) among 331 Dhaka University teachers and also by survey of Haque (2002).⁴ Panel speakers at World Hypertension Day 2008 seminar in Bangladesh also declared the prevalence being 15-20% after analysis of several reports with about 15 million people suffering from high blood pressure.²⁷ Other recent studies in Bangladesh also reported the prevalence rate of around 14-27% in populations of different age group in the urban areas.^{28,29} An Iranian study showed similar statistics of 25.2% hypertension in 25-64 year of age.³⁰ Extensive studies on adult Chinese population aged 35 to 74 years were done

to find out the sickness pattern in the community. Hypertension was found to be present among 27.2% of the people. But the population in that particular study was a little older by age group.³¹

Mean change of systolic/ diastolic blood pressure was -9.1/-8.4 mmHg after 18 month behavioural risk reduction intervention. This is consistent and comparable to study outcome of Apple (1997).^{13-14,32} He reported reduction of BP by -11.4/-5.5 mmHg on 133 respondents in 3 weeks and -5.5/-3.0 mmHg on 459 respondents in 11 weeks by DASH plus intervention comparing to controlled diet. Canadian study on 309 cases with hypertension reported reduction of -7.2/-14.3 mmHg BP by non-pharmacological approaches over 24 month period.³³

UK researcher Aucott (2005) reviewed literature published during the period 1966 to 2001 describing about effect of weight reduction on reversal of high blood pressure. After analyses he concluded that reduction of 10 kg body weight could reduce -4.6/-6.0 mmHg BP in 24 months.³⁴

STEPS study in the Department of Community and Family Medicine, University of Missouri-Kansas City, USA recommended that low calorie diet could reduce 5-6 mmHg sBP (40% people can reduce sBP 10mmHg in 1 year), exercise can reduce 3-5 mmHg sBP (30% people can reduce sBP 10mmHg over 1 year) and these factors in combination can reduce 4-5 mmHg sBP and up to 25% people can reduce sBP by 10mmHg in 1 year.³⁵ National Institute for Clinical Excellence also recommended similar study findings in the United Kingdom.³⁶

Trials of Mild Hypertension Study (TOMHS) was a four-year trial on 902 cases with stage-I hypertension (62 % males, 80 % non-Black, mean age 55 years). It tested the BP effects by multifactorial intervention- weight loss, sodium reduction, physical activity, and reduced alcohol intake. Average within-group BP changes were 10.6 mmHg reduction in sBP and 8.1mmHg reduction in dBP. This study results were similar to our present study outcome.³⁷

Percent reduction of blood pressure in this study is encouraging (7.0% sBP vs. 9.9% dBP after 18 month intervention). Mean sBP reduced more than mean change of dBP (-9.1/-8.4 mmHg). But percent

reduction of blood pressure was less in case of dBP. This is due to the lower baseline value of dBP than sBP and also the low range value of dBP than sBP. The Trials of Hypertension Prevention-Phase II (TOHP2), multicenter 2x2 factorial designs, study conducted to test the long-term effects of weight loss and/or a reduced salt intake on hypertension. The study was done on 2,383 overweight middle-aged adults.³⁸ After six months intervention, the incidence of hypertension was lowest in the combined weight loss/reduced sodium group (2.7%), intermediate in the weight loss (4.2%) and sodium reduction (4.5%) groups, and highest in the usual care group (7.3%). At 18 months, same scenario persisted.³⁸

Another aspect of the study outcome is the reversal of hypertension. After 18 months intervention, reversal of 56.7% respondents with stage-I hypertension is an encouraging outcome. Duff (2003) gave intervention for 6 months and followed for one year and found reversal of 28% hypertension to normal at the end of six month and 26% at the end of 1 year through life style modification counseling.³⁹ His result was much influenced by number of drop-out cases since it was a hospital based study. Careful case inclusion of the at the beginning, routine follow-up, quality information dissemination and holistic health care support to the respondents and their families were the steps taken to minimize drop-out at the present study.

Extra salt intake was reduced at the end of 18 month intervention. Such reduction of salt intake significantly influenced the change of both systolic and diastolic blood pressure. And again when tested in reduced model by multiple regression analysis salt reduction was found to be the best predictor ($t=4.148$; $p=0.000$ for sBP and $t=2.462$; $p=0.015$ for dBP) for reducing both systolic and diastolic blood pressure compared to other behavioural determinants. Salt reduction contributed more for systolic blood pressure reduction in comparison to diastolic blood pressure reduction. Change of mean body weight is significantly reduced from 63.2 kg at baseline to 62.6 kg after 6 month, 61.5 kg after 12 month and 61.1 kg after 18 month intervention. Change of body weight significantly reduced both systolic and diastolic blood pressure ($F=3.129$, $p=0.000$, $r^2=0.378$ for sBP and $F=3.129$, $p=0.000$,

$r^2=0.378$ for dBP). Impact of isolated weight reduction was found more on systolic blood pressure. Percent contributors for change of body weight ranked second for diastolic blood pressure and ranked third for systolic blood pressure as predictors to influence blood pressure.

Increment of physical activity influenced systolic blood pressure more than diastolic blood pressure ($F=4.389$; $p=0.037$ for change of METs). Smoking influenced diastolic blood pressure ($t=0.340$, $p=0.735$) more than systolic blood pressure ($t=0.124$, $p=0.902$). Smoking was not a significant predictor for reduction of blood pressure in this particular study, however smoking has many other deleterious and life threatening effects on human health and survival. So impact of smoking is not ethically highlighted here.

Conclusion

Hypertension is no more a myth but rather a social reality and a real threat for the developing countries. Hypertension prevalence is increasing very silently but significantly. This study on a moderately middle class community of Dhaka city indicated shifting of the disease trend towards middle class. Changing life style and behaviour pattern are crucial modifiable risk factors for causation of hypertension. However the study showed that hypertension is preventable. More than 50% reversal of hypertension was possible by behavioural risk reduction. This study also showed that a better quality of life can be ensured, along with reduction of blood pressure, through behavioural counseling. Predictors for systolic BP reduction were reduction of salt intake, increment of physical activities, and reduction of weight in order. Determinants for dBP determinants were, in rank order, salt reduction, weight reduction, and METs increment. However, eighteen month intervention was reasonably brief for such a big issue and hence prolonged intervention with cohort follow-up model could better explain many marginal debates. The study concluded with expectation that blood pressure treating clinicians shall pay attention to this study finding and add these findings while managing hypertensive patients. Also this study recommends immediate initiation of a state-based STOP-Hypertension programme at community level.

Reference

1. Ghaffar A, Reddy KS, Singhi M. Burden of non-communicable diseases in South Asia. *BMJ* April 2004;328:807-810 doi:10.1136/bmj.328.7443.807
2. WHO Regional Office for South-East Asia. Non-communicable diseases. Geneva, 2009 <http://www.searo.who.int/en/Section1174/Section1459.htm> accessed on 26 March, 2009.
3. Malik A. Congenital and acquired heart diseases. *Bangladesh Med Res Council Bull* 1976;11:14
4. Haque KMHSS. Prevention and control of cardiovascular diseases- Bangladesh perspective. *Proceedings of Japan-Bangladesh Joint Conference on Cardiovascular Diseases, Dhaka; 2002; 17 : 23-24*
5. Ali SMK, Chowdhury MMH, Halim A, Quazi S, Islam N, Rahman M, Mohiduzzaman M, Malek MA. Pattern of cardiovascular disease among Dhaka University teachers. *Bang J Nutr Dec* 1987;1(1):26-33.
6. Ullah W. Hypertension in a mixed community. *Bangladesh Med Res Council Bull, Dec* 1976; 2(2): 95-99.
7. Islam N, Janan FAJ, Chowdhury A, Ahmed Z, Mathura KC. Hypertension in secretariat population of Bangladesh. *Bangladesh Med Res Council Bull, June* 1979; 5(1):19-24.
8. Chowdhury AKMN, Alam MN, Ali SMK. Dasherbandi Project Studies: Demography, morbidity and mortality in a rural community of Bangladesh. *Bangladesh Med Res Council Bull* 1981;7: 22–39.
9. Islam N, Khan M, Latif ZA. Hypertension in the rural population of Bangladesh- a preliminary survey. *Bangladesh Med Res Council Bull, June* 1983; 9(1):11-14.
10. Begum JA, Shahidullah M, Saiduzzaman AF, Zaman S. Comparative study of hypertension in three different places of Bangladesh. *JOPSOM, Dec* 1984; 3(2): 17-22.
11. Sayeed MA, Banu A, Haq JA, Khanam PA, Mahtab H, Khan AKA. Prevalence of hypertension in Bangladesh: effect of socioeconomic risk factor on difference between rural and urban community. *Bangladesh Med Res Council Bull. 2002 Apr*;28(1):7-18.
12. Rahman AKMF, Haque KMHSS, Hossain N, Chowdhury AHK, Uddin MJ, Ali M. Acute myocardial infarction in hypertensive patients: a comparison of clinical outcome in hypertensive and normotensive patients. *Chest and heart journal, 2000*;14(2):69-76.
13. Appel LJ, Champagne CM, Harsha DW, Cooper LS, Obarzanek E, Elmer PJ, et al. Writing group of the PREMIER Collaborative Research Group. Effects of comprehensive lifestyle modification on blood pressure control: main results of the PREMIER clinical trial. *JAMA. 2003 Apr* 23-30; 289(16):2083-93.
14. Svetkey LP, Erlinger TP, Vollmer WM, Feldstein A, Cooper LS, Appel LJ, Ard JD, Elmer PJ, Harsha D, Stevens VJ. Effect of lifestyle modifications on blood pressure by race, sex, hypertension status, and age. *J Hum Hypertens, 2004 Sept* 23. doi:10.1038/sj.jhh.1001770 viewed on 06 Oct, 2006.
15. Harris GD, White RD. Lifestyle modifications for the prevention and treatment of cardiovascular disease: an evidence-based approach. *Mo Med. 2004 May-Jun*; 101(3): 222-6.
16. Bennett S, Parpia T, Hayes R, Cousens S. Methods for the analysis of incidence rates in cluster randomized trials. *Int J Epid. 2002*;31:839-846.
17. Voter list. <http://www.ecs.gov.bd> Election Commission of Bangladesh accessed on 06.02.2006.
18. World Health Organization. STEPS Field manual guidelines for field staff. The WHO STEPwise approach to Surveillance of noncommunicable diseases (STEPS). WHO/NMH/CCS/03.05. Geneva 2003:38-39.
19. WHO. STEPS Field manual guidelines for field staff. WHO/NMH/CCS/03.05. Geneva: WHO 2004:30-31.
20. Pickering TG, Hall JE, Appel LJ, Falkner BE, Graves J, Hill MN, Jones DW, Kurtz T, Sheps SG, Roccella EJ. Recommendations for blood pressure measurement in human and experimental animals - Part 1: blood pressure measurement in human: A statement for professionals from the subcommittee of professional and public education of the American Heart Association Council on high

- blood pressure research. *Hypertension*. 2005;45:142-185.
21. Willmott SA, Boardman JAP, Henshaw CA, Jones PW. Understanding General Health Questionnaire (GHQ-28) score and its threshold. *Soc Psychiatry Psychiatr Epidemiol* 2004;39(8):613-617.
 22. Ramos FI, Fernandez-Palacín F. Comparison between the GHQ-28 and SF-36 (MH 1–5) for the assessment of the mental health in patients with ischaemic heart disease. *Euro J Epidemiol*. 2000;16(4):311-316.
 23. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand* 1983, 67:361-370.
 24. Baecke JA, Burema J, Frijters JE. A short questionnaire for the measurement of habitual physical activity in epidemiological studies. *Am J clinic nutri* 1982; 36:936-942.
 25. Evenson KR, Rosamond WD, Cai J, Toole JF, Hutchinson RG, Shahar E, et al. Physical activity and ischemic stroke risk. The atherosclerosis risk in communities study. *Stroke* 1999;30:1339-1339.
 26. Guidelines for Data Processing and Analysis of the International Physical Activity Questionnaire (IPAQ). Revised April 2004. www.ipaq.ki.se viewed on 12.02.09.
 27. Haque KMHSS, Khandaker RK, Malik A, Islam S. Declaration of national observance of world hypertension day 2008. Dhaka: NHF, 17 May 2008.
 28. Karim SR, Ferdousi SF, Mahmood AR, Morshed M, Hoque GMS. Hypertension and the related factors among the low socio-economic group of people. *Bangladesh Med J*, 2004; 33(3):86-89.
 29. Alamgir AKM, Akhter SFU. Hypertension Prevalence and Related Factors in an Urban Affluent Community in Bangladesh. *Bang J Med Sci*, March 2005 ; 11(1): 22-25.
 30. Asgari F, Aghajani H, Haghazali M, Heidarian H. Non-communicable diseases risk factors surveillance in Iran. *Iranian J Publ Health*, 2009;38 (Suppl. 1):119-122.
 31. Gu D, Reynolds K, Wu X, Chen J, Duan X, Muntner P, et al, for the InterASIA Collaborative Group. Prevalence, awareness, treatment, and control of hypertension in China. *Hypertension*, 2002;40:920.
 32. Appel LJ, Moore TJ, Obarzanek E, et al. A clinical trial of the effects of dietary patterns on blood pressure. *NEJM*, 1997;336: 1117-1124.
 33. Hill MN. HBP Care : Comprehensive HBP care in young urban black men. *Clin Cardiol* 2000;23:56-58.
 34. Aucott L, Poobalan A, Smith WCS, Avenell A, Jung R, Broom J. Effects of weight loss in overweight/obese individuals and long-term hypertension outcomes. *Hypertension*. 2005;45:1035.
 35. Harris GD, White RD. Lifestyle Modifications for the Prevention and Treatment of Cardiovascular Disease:an Evidence-based Approach. *Mo Med*. May-Jun 2004;101(3):222-6.
 36. NICE Technology Appraisal No. 39, March, 2002. Developed by the Newcastle Guideline Development and Research Unit. National Institute for Clinical Excellence. Clinical Guideline 18. Hypertension: management of hypertension in adults in primary care. August 2004:12-15. <http://www.nice.org.uk/> viewed on 15-08-2006
 37. TOMHS. The Treatment of Mild Hypertension Research Group. The treatment of mild hypertension study: A randomized, placebo-controlled trial of nutritional-hygienic regimen along with various drug monotherapies. *Arch Intern Med* 1991; 151:1413-1423.
 38. TOHP2. The Trials of Hypertension Prevention Collaborative Research Group. Effects of weight loss and sodium reduction intervention on blood pressure and hypertension incidence in overweight people with high-normal blood pressure: The Trials of Hypertension Prevention, Phase II. *Arch Intern Med* 1997; 157:657-667.
 39. Duff EM, Wilks R. Six-month hypertension intervention study. One year follow-up. *West Indian Med J*. 2003;52(3):219-22.

REVIEW ARTICLE

Non-Invasive Ventilation and its Role in COPD

MN Haque¹, SAHMM Islam², BA Hossain³, MR Hassan⁴, MB Ullah¹, SR Huq¹

Abstract:

Non-invasive ventilation (NIV) in the management of acute type 2 respiratory failure in patients with chronic obstructive pulmonary disease (COPD) represents one of the major technical advances in respiratory care over the last decade. The National Institute for Health and Clinical Excellence (NICE) recommends that NIV be available in all hospitals admitting patients with COPD. Patients with underlying chronic obstructive pulmonary disease (COPD) who present with an exacerbation of their COPD and hypercapnic respiratory distress or respiratory failure are the group most likely to be successfully treated with noninvasive ventilation (NIV). Exacerbations increase the respiratory load in these patients, exceeding their ability to adequately ventilate through a variety of mechanisms, including increasing hyperinflation with decreased diaphragmatic excursion and strength, increasing intrinsic positive end-expiratory pressure (PEEP), ineffective or inadequate tidal volume generation, respiratory patterns, and increased respiratory frequency. Noninvasive ventilation effectively unloads the respiratory muscles, increasing tidal volume, decreasing the respiratory rate, and decreasing the diaphragmatic work of breathing, which translates to an improvement in oxygenation, a reduction in hypercapnia, and an improvement in dyspnea.

Noninvasive ventilation is an important adjunct to other conventional therapy (eg, bronchodilators, corticosteroids, antibiotics). COPD is an ideal condition for noninvasive ventilation, given the rapid reversibility w treatment and added support that can be provided by noninvasive ventilation. Most experience with noninvasive ventilation has accrued with either bilevel positive airway pressure (BiPAP) or pressure support ventilation, less so with volume ventilation and continuous positive airway pressure (CPAP), which is infrequently used as a mode of ventilatory support in these patients.

[Chest & Heart Journal 2009; 33(1) : 59-65]

Introduction

Noninvasive ventilation (NIV) refers to the administration of ventilatory support without using an invasive artificial airway (endotracheal tube or tracheostomy tube). The use of noninvasive ventilation has markedly increased over the past two decades, and noninvasive ventilation has now

become an integral tool in the management of both acute and chronic respiratory failure, in both the home setting and in the critical care unit. Noninvasive ventilation has been used as a replacement for invasive ventilation, but its flexibility also allows it to be a valuable complement in patient management.

1. Assistant Professor, Respiratory Medicine, National Institute of Diseases of Chest and Hospital, Mohakhali, Dhaka, Bangladesh.
2. Medical Officer, ICU Unit, National Asthma Center, National Institute of Diseases of Chest and Hospital, Mohakhali, Dhaka, Bangladesh.
3. Superintendent, National Institute of Diseases of Chest and Hospital, Dhaka.
4. Professor, Chest Medicine, National Asthma Center, National Institute of Diseases of Chest and Hospital, Dhaka.

Correspondence to: Dr. Md. Naimul Hoque, Assistant Professor, Respiratory Medicine, National Institute of Diseases of Chest and Hospital, Mohakhali, Dhaka, Bangladesh.

Noninvasive positive pressure ventilation

Positive-pressure ventilation delivered through a mask has become the predominant method of providing noninvasive ventilatory support and is the focus of this and subsequent sections. Early bedside physiologic studies in healthy patients and in patients with respiratory conditions document successful ventilatory support.¹

Ventilatory support can be achieved through a variety of interfaces (mouth piece or nasal, face, or helmet mask using a variety of ventilatory modes (eg, volume ventilation, pressure support, bilevel positive airway pressure [BiPAP], proportional-assist ventilation [PAV], continuous positive airway pressure [CPAP]) with either ventilators dedicated to noninvasive ventilation (NIV) or those capable of providing support through an endotracheal tube or mask. Older models of noninvasive ventilators required oxygen to be bled into the system, but current models incorporate oxygen blenders for precise delivery of the fraction of inspired oxygen (FI_{O2}).

Absolute contraindications of NIV

- Coma
- Cardiac arrest
- Respiratory arrest
- Any condition requiring immediate intubation
- Other contraindications (rare exceptions)
- Cardiac instability
- Shock and need for pressor support
- Ventricular dysrhythmias
- Complicated acute myocardial infarction
- GI bleeding - Intractable emesis and/or uncontrollable bleeding
- Inability to protect airway
- Impaired cough or swallowing
- Poor clearance of secretions

Patient inclusion criteria

- Patient cooperation (an essential component that excludes agitated, belligerent, or comatose patients)
- Dyspnea (moderate to severe, but short of respiratory failure)
- Tachypnea (>24 breaths/min)
- Increased work of breathing (accessory muscle use, pursed-lips breathing)

- Hypercapnic respiratory acidosis (pH range 7.10-7.35)
- Hypoxemia (PaO₂/FIO₂ <200 mm Hg, best in rapidly reversible causes of hypoxemia).²

Suitable clinical conditions for noninvasive ventilation (most patients)

- Chronic obstructive pulmonary disease
- Cardiogenic pulmonary edema
- Suitable clinical conditions for noninvasive ventilation (selected patients)
- After discontinuation of mechanical ventilation (COPD)
- Community-acquired pneumonia (and COPD)
- Asthma
- Immunocompromised state
- Postoperative respiratory distress and respiratory failure
- Do-not-intubate status
- Neuromuscular respiratory failure
- Decompensated obstructive sleep apnea/cor pulmonale
- Cystic fibrosis
- Acute respiratory distress syndrome
- Mild Pneumocystis carinii pneumonia

Application of Noninvasive Ventilation^{3,4}

Several considerations can enhance the likelihood of successful noninvasive ventilation (NIV). In addition to these factors, the experience and expertise of front-line health care providers, specifically nursing and respiratory therapy staff, cannot be underestimated. This is not a concern in hospitals where noninvasive ventilation is well established, but it is an important factor in facilities where noninvasive ventilation has been infrequently administered or not used at all.

Location of application

- ICU (especially if possibility of intubation)
- Step-down unit (lower severity of illness)
- Moderately severe COPD (pH >7.30)
- Do-not-intubate status
- Intermittent or nocturnal ventilatory support
- Ward setting (not recommended if intubation is a consideration)
- Suitable in specialized units
- Same considerations as step-down unit

- Emergency department - Local considerations, expertise may mirror ICU or step-down unit

Patient interfaces

1. Masks 2. Ventilators.

Orofacial masks (general advantages)

- Best suited for less cooperative patients
- Better in patients with a higher severity of illness
- Better for patients with mouth-breathing or pursed-lips breathing
- Better in edentulous patients
- Generally more effective ventilation

Orofacial masks (cautions, disadvantages)

- Claustrophobic
- Hinder speaking and coughing
- Risk of aspiration with emesis

Nasal masks (general advantages)

- Best suited for more cooperative patients
- Better in patients with a lower severity of illness
- Not claustrophobic
- Allows speaking, drinking, coughing, and secretion clearance
- Less aspiration risk with emesis
- Generally better tolerated

Nasal masks (cautions, disadvantages)

- More leaks possible (eg, mouth-breathing or edentulous patients)
- Effectiveness limited in patients with nasal deformities or blocked nasal passages.

Ventilators

The choice of ventilators available to provide noninvasive ventilatory support has continued to expand. Early noninvasive ventilatory support was applied using either large bedside critical care volume ventilators or smaller volume or pressure specialty ventilators devoted to noninvasive ventilation. While the critical care ventilators had more options, they were also less tolerant of leaks. The specialty ventilators had fewer options and range, but they were more leak tolerant^{5,6,7}.

Many critical care ventilators currently in use also have a noninvasive ventilation option, either as part of the original device or available as an upgrade option. The ideal device is dependent of a

number of factors, including familiarity by staff and available options. The differences between the bedside critical care ventilator and specialty noninvasive ventilator continue to diminish as differences related to ventilator options, range of support, and leak tolerance are corrected in both devices. However, most hospitals continue to provide noninvasive support with the specialty ventilator.

Modes of ventilation

Choosing the initial mode of ventilation is based in part on past experience, in part on the capability of ventilators available to provide support, and in part on the condition being treated. Most patients who are provided noninvasive ventilation are provided support with pressure ventilation, with continuous positive airway pressure (CPAP), which is the most basic level of support. CPAP may be especially useful in patients with congestive heart failure or obstructive sleep apnea.

Bilevel positive airway pressure (BiPAP) is probably the most common mode of support and requires provision of inspiratory positive airway pressure (IPAP) and expiratory positive airway pressure (EPAP). The difference between IPAP and EPAP is a reflection of the amount of pressure support ventilation provided to the patient, and EPAP is synonymous with positive end-

expiratory pressure (PEEP). Some noninvasive ventilation is provided using proportional-assist ventilation (PAV), which provides flow and volume assistance with each breath.

While volume ventilators can be used to provide noninvasive ventilatory support, the previously described modes are preferred because they provide better patient comfort and synchrony and are more tolerant of the leaks that accompany all noninvasive ventilatory interfaces.

Initial ventilator settings and adjustments

Adequate ventilation and oxygenation, correction of respiratory failure, and adequate patient tolerance and comfort are the primary goals of noninvasive ventilation, and adjustments are made to achieve these endpoints. Initial settings focus on achieving adequate tidal volumes, usually in the range of 5-7 mL/kg. Additional support is provided to reduce the respiratory rate to less than 25 breaths/minute. Oxygen is adjusted to achieve

adequate oxygenation, with a pulse oximetry goal of greater than 90%. Serial arterial blood gas measurements are essential to monitor the response to therapy and to guide further adjustments in the ventilator.

Initial IPAP/EPAP settings

- Start at 10 cm water/5 cm water
- Pressures less than 8 cm water/4 cm water not advised as this may be inadequate
- Initial adjustments to achieve tidal volume of 5-7 mL/kg (PAP and/or EPAP)
- Subsequent adjustments based on arterial blood gas values
- Increase IPAP by 2 cm water if persistent hypercapnia
- Increase IPAP and EPAP by 2 cm water if persistent hypoxemia
- Maximal IPAP limited to 20-25 cm water (avoids gastric distension, improves patient comfort)
- Maximal EPAP limited to 10-15 cm water
- F102 at 1.0 and adjust to lowest level with an acceptable pulse oximetry value
- Back up respiratory rate 12-16 breaths/minute.⁸

Predictors of successful noninvasive ventilation

Predictors of success - Response to trial of NIV (1-2 h)

- Decrease in PaCO₂ greater than 8 mm Hg
- Improvement in pH greater than 0.06
- Correction of respiratory acidosis

Predictors of failure

Severity of illness

- Acidosis (pH <7.25)
- Hypercapnia (>80 and pH <7.25)
- Acute Physiology and Chronic Health Evaluation II (APACHE II) score higher than 20
- *Level of consciousness*
- Neurologic score (>4 = stuporous, arousal only after vigorous stimulation; inconsistently follows commands)
- Encephalopathy score (>3 = major confusion, daytime sleepiness or agitation)
- Glasgow Coma Scale score lower than 8

Failure of improvement with 12-24 hours of noninvasive ventilation.^{9,10}

Late failures (>48 h after initiation of noninvasive ventilation) Admission predictors of failure

- Lower functional status (Activity score < 2 = dyspnea light activity)
- Initial acidosis (pH <7.22)
- Hospital complications (pneumonia, shock, coma)

Noninvasive Ventilation in COPD

Patients with underlying chronic obstructive pulmonary disease (COPD) who present with an exacerbation of their COPD and hypercapnic respiratory distress or respiratory failure are the group most likely to be successfully treated with noninvasive ventilation (NIV). Exacerbations increase the respiratory load in these patients, exceeding their ability to adequately ventilate through a variety of mechanisms, including increasing hyperinflation with decreased diaphragmatic excursion and strength, increasing intrinsic positive end-expiratory pressure (PEEP), ineffective or inadequate tidal volume generation, respiratory patterns, and increased respiratory frequency. Noninvasive ventilation effectively unloads the respiratory muscles, increasing tidal volume, decreasing the respiratory rate, and decreasing the diaphragmatic work of breathing, which translates to an improvement in oxygenation, a reduction in hypercapnia, and an improvement in dyspnea.¹¹

Non-invasive ventilation (NN), within both the intensive care unit (ICU) and the ward environment, has been shown in randomised controlled trials (RCTs) and systematic reviews to reduce intubation rate and mortality in COPD patients with decompensated respiratory acidosis (pH <7.35 and PaCO₂ >6 kPa) following immediate medical therapy. NIV should therefore be considered within the first 60 minutes of hospital arrival in all patients with an acute exacerbation of COPD in whom a respiratory acidosis persists despite maximum standard medical treatment, which includes:

- controlled oxygen to maintain SaO₂ 88-92%
- nebulised salbutamol 2.5-5 mg
- nebulised ipratropium 500 µg
- prednisolone 30 mg
- antibiotic agent (when indicated).

Recommended inclusion and exclusion criteria for potential NIV are shown below.

Clinical inclusion and exclusion criteria for NIV.

Inclusion criteria

Primary diagnosis of COPD exacerbation (known diagnosis or history and examination consistent with diagnosis)

- Able to protect airway
- Conscious and cooperative
- Consider NN if unconscious and endo-tracheal intubation deemed inappropriate or NIV to be provided in a critical care setting.

Exclusion criteria

- Life-threatening hypoxaemia
- Severe co-morbidity
- Confusion/agitation/severe cognitive impairment
- Facial burns/trauma/recent facial or upper airway surgery
- Vomiting
- Fixed upper airway obstruction
- Undrained pneumothorax
- Upper gastrointestinal surgery
- Inability to protect the airway
- Copious respiratory secretions
- Haemodynamically unstable requiring inotropes/pressors (unless in a critical care unit)
- Patient moribund
- Bowel obstruction
- NIV is not the treatment of choice for patients whose primary diagnosis is heart failure or pneumonia but may be used in COPD patients with these complications if escalation to intubation and ventilation is deemed inappropriate^{12,13}.

Patient selection

NIV should be considered in all patients with an acute exacerbation of COPD in whom a respiratory acidosis (pH <7.35 Pa.CO₂ >6 kPa), persists despite immediate maximum standard medical treatment on controlled oxygen therapy for no more than 1 hour. Set-up

The decision to commence NIV should be made by a doctor of specialty training (ST) level 2 or above who is competent to do so. A trained and competent healthcare professional should initiate NIV.

The patient should be in a sitting or semi-recumbent position in bed and the following are recommended:

- A full-face mask should be used for the first 24 hours, followed by switching to a nasal mask if preferred by the patient.
- An initial inspiratory positive airway pressure (IPAP) of 10 cm H₂O and expiratory positive airway pressure (EPAP) of 4-5 cm H₂O should be used.
- IPAP should be increased by 2-5 cm increments at a rate of approximately 5 cm H₂O every 10 minutes, with a usual pressure target of 20 cm H₂O or until a therapeutic response is achieved or patient tolerability has been reached.
- Oxygen, when required, should be entrained into the circuit and the flow adjusted to achieve the target saturation, usually 88-92%.
- Bronchodilators, although preferably administered off NIV, should as necessary be entrained between the expiration port and face mask.
- If a nasogastric tube is in place, a fine bore tube is preferred to minimise mask leakage.

Monitoring

Monitoring should include a mixture of physiological measures and clinical parameters.

These parameters should be used to assist in formulating a management plan and within the first 4 hours of NIV assist in the decision as to the need to escalate to intubation.

Staff involved in the care and monitoring of NN patients should be appropriately trained and experienced.

The following should be recorded and be used to formulate an iterative management plan:

- Baseline observations:
 - arterial blood gas (ABG)
 - respiratory rate
 - heart rate

- Continuous pulse oximetry and electrocardiogram (ECG) recording during the first 12 hours
- Repeat ABGs:
 - after 1 hour of NIV therapy and 1 hour after every subsequent change in settings
 - after 4 hours, or earlier in patients who are not improving clinically
- Frequent clinical monitoring of acutely ill patients:
 - every 15 minutes in the first hour
 - every 30 minutes in the 1- to 4-hour period
 - hourly in the 4- to 12-hour period
- Observations including:
 - respiratory rate, heart rate
 - level of consciousness, patient comfort
 - chest wall movement, ventilator synchrony, accessory muscle use^{13,14}.

Duration of treatment

6.1 Patients who benefit from NIV during the first 4 hours of treatment should receive NIV for as long as possible (a minimum of 6 hours) during the first 24 hours.

6.2-Treatment should last until the acute cause has resolved, commonly after about 3 days.

6.3 In patients in whom NIV is successful (pH 7.35 achieved, resolution of underlying cause and symptoms, respiratory rate normalised) following the first 24 hours or longer, it is appropriate to start a weaning plan:

- gradual reduction of the duration of NIV should be determined by clinical improvement
- the use of a profoina to chart physiological indices has been shown to improve successful weaning from NIV¹⁴.

Weaning

Initially weaning should be during the day with extended periods off the ventilator for meals, physiotherapy, nebulised therapy etc. After successfully weaning during the day, many patients will require an additional night on NIV.

The weaning strategy should be documented in the medical and nursing records. The following is recommended:

- continue NIV for 16 hours on day 2 A
- continue NI:V for 12 hours on day 3 including 6-8 hours overnight use
- discontinue NIV on day 4, unless continuation is clinically indicated. Note that some patients may:
 - show at an earlier stage that they no longer require NIV and self-wean
 - improve rapidly, prompting a clinical decision to wean early
 - require long-term nocturnal support, indicated following assessment by the respiratory team¹⁵.

Palliation

Palliation of symptoms is appropriate in some patients, where standard medical treatment and NIV fails and a decision has been made and documented not to escalate to intubation and mechanical ventilation, or where a patient chooses not to have NIV or other interventionist treatment:

- If the patient gains symptom relief, continued NIV may be appropriate for palliation of breathlessness, but normally would be withdrawn.
- Opiates and benzodiazepines can be used to treat breathlessness in this situation.
- The palliative care team should be involved and a suitable care pathway followed after discussion with the patient and family.

Conclusion

The indications for NPPV are not as clear in patients with non-COPD causes of acute respiratory failure. For acute pulmonary edema, CPAP alone drastically reduces the need for intubation, although studies have not demonstrated reductions in morbidity or mortality rates. NPPV avoids intubation and reduces complication rates in patients with hypoxemic respiratory failure, but more controlled trials are needed to establish precise indications. In the meantime, NPPV administration to patients with non-COPD causes of acute respiratory failure appears to be safe as long as patients are selected carefully with particular attention to the exclusion of inappropriate candidates.

For chronic respiratory failure, a wide consensus now favors the use of NPPV as the ventilatory mode of first choice for patients with neuromuscular diseases and chest wall deformities, despite a lack of randomized controlled trials. Central hypoventilation and failure of obstructive sleep apnea to respond to CPAP are also considered acceptable indications, although evidence to support these latter applications is sparse. For patients with severe stable COPD, some evidence supports the use of NPPV in severely hypercapnic patients, particularly if there is associated nocturnal hypoventilation. However, the data are conflicting and do not permit the formulation of firm selection guidelines.

References:

1. Corrado A, Gorini M, Melej R, et al. Iron lung versus mask ventilation in acute exacerbation of COPD: a randomised crossover study. *Intensive Care Med.* 2009;35(4):648-55. [Medline].
2. Brochard L, Isabey D, Piquet J, et al. Reversal of acute exacerbations of chronic obstructive lung disease by inspiratory assistance with a face mask. *N Engl J Med.* 1990;323(22):1523-30. [Medline].
3. Brochard L, Mancebo J, Wysocki M, et al. Noninvasive ventilation for acute exacerbations of chronic obstructive pulmonary disease. *N Engl J Med.* Sep 28 1995;333(13):817-22. [Medline].
4. Plant PK, Owen JL, Parrott S, Elliott MW. Cost effectiveness of ward based non-invasive ventilation for acute exacerbations of chronic obstructive pulmonary disease: economic analysis of randomised controlled trial. *BMJ.* 3 2003;326(7396):956. [Medline].
5. Keenan SP, Sinuff T, Cook DJ, Hill NS. Which patients with acute exacerbation of chronic obstructive pulmonary disease benefit from noninvasive positive-pressure ventilation? A systematic review of the literature. *Ann Intern Med.* 2003;138(11):8b1-70. [Medline].
6. [Best Evidence] Lightowler JV, Wedzicha JA, Elliott MW, Ram FS. Non-invasive positive pressure ventilation to treat respiratory failure resulting from exacerbations of chronic obstructive pulmonary disease: Cochrane systematic review and meta-analysis. *BMJ.* 2003;326(7382):185. [Medline].
7. Confalonieri M, Garuti G, Cattaruzza MS, et al. A chart of failure risk for noninvasive ventilation in patients with COPD exacerbation. *Eur Respir J.* 2005; 25(2): 348-55. [Medline].
8. Diaz GG, Alcaraz AC, Talavera JC, et al. Noninvasive positive-pressure ventilation to treat hypercapnic coma secondary to respiratory failure. *Chest.* Mar 2005;127(3):952-60. [Medline].
9. Scala R, Naldi M, Archinucci I, Coniglio G, Nava S. Noninvasive positive pressure ventilation in patients with acute exacerbations of COPD and varying levels of consciousness. *Chest.* 2005;128(3):1657-66. [Medline].
10. Girou E, Brun-Buisson C, Taille S, Lemaire F, Brochard L. Secular trends in nosocomial infections and mortality associated with noninvasive ventilation in patients with exacerbation of COPD and pulmonary edema. *JAMA.* 2003;290(22):2985-91. [Medline].
11. Girou E, Schortgen F, Delclaux C, et al. Association of noninvasive ventilation with nosocomial infections and survival in critically ill patients. *JAMA.* 2000;284(18):2361-7. [Medline].-
12. [Guideline] Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. National Guideline Clearinghouse. 2008.
13. Masip J, Roque M, Sanchez B, Fernandez R, Subirana M, Exposito JA. Noninvasive ventilation in acute cardiogenic pulmonary edema: systematic review and meta-analysis. *JAMA.* 2005;294(24):3124-30. [Medline].
14. Gray A, Goodacre S, Newby DE, Masson M, Sampson F, Nicholl J. Noninvasive ventilation in acute cardiogenic pulmonary edema. *N Engl J Med.* 2008;359(2):142-51. [Medline].
15. British Thoracic Society: n chronic obstructive pulmonary disease: management of acute type 2 respiratory failure: National Guidelines: October 2008.

ORIGINAL ARTICLE

Location and Histological Pattern of Lung Carcinoma in Relation to the Smoking Habit

Rokeya Sultana¹, Mirza Mohammad Hiron², AKM Mustafa Hussain³,
Mostafizur Rahman⁴, Abdur Rouf⁵, Syed Rezaul Huq⁵

Abstract

Background : Lung cancer is the leading cause of cancer death world wide. It is the most common cancer among men with an incidence of 37.5 new cases per million population. The most important risk factor for lung cancer is cigarette smoking. In different studies it was established that smoking influences both location & Histological pattern of lung carcinoma. There is a lack of local data in Bangladesh concerning location of lung carcinoma in relation to the smoking habit & recent histological pattern of lung cancer among smokers & non-smokers.

Objectives : The main objectives of the study was to assess the relationship of cigarette smoking with the location and histological pattern of lung cancer and to observe recent in histological type of lung cancer in both smokers and non-smokers & non-smokers.

Method : This cross sectional study was conducted in the Respiratory Medicine Department of National Institute of Diseases of Chest & Hospital (NIDCH) from July 2007 to June 2008. Total number of 98 Histologically proven primary lung cancer cases were included in the study. Location of tumour were evaluated by Chest X-ray lateral view, Fiber Optic Bronchoscopy (FOB) & CT scan of chest. For histological typing bronchial biopsy, brushing & BAL were taken. CZT guided FNAC were performed in cases of peripheral lesion & where bronchial biopsy couldn't be taken due to technical reason.

Result : We found that bronchogenic carcinoma occurring in smokers were more frequently in the upper lobes, whereas those occurring in nonsmokers were more frequently located in lower lobes. Squamous cell and small cell carcinoma were more common in upper lobes (97.7%) than lower lobes (2.3%), whereas adenocarcinoma and others were more common in lower lobes (53.7%) than in upper lobes (46.3%). In both smokers and non-smokers adenocarcinoma were most common histological type of lung cancer at present.

Conclusion: From the study it can be concluded upper lobe lung cancer is more common among smokers & histologically most of them are small cell & squamous cell type.

[Chest & Heart Journal 2009; 33(1) : 48-53]

1. Medical Officer, National Institute of Diseases of the Chest & Hospital, Dhaka, Bangladesh
2. Director and Professor of Respiratory Medicine, National Institute of Diseases of the Chest & Hospital, Dhaka, Bangladesh
3. Associate Professor of Respiratory Medicine, National Institute of Diseases of the Chest & Hospital, Dhaka, Bangladesh.
4. Professor of Respiratory Medicine, National Institute of Diseases of the Chest & Hospital, Dhaka, Bangladesh.
5. Assistant Professor of Respiratory Medicine, National Institute of Diseases of the Chest & Hospital, Dhaka, Bangladesh.

Correspondence to: Dr. Rokeya Sultana, MD (Chest), Medical Officer, National Institute of Diseases of the Chest & Hospital, Dhaka, Bangladesh

Introduction

Lung cancer is the leading cause of cancer death world wide. It is the most common malignancy with an estimated 12.8% of new cancer cases each year world wide. It is the most common cancer among men with an incidence of 37.5 new cases per 1 million populations and in female the incidence is 10.8 cases per million populations. The main aetiological factor of the disease is the smoking habit. In the USA active smoking is responsible for 90% of lung cancer cases. Compared to the non-smokers, smokers have about 20 fold increase in lung cancer risk at present¹.

Smoking has definite role on location as well as on histological pattern of lung cancer. In one study it was found that lung tumor which arises in association with smoking exposure tends to occur in upper lobe, with typical upper and lower ratio being roughly 2.5:1. The pathophysiological basis for the predominance of upper lobe location of lung cancer is that toxins and carcinogens persist in the upper lobe for a longer period due to the lower efficiency of lymphatic depuration and there is less efficient delivery of food derivatives or protective substances via circulation to the upper lobe, when compared with the lower lobe. Ventilation perfusion ratio is greater in the upper lobe than in the lower lobe creating favorable condition for this predominance⁸.

Cigarette smoking also has strong influence on histological type of lung cancer. Studies conducted in the USA, Europe, and China, Observed a higher smoking related risk of squamous cell carcinoma and small cell carcinoma than that of adenocarcinoma¹⁴. But in recent decades it has been seen there is an increase of lung adenocarcinoma incidence compared with squamous cell carcinoma of the lung among smokers. Two concepts that are regarded as contribution to this changes in the histological type of lung cancer; one major factor for the reduced emission of smoke relate to changes in the composition of cigarette tobacco blend. And another general acceptance of cigarette with filter tips and low tar.

Materials and Methods:

This was a cross-sectional study which was conducted during the period from July, 2007 to June, 2008 in the department of Respiratory

Medicine in collaboration with Department of Pathology and Radiology of National Institute of Diseases of chest and hospital (NIDCH), Mohakhali, Dhaka- 1212. A total number of 98 patients with lung cancer fulfilling the inclusion criteria were included in the study.

It was a consecutive method of sampling. Patients were selected according to the following inclusion and exclusion criteria.

Inclusion criteria:

Following inclusion criteria were used to select the patients-

- a) Both smokers or non-smokers diagnosed cases of primary lung cancer with solitary lesion.
- b) Suspected cases of lung cancer with following features.

Clinical: cough, hemoptysis, dyspnoea, chest pain, weight loss, anorexia, hoarseness of voice, clubbing, palpable lymph node both in smokers and non-smokers.

Radiological: Consolidation of lung, complete or partial collapse of lung, enlargement of hilar shadow with sunray appearance etc. both in smokers and non-smokers.

Exclusion criteria:

Following exclusion criteria were used to select the patients-

- a) Diagnosed cases of metastatic lung cancer
- b) Both diagnosed or suspected cases of primary lung cancer with bilateral involvement or involvement of both lobe.
- c) Both suspected and diagnosed cases of lung cancer with features contraindicating FOB such as-
 - 1 Patient who did not give consent
 - 2 Non co-operative patient during the procedure
 - 3 Very old and disabled patient
 - 4 Patient having major concomitant diseases- recent MI, cerebrovascular disease or unstable angina (within last 3 months), poorly controlled bronchial asthma
 - 5 Sputum positive for AFB

6 Patient having bleeding diathesis

- In final analysis suspected patients not diagnosed as lung cancer by bronchial biopsy or CT guided FNAC were excluded.

Study Procedure:

In each case consent from the patient was obtained after discussing with the patient about the study procedure. The relevant sociodemographic characteristics and history of smoking habit were collected.

Operational definition of upper lobe tumour

In this study upper and middle lobe tumour of right lung and upper lobe tumour of left lung are labeled as upper lobe tumour.

Study proper:

After selection of the patients initially CT scan of chest and Flexible Fibreoptic Bronchoscopy (FOB) were done in patient having suspected lesion as per standard procedure. Location of the tumour was seen and recorded according to upper lobe or lower lobe tumour. Tumour which extend to both lobe or involve both (right and left) side were excluded from study. Bronchial biopsy, bronchial brushing, BAL were taken.

In patients where no definite lesion were seen in bronchoscopy due to peripheral lesion or in cases where biopsy could not be taken (for technical reason) CT guided FNAC were done as far standard procedure. Slides and materials were immediately sent to the laboratory.

In diagnosed cases of primary lung cancer for location of tumour report of FOB and or CT scan of chest and for cancer cell typing report of bronchial biopsy, brushing and or CT guided FNAC were collected and recorded in data sheet.

Results & Observation:

To find the relationship of smoking with location and cell type of lung cancer a total of 125 cases were included initially. Of them 5 were diagnosed cases of primary lung cancers and 120 were suspected cases of lung cancer based on clinical and radiological findings. All the suspected cases were then subjected to fiber optic bronchoscopy (FOB) and CT scan of chest to see the location of the tumour. Six patients were excluded due to both lobe involvement and another 4 because of bilateral involvement of lungs. On the basis of FNAC and

histopathological reports 17 more patients were excluded because of benign lesion and inflammatory conditions. Therefore 98 confirmed cases of lung cancer were included for final analysis.

Table-I

Distribution of patients by smoking habit (n = 98)

Smoking habit	Frequency	Percentage
Present smokers	41	41.8
Past smokers	40	40.8
Non-smokers	17	17.2

Table-II

Age distribution of smokers and non-smokers (n=98)

	Group		
	Smokers (n = 81)	Non-smokers (n = 17)	
< 50	10(12.3)	1(5.9)	
50 – 55	19(23.5)	7(41.2)	
55 – 60	14(17.3)	2(11.8)	
60 – 65	22(27.2)	2(11.8)	
e" 65	16(19.8)	5(29.4)	
Mean ± SD	57.6 ± 10.6	58.1 ± 10.3	0.851

*Data were analysed using Student's t-Test; Figures in the parentheses denote corresponding %.

Table-III

Comparison of smoking habit between sex (n = 98)

	Sex		
	Male (n = 87)	Female (n = 11)	
Smokers	79(90.8)	2(18.2)	
Non-smokers	8(9.2)	9(81.8)	< 0.001

Figures in the parentheses denote corresponding %.

*Data were analysed by using Chi-square, Test with Yate's correction;

Table-IV

Distribution of patients by history of smoking (n = 81)

History of smoking	Mean	SD
Age at starting smoking (yrs)	23.9	4.3
Duration of smoking (yrs)	27.5	11.8
Number sticks consumed (per day)	22.0	11.0
Pack-years of smoking	32.8	21.2
Time since quitting smoking (yrs)	12.1	10.3

Table-V
Location of lung cancer detected by imaging and FOB (n=98)

Radiological examination and FOB	Frequency	Percentage
Side of lung affected		
Right	58	59.2
Left	40	40.8
Lobe affected		
Upper	68	69.4
Lower	30	30.6

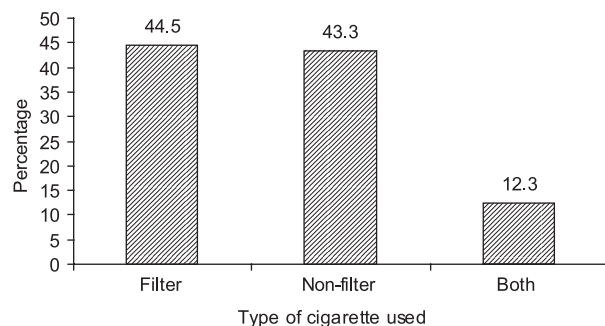


Fig-1: Distribution of patients by type of cigarettes used (n = 81)

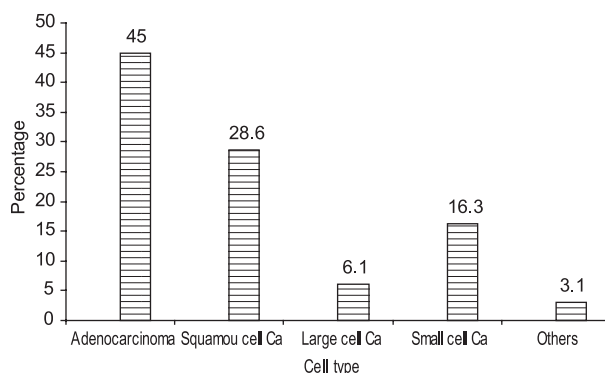


Fig-2: Distribution of patients by type of cell (n = 98)

Table-VI
Association between histologic cell type and smoking habit

	Smoking habit		
	Smoker (n = 81)	Non-smoker (n = 17)	
Adenocarcinoma	30(37.0)	15(88.2)	
Squamous cell carcinoma	27(33.3)	1(5.9)	
Large cell carcinoma	5(6.2)	1(5.9)	0.001
Small cell carcinoma	16(19.8)	0(0.0)	
Others	3(3.7)	0(0.0)	

Table-VII

Association between smoking habit and pulmonary lobe affected

	Affected lobe of lung		
	Upper (n = 68)	Lower (n = 30)	
Smoker	64(94.1)	17(56.7)	< 0.001
Non smoker	4(5.9)	13(43.3)	

Figures in the parentheses denote corresponding percentage. # Chi-square, Test was employed to analyse the data

Table-VIII

Association between smoking related variables and cell type (n=81)

	Cancer cell type		
	SCC & SCLC (n = 44)	Adeno-carcinoma & others (n = 54)	
Age at starting smoking (yrs)	22.1 ± 3.9	26.0 ± 3.7	< 0.001
Duration of smoking (yrs)	34.5 ± 8.9	18.5 ± 8.5	< 0.001
Pack-years of smoking	48.1 ± 12.5	12.8 ± 11.0	< 0.001
Time since quitting smoking (yrs)	4.1 ± 5.4	17.2 ± 9.9	< 0.001

Data were analysed using Student's t-Test and were presented as mean ± SD.

Table-IX

Association between type of cigarette used and cell type (n=71)

	Cancer cell type		
	SCC & SCLC (n = 35)	Adeno-carcinoma & others (n = 36)	
Filter	7(20.0)	29(80.6)	< 0.001
Non-filter	28(80.0)	7(19.4)	

Figures in the parentheses denote corresponding percentage. # Chi-square, Test was employed to analyse the data.

Discussion

The study was completed with 98 patients. The sociodemographic data of the study population demonstrated that there was no significant

difference between smokers and non-smokers in term of age. Males were predominant compared to females, with male: female ratio 8:1. In this study 81 cases were smokers and 17 were non-smokers. Regarding type of cigarette smoked 44.5% of the patients used filter cigarettes, other 43.3% non-filter cigarettes and 12.3% used both filter and non filter cigarettes.

The location of the tumour was determined through the examination of images (chest x-ray and CT scan of the chest) and by direct visualization of tumour by fibre-optic bronchoscopy.

In this study the tumour localized in the upper and middle lobes of the right lung were considered as upper lobe tumours, since these were equivalent to the left upper lobe tumour (upper division plus lingula). Out of 98 patients majority had lesion in the right lung. Regarding involvement of lobe, upper lobe was found to be affected predominantly.

Histological typing of lung cancer was done by FOB followed by bronchial biopsy, brushing and BAL (Bronchoalveolar lavage) and CT guided FNAC where applicable. Among 98 patients, 45% of patients exhibited adenocarcinoma, 28.6% squamous cell carcinoma, 16.3% small cell lung cancer 6.1% large cell carcinoma and 3.1% other cell type. But in Hussain² s (2005) study in Bangladesh, it was found adenocarcinoma (25.8%), squamous cell carcinoma (40%), small cell carcinoma (26.7%), large cell carcinoma (5.0%) others (2.4%) which was not consistent with present study.

Regarding affected lobe in relation to smoking habit, there was a clear predominance of upper lobe tumours among smokers (94.1%), whereas the majority of tumours found among non-smokers were lower lobe tumours (43.3%). This difference was statistically significant ($P < 0.001$). Ratio of upper: lower lobe tumour among smoker was roughly 4:1.

This predominance of upper lobe tumour among smokers is not well understood, though there are some suppositions. As the ventilation perfusion ratio (V/Q) is higher in the upper lobes compared with the lower lobes, it can be hypothesized that the balance between cigarette derived carcinogenic substances delivered via the airways and diet-derived protective substances delivered via

circulation would be less favorable in the upper lobes compared with the lower lobes (Lee et al., 1998).

Among 81 smoker patients distribution of histological cell types revealed that the highest percentage of lung cancer was adenocarcinoma 37%, followed by squamous cell cancer 33.3%, small cell lung cancer 19.8%, large cell cancer 6.2%, other 3.7%. But in Hussain² s (2005) study it was found among smokers highest percentage had squamous cell carcinoma (40.8%) followed by small cell carcinoma (26.7%), adenocarcinoma (25.8%), large cell carcinoma (5%) and others (2.4%). So it is observed from present study among smokers the percentage of adenocarcinoma had increased than squamous cell carcinoma as compared with the previous study. The dramatic rise in adenocarcinoma among smokers appears to be directly related to the tobacco industry's decision to manufacture, market and sell what is so called "Safe cigarette" with filter tips and low-tar.

During 1950, unfiltered cigarettes and high tar yields were common. This product was too toxic to allow smokers to inhale deeply in to the lung, but public concern about health hazards led the industry to change cigarette design and increase production of filtered and low tar cigarettes. Smokers tend to inhale low yield filtered cigarettes more deeply than high-yield cigarettes to satisfy their craving for nicotine, (Franceschi, 1999). Accordingly, the periphery of the lung tends to be more heavily exposed to tobacco-related carcinogens, which is the location of adenocarcinoma (Gazdar and Minna, 1997).

To see of the relationship between histological pattern of lung cancer with location and smoking related variables, squamous cells carcinoma and small cell lung cancer is placed in one group and adenocarcinoma and others type of lung cancer in another group. It was found among the upper lobe tumour most were of squamous cell and small cell carcinoma (97.7%) and whereas among lower lobe tumour most were of adenocarcinoma and others type of lung cancer (53.7%).

Regarding the comparison of smoking related variables with major histological lung cancer, it was observed, the mean age at starting smoking was significantly lower in squamous cell and small cell carcinoma group than that of adenocarcinoma

and other cell types. The mean duration of smoking was much higher in squamous cell and small cell carcinoma group than that in adenocarcinoma group. The mean pack-years of smoking was found higher in the former group than that in the later group. A significantly longer lag time since quitting smoking was found in adenocarcinoma group than squamous cell and small cell carcinoma group.

Conclusion:

We conclude that Upper lobe tumour is more common among smokers and lower lobe tumour more common among non-smokers. Squamous cell carcinoma and small cell lung cancer are more predominant in upper lobe than lower lobe. The most common histological type of lung cancer in both smoker and non-smoker patients in Bangladesh is adenocarcinoma. Age at starting of smoking, duration and pack-years of smoking, time since quitting smoking and type of smoking all have definite role on lung cancer histology.

References:

1. Alberg AJ and Samet JM. Epidemiology of lung cancer. *Chest* 2003; 123: 21-49.
2. Auerbach O, Garfinkel L and Parks VR. Histologic type of lung cancer in relation to smoking habits, year of diagnosis and sites of metastases. *Chest* 1975; 67: 382-87.
3. Bilello KS, Murin S, Matthay RA. Epidemiology, etiology and prevention of lung cancer. *Clin Chest Med* 2002; 23: 1-25.
4. Hussain AKMM. Histopathological pattern of bronchial carcinoma in smokers in Bangladesh, MD thesis 2005, University of Dhaka.
5. Jamnik S, Uehara C, Silva VVD, Location of lung carcinoma in relation to the smoking habit and gender. *J Bras Pneumol* 2006; 32: 510-4.
6. Jemal A, Murray T, Ward E et al. Cancer statistics, *CA cancer J Clin* 2005; 55: 10-30.
7. Khuder SA and Mutgi AB. Effect of smoking cessation on Major Histologic Types of Lung cancer 2001; 120: 1577-83.
8. Lee BW, Wain JC, Kelsey KT, Wiencke JK, Christiani DC, Association of cigarette smoking and asbestos exposure with location and histology of lung cancer. *Am J Respir Crit Care Med* 1998; 157: 748-755.
9. Lubin JH and Blot WJ. Assessment of lung cancer risk factors by histologic category. *J. Natl Cancer Inst* 1984; 73: 383-92.
10. Paris C, Benichou J, Saunier F et al. Smoking status, occupational asbestos exposure and bronchial location of lung cancer. *Lung cancer*. 2003; 401:17-24.
11. Strauss GM and Rathore R. lung cancer. In Baum's Textbook of pulmonary diseases. Crapo JD, Glassroth J, Karlinsky JB, King TE (Editors), 7th edition, Lippincott Williams & Wilkins's, Philadelphia 2004; 798.
12. Strauss GM, Cummings KM, Smoking related adenocarcinoma of the lung: Now the most common cause of cancer death in the United States. *Proc Am Soc Clin Oncol* 2003; 22: 638.
13. Wynder EL and Muscat JE. The changing epidemiology of smoking and lung cancer histology, *Environmental health perspect* 1995; 103: 143-8.
14. Wynder EL, Kabat GC. The effect of low yield cigarette smoking on lung cancer risk. *Cancer* 1988; 62: 1223-30.
15. Gazdar AF and Minna JD. Cigarettes, sex and lung adenocarcinoma. *Journal of the National Cancer Institute* 1997; 89: 1563-65.

ORIGINAL ARTICLE

Down Syndrome with Congenital Heart Disease: Analysis of Cases Over Two Years in A Non-Invasive Laboratory of A Tertiary Hospital

Lt. Colonel Nurun Nahar Fatema

Abstract:

Background: Trisomy 21 or Down syndrome is the most frequent chromosomal aberration affecting live birth infants with an incidence of 1 in 660 live births. This syndrome is often associated with congenital cardiac lesions, Incidence of which is 40-60 percent. This study was conducted to see the frequency of Down Syndrome cases and pattern of heart diseases they have in the most busy non-invasive pediatric cardiac laboratory of the country.

Methods: It was a retrospective study conducted in the non-invasive pediatric cardiac laboratory and pediatric cardiac outpatient clinic of a tertiary hospital over a period of two years (November 2007 to October 2009). All the patient who had Down Syndrome and had Doppler echocardiography were included in the study.

Results: Out of total six thousand and fifty echocardiography, Down Syndrome case was 205 (3.38%). Out of 205 cases, 185 cases were followed up in pediatric cardiac out patient clinic. Twenty cases had not reported in the out patient clinic. Seventeen of those patients had normal cardiac anatomy in Doppler echocardiography. Male were 43.90% and female were 56.09% amongst study group. Most of the patients are young infant (47.32%). Only 2.44% are in more than 10 years age group. Murmur was audible in 86.49% cases in study group and developmental delay was present 'in 100% of the cases. Doppler Echocardiography was found as most sensitive and specific investigation for detecting congenital heart disease. A-V canal defect was the commonest association (15.60%). Congenital heart disease was not detected in 8.29% cases. Surgical treatment was advised in 52.19% cases, Device closure was advised in 16.59% cases, medical management was advised in 21.46% cases.

Conclusion: Down syndrome is a very common chromosomal anomaly in our country. Incidence of this syndrome is increasing as number of working women, late marriage and elderly mother increasing. So multidisciplinary approach for managing this disease should be adapted immediately.

[Chest & Heart Journal 2009; 33(1) : 54-58]

Introduction:

Down Syndrome, also called Trisomy 21, is the commonest genetic pattern of malformation in human being¹. Most of the textbooks and authors quote the incidence of this malformation as one in

700 to 800 live births. Down syndrome was first described by John Langdon Haydon Down with characteristic physical features and problems and so known as Down syndrome'. Children with down syndrome are at much higher risk of congenital

Correspondence to: Lt. Colonel Nurun Nahar Fatema, Pediatric Cardiologist Department of Cardiology CMH Dhaka

heart disease². The incidence of congenital heart disease (CHD) in general population is 0.8 percent whereas the incidence of CHD in children with down syndrome is between 40-60 percent³. The aim of this study was to find out the pattern of congenital heart disease among the Down syndrome cases who were analyzed over a period of two years. Among 6050 cases of total echocardiography performed over two years, 205 (3.38%) were with Down syndrome. Most commonest type of congenital heart lesion was AV canal defect (15.60%). Normal cardiac anatomy was found in 17 (8.29%) cases.

Materials and Methods:

This is a retrospective study carried out in the pediatric echocardiography laboratory and pediatric cardiac out patient clinic of Lab Aid cardiac hospital from November 2007 to October 2009. Patients were referred either to the out patient clinic for cardiac evaluation or to the Echo laboratory for color Doppler echocardiography. All the cases who were less than 3 years of age were sedated first with syrup promethazine hydrochloride 1 mg/kg body weight. Sequential segmental analysis of the heart was done using color Doppler, M-mode and 2-D Echocardiography. Echocardiography was advised to all out patient cases also even if there was no audible murmur. This was done for screening purpose. All the cases who were referred for echocardiography only were sent back to their 'referral center. Most of the cases who were positive for various type of congenital heart lesions were again referred back to the pediatric cardiologist for further management. Management plan was designed for each and every patient depending on the individual requirement. Before doing that, history, clinical examination, chest X-ray, ECG were done and analyzed thoroughly. Most of the patients had history of developmental delay, constipation, recurrent respiratory tract infection, feeding difficulties etc. Surgical correction was planned for those who had no chance of cure with medical management. Medical treatment was planned for those who had chance for cure with medicine and moreover there was no complications related to their heart lesions.

Device closure was advised for those cases who will never require open heart surgery for any other existing lesions. All patients with congenital heart lesions were advised to attend out patient clinic at regular intervals. Interval was more for less serious lesions and less for more serious lesions. Post operative and post intervention cases were followed up according to the protocol. For device cases, follow up plan was as 1, 3, 6, 9, 12, 18, 24 month of intervention and yearly thereafter for 02 years. For surgery, follow up plan was at 6 weeks, 03 months, 06 months, 01 year of surgery and yearly thereafter for 05 years.

Results:

Table-I showed frequency of down syndrome cases amongst all who had Doppler echocardiography over a period of two years. Amongst 605 of total cases, 205 (3.38%) cases had Down syndrome.

Table-I

Frequency of Down syndrome cases amongst total pediatric echocardiography load.

Subject	No	Percentage
Total Echocardiography	6050	100%
Down syndrome Baby	205	3.38%

Table-II showed sex distribution of the Down syndrome cases. Among 205 cases of Down baby, 90 (43.90%) were male and 115 (56.09%) were female. So female outnumbered male cases.

Table-II

Sex distribution of patients N=205.

Sex	No	Percentage
Male	90	43.90%
Female	115	56.09%

Table-III showed age distribution of patients. Ninety seven (47.32%) cases were in 0-6 months age group, 69 (33.66%) cases were in more than 6 months to 3 years age group, 34 (16.59%) cases were in more than 3 years to 10 years age group and 5 (2.44%) cases were in more than 10 years age group.

Table-III
Age distribution of patients N=205

Age	0-6 months	> 6 months to 3 yrs	>3 years to 10 yrs	> 10 years
Number	97	69	34	5
Percentage	47.32%	33.66%	16.59%	2.44%

Table-IV showed clinical findings in Down syndrome cases. As 20 patient had only echocardiography and not reported to pediatric out patient clinic for other work up, total case here was 185. History of recurrent respiratory tract infection was present in 127 (68.64%) cases, Murmur was detected with stethoscope in 160 (86.49%) cases. Developmental delay was present in 185 (100%) cases and murmur was not detected in 25 (13.51 %) cases.

Table-IV
*Clinical findings in Down syndrome cases
N=185*

Symptoms-and signs	No	Percentage
Recurrent RTI	127	68.64%
Presence of murmur	160	86.49%
Developmental Delay	185	100%
G I Tract abnormality	25	13.51%
Hypothyroidism	8	4.32%
Eye problem	4	2.15% ‘
Hearing defect	1	0.44%

20 cases had not reported to out patient clinic after echocardiography.

Table-V Showed investigation findings in study cases. Cardiomegaly was observed in 108 (52.68%) cases, Extreme axis in ECG was noticed in 32 (15.6%) cases, Doppler echocardiography showed presence of various types of congenital heart diseases in 188 (91.71%) cases.

Table-V
Investigation findings in study cases = 205

Investigation	No.	Percentage
CXR	Cardiomegaly	108 52.68%
	Boot shaped heart	9 4.39%
ECG	Extreme axis	32 15.61%
	LVH	82 40%
	RVH	42 20.49%
Doppler echocardiography	Abnormal	188 91.71%
	Normal	17 8.29%

Table-VI Showed pattern of heart disease amongst Down syndrome cases. A-V canal defect was found amongst maximum cases (15.60%), ASD amongst 13.17% cases, VSD amongst 14.63% cases, PDA amongst 5.85% cases and TOF amongst 2.44% cases.

Table-VI
Pattern of heart disease in down syndrome cases

Outcome	No	Percentage
AV canal defect	32	15.60%
VSD	30	14.63%
ASD	27	13.17%
ASQ with PDA	27	13.17%
ASD and VSD	17	8.29%
NAD	17	8.29%
PDA	12	5.85%
CoA with VSD or PDA	12	5.85%
ASD VSD PDA	7	3.41%
VSD PDA	7	3.41%
TOF	5	2.44%
DORV	5	2.44%
PS	5	2.44%
MVP	2	.98%

Note; VSD-ventricular septal defect, ASD- atrial septal defect, PDA-patent ductus arteriosus, CoA- coarctation of aorta, TOF- tetralogy of Fallot, DORV-double outlet right ventricle, PS-pulmonary stenosis , MVP- mitral valve prolapse

Table-VII Showed outcome of the cases. Surgical treatment was offered in 52.19% cases, device closure of ASD, PDA and VSD was performed in 16.59% cases. Medical management was advised in 21.46% cases and 9.76% cases had not reported to pediatric cardiac OPD after echocardiography.

Table-VII
*Outcome of Down syndrome cases
N=185*

Outcome	No	Percentage
Surgery	107	52.19%
Device closure	34	16.59%
Medical management	44	21.46%
Not reported to Pediatric cardiac OPD	20	9.76%

Discussion:

Down Syndrome (DS) is a major cause of congenital heart disease (CHD) and the most frequent known cases of atrioventricular septal defects (AVSDs)⁴. A normal human cell contains 23 pairs of chromosomes which carry all of a person's genetic information. Due to several possible abnormal mechanisms of cell reproduction, patients with Down syndrome have an extra copy of the 21st chromosome^{1,2,3}. Advanced maternal age is associated with a high incidence of Trisomy 21, but even women of any age can have affected babies⁵. Molecular studies of rare individuals with CHD and partial duplications of chromosome 21 established a candidate region that included D21s55 through the telomere. One study reports DSCAM (Down syndrome cell adhesion molecule) as a candidate gene⁴. The type of heart defects in children with Down syndrome can be broken down into three broad categories.

1. Atrio-ventricular septal defects.
2. Ventricular septal defect, Atrial septal defect or patent ductus arteriosus.
3. Other complex heart disease.

AV canal defect comprises 60% of CHD in Down's syndrome in Cincinnati Children's Hospital Medical Center report. But in our study it comprises only 15.60% of the CHD in Down syndrome. Ventricular septal defect (VSD), Atrial septal defects (ASD) and patent ductus arteriosus (PDA) comprises another 20% of the CHD in some report. But in our study these three defects comprise 33.65% of the cases. Reasons here is that, most of the cases included in this study are very young infants and in this age group ASD, VSD and PDA is very common. Many of these cases close spontaneously once the baby grows older but A-V canal never cures unless operated. In present study female outnumbered male, but sex prevalence was not mentioned in other studies. Non cardiac medical problems associated with Down syndrome found in this study is a) developmental delay in 100% cases b) hypothyroidism in 4.32% cases c) Recurrent RTI in 63.64% cases d) GI tract abnormality in 13.51% cases. Other study showed 100% developmental delay, 2%-5% gastrointestinal abnormalities, 40-75% hearing loss, 60% eye disorder, 1% leukemia and 5% has thyroid disorders^{4,5-10}. Most cardiologists would agree that all babies that have

been diagnosed with Down Syndrome should have a cardiac evaluation because of the high incidence of associated congenital heart defects. In our center, we do screening of all babies with Down syndrome for congenital heart disease and thyroid disorders. So among 6050 cases of Doppler echocardiography performed, 205 had Down syndrome (3.38%). Number of Down Syndrome was high because all cases of Down syndrome were screened. In our center we use Doppler echocardiography for screening as we found this test almost 100% sensitive and specific. Among 205 cases of Down patient, 185 patients were detected to have heart diseases by this test. But CXR and ECG was not sensitive in all cases though they were specific for the defects. One study showed individual examination methods were insensitive but highly specific¹¹. This study concluded that echocardiography performed early in life can detect congenital heart disease that might otherwise be missed". Children with Down Syndrome are initially managed medically with the use of diuretics, Digoxin etc. In general, ASD, VSD and AV canal defects are closed surgically if the child is symptomatic and cannot be controlled with medication¹¹. A-V canal are usually repaired by 3.6 months of age. Atrial septal defect, VSD and PDA can be closed with devices if the patient can fulfill the criteria for such. Depending on size of ASD, VSD, surgery can be postponed even longer, keeping in mind the development of Eisenmenger Syndrome^{12,13}. Overall survival beyond one year is 85%. Over 50% of individuals with Down syndrome live to be greater than 50 years old. Pneumonia and congenital heart disease is the most common cause of death in 1st year of life.

Conclusion:

Diagnosis of Down Syndrome is strongly suggested by characteristic physical findings, but the final diagnosis is often made only after chromosome analysis which includes a complete count and visualization under microscope of the chromosome taken from blood cell. A Down Syndrome baby must have cardiac evaluation as 40-60% of them have congenital heart lesions. Multidisciplinary approach of management should be planned for these children to address neurodevelopmental delay, GIT abnormalities, thyroid disorders, cardiac problems and others.

References:

1. <http://www.Cincinnatichildrens.Org/health/heart-encyclopedia/disease/syndrome/down.htm>.
2. Judith G. Hall. Chromosomal clinical abnormalities. In: Richard E Behrman, Robert M. Kliegman, Hal B Jenson. Eds. Nelson textbook of paediatrics. Philadelphia: WB Saunders, 2000: 328-329.
3. Ronald. V. Lacro. Dysmorphology. In: Donald C. Fyler MD. Eds. Nadas' Pediatric Cardiology. Philadelphia: Hanley and Belfus, 1992: 41-47.
4. Barlow GM, Chen XN, Shi Zy, Lyons GE, Kurnit DM, Celle L et al. Down Syndrome and congenital heart disease: a narrowed region and a candidate gene. *Genet~Med* 2001; 3(2): 91-101.
5. Cullum L, Liebman J. The association of congenital heart disease with Down's Syndrome. *J Am col cardiol* 1969; 24 (3): 354-357.
6. Elwood JH, Darrong PM. Severe mental handicap in Northern Ireland. *J. Ment Defic Res*, 1981; 25 (3): 147-155.
7. Rowe RD, Uchida IA. Cardiac malformation in mongolism: a perspective study of 184 mongolism: a prospective study of 184 mongoloid children. *Am J Med* 1961; 24(3):726-735.
8. Shaher RM, Farina MA, Porter IH, Bishop M. Clinical aspects of congenital heart disease in mongolism. *Am J cardiol* 1972; 29 (4): 497-503.
9. Tandor R, Edward JE. Cardiac malformations associated with Down's Syndrome. *Circulation* 1973; Jun 47 (6): 1349-1355.
10. Dark SC, Mathews RA, Zuberbuhler JR; Row RD, Neches wh, Lenox CC. Down Syndrome with congenital heart malformation. *Am J Dis child* 1977; 131 (1): 29-33.
11. TR Tubman, MD Shields, BG Craig, HC Mulholland, Nc Nevin. Congenital heart disease in Down's Syndrome: two years prospective early screening study. *BMJ* 1991; 302 (6790): 1425-1427.
12. Greenwood RD, Nadas AS, The clinical cause of cardiac disease in Down's syndrome. *Pediatrics* 1976; 58 (96): 893-897.
13. Soudon P, Stijns M, Tremouroux wattier M, Vliers A. Precocity of pulmonary vascular obstruction of Down's syndrome. *Eur J cardiol* 1975; 2 (4): 473-476.

CASE REPORT

Tender Hepatomegaly As Presentation of Disseminated Tuberculosis - A Case Report

MU Jalal¹, KC Ganguly², K Hassan³, SMS Rahman⁴, M Ilias⁵, AKM Hussain⁶, MM Hiron⁷

Abstract:

Hepatic involvement of disseminated tuberculosis may mimic multiple SOL in the liver and in that case ultrasonography and CT scan may create confusion, only tissue diagnosis can reduce patient's suffering and initiate early management. When hepatic TB occurs as a part of disseminated TB and diagnosis can not be established from lung lesion the diagnosis have to be relied upon identification of granulomatous lesion in the liver through FNAC.

[Chest & Heart Journal 2009; 33(1) : 66-70]

Case Report:

Emran Hossain of 45 years old shopkeeper in Saudi Arabia was suffering from fever and cough for three months and feeling of heaviness and pain in right upper abdomen for one month. His cough was productive with scanty amount of sputum, which was colourless and odorless but mucoid in nature and not blood stained. There was no diurnal variation of cough and it was not associated with wheeze, shortness of breath or chest pain. He developed continued low grade fever with evening rise. It was not associated with chill and rigor. Highest recorded temperature was 101°F. Fever used to subside with antipyretic. He was also feeling heaviness and a dull aching pain in the right upper abdomen which was not associated with yellow colouration of urine or sclera. He had loss of appetite associated with gross reduction of his weight. He didn't have headache, visual disturbance diplopia or vomiting. With these complains he attended a clinic in Saudi Arabia and with the help of USG he was diagnosed as multiple SOL in liver with ascites. For this reason he was sent back to Bangladesh. Patient suffered from hepatitis at the age of 20yrs. He is not diabetic. He gave no history of contact with patient of

tuberculosis. All his family members are in good health.

Patient felt comfortable in left lateral position. Patient was moderately anaemic but cyanosis and jaundice were absent. Clubbing and koilonychia were absent. Lymph nodes were not palpable. He had tender hepatomegaly with irregular surface and firm consistency. Shifting dullness was present in the abdomen. There was no other organomegaly. Examination of the respiratory system and other systemic examination revealed normal findings. His blood counts showed TWC of 4500/cmm with N-60%,L-32%,M-04%,E-04% and Hb-11gm/dl, an ESR of 45 mm in 1st hr. MT was negative. Serum bilirubin: 1.4mg/dl, SGOT: 51U/L, SGPT: 62U/L, Alkalinephosphatase:350U/L,RBS:110mg/dl, Serum creatinine: 0.68mg/dl,Serum albumin: 4.5gm/dl, HBsAg -negative, Anti-HCV: negative. Tumour markers like CEA, á-fetoprotein, PSA were not raised and HCG absent.

X-ray chest showed a small area of non-homogenous opacity in left upper zone suggestive of pulmonary tuberculosis but the left dome of diaphragm was elevated and there was slight shifting of mediastinum towards left with a linear

1. Medical Officer, National Institute of Diseases of the Chest and Hospital (NIDCH), Dhaka
 2. Assistant Professor of Respiratory Medicine, National Institute of Diseases of the Chest and Hospital, Dhaka
 3. Assistant Professor of Respiratory Medicine, National Institute of Diseases of the Chest and Hospital, Dhaka
 4. Registrar-Medicine, NIDCH, Dhaka,
 5. Medical officer, NIDCH, Dhaka
 6. Associate Professor of Respiratory Medicine, National Institute of Diseases of the Chest and Hospital, Dhaka
 7. Professor and Director, National Institute of Diseases of the Chest and Hospital, Dhaka
- Correspondence to:** Medical Officer, National Institute of Diseases of the Chest and Hospital (NIDCH), Dhaka



Fig-1: Chest X-Ray Postero-Anterior view - left upper zone opacity, elevated left dome of diaphragm with linear cardiac left border.

left border of cardiac silhouette suggesting collapsed lung margin. Lateral view chest X-ray showed collapse of posterior basal segment of lower lobe.

Three samples of his sputum smear were examined for AFB and found to be negative and a sputum culture in Lowenstein-Jensen medium yielded no growth after six weeks.



Fig-2: X-Ray Chest left lateral view - Collapsed posterior basal segment of left lower lobe

USG of whole abdomen showed multiple space occupying lesions (SOL) within the liver suggestive of multiple metastases with ascites. CT scan of liver showed multiple hypo dense areas within the hepatic parenchyma, suggestive of metastatic lesions.

CT guided FNAC from hepatic lesions were done and it showed granulomatous lesion with caseation necrosis suggestive of tuberculosis. At this stage the patient was given anti-TB chemotherapy and he began to improve with remission of fever, regaining

his appetite, body weight and disappearance of abdominal pain Though USG and CT- scan findings



Fig-3: CT scan of abdomen - multiple SOL in the liver.

suggested the case as a malignant one ultimately it has been proven to be a case of Disseminated tuberculosis involving liver, lung and peritoneum .

Discussion:

Bangladesh ranks 6th on the list of 22 highest burden TB countries in the world¹. In Bangladesh's settings it is easy to diagnose pulmonary tuberculosis when the sputum smear is positive but it is difficult to diagnose extra pulmonary tuberculosis where in most of the time diagnosis relies on identification of typical granulomatous lesion with central caseous necrosis or on clinical judgement. The most important step in making a diagnosis of tuberculosis is to think of it in the first place². Extra-pulmonary tuberculosis is found in 15-20% of all cases of tuberculosis diagnosed. Extrapulmonary tuberculosis can be generalized or confined to a single organ. Extrapulmonary dissemination may occur via lymphatic or hematogenous route. In order of frequency, the extrapulmonary sites most commonly involved in tuberculosis are the lymph nodes, pleura, genitourinary tract, bones and joints, meninges, peritoneum, and pericardium. However, virtually all organ systems may be affected. As a result of hematogenous dissemination in HIV-infected individuals, extrapulmonary tuberculosis is seen more commonly today than in the past³

Disseminated tuberculosis is often difficult to diagnose especially hepatic TB. Moreover hepatic TB may present as cirrhosis of liver, multiple secondaries or hepatocellular carcinoma, liver abscess or diffuse non specific enlargement. Ultrasonologic findings often can not differentiate tubercular seedlings in the liver from multiple

secondaries. In those cases diagnosis is likely to be misleading unless a cytologic analysis of the tissue from the lesion is done.

Acute dissemination of tubercle bacilli via the blood stream causes miliary tuberculosis which is in fact a radiological diagnosis of diffuse, discrete, nodular pulmonary shadowing of size <2mm. Hematogenous spread of TB bacilli can occur in immunosuppressed or in case of overwhelming primary infection or it can also occur when bacilli are discharged from reactivation of an old primary lesion into an eroded blood vessel. Thirdly vascular invasion may occur from active post primary lesion⁴.

Lymphatic spread may also cause disseminated tuberculosis. In disseminated tuberculosis the distribution of the lesion is variable, though any organ may be affected but the lungs are virtually always affected, sometimes only microscopically. Involvement of other organs varies from case to case. Involvement of any serous sacs results into effusions. The spleen and liver may be enlarged and studded with irregular necrotic foci, usually less than 1cm in diameter or only visible microscopically. Although this patient had no sign of raised intracranial pressure or features of meningitis, tuberculous meningitis is the most common CNS manifestation of TB. Diagnosis of TB meningitis is often difficult and requires a high degree of suspicion and diagnosis often rests upon the astute judgement of the clinician with a high degree of suspicion based on epidemiological and clinical clues. Presumptive therapy is frequently necessary to avoid the disastrous consequences as the disease is uniformly fatal if left untreated. Bone marrow biopsy has no serious adverse effect. The yield is approximately 50% in case of hematogenous dissemination.

Another form of disseminated tuberculosis is 'cryptic' where it is difficult to diagnose radiologically but usually it presents as PUO with systemic constitutional features. Abdominal tuberculosis may involve the gastrointestinal tract, peritoneum, mesenteric lymph nodes, or genito-urinary tract. Other organs e.g., liver, spleen, adrenal glands usually are affected as a consequence of miliary tuberculosis. In this particular case pulmonary lesion was not miliary, rather a small localised lesion in the left upper zone. It can be presumed that TB

bacilli spread from the pulmonary lesion and the main involvement was hepatic parenchyma and peritoneum (ascites) as well as the left lung, though diagnosis could not be established from pulmonary lesion. This is a common happening when sputum smear and culture become negative. Isolated liver involvement is unusual and that can occur when *Mycobacterium tuberculosis* in GIT is carried to liver by portal circulation. There are 3 types of involvement 1) Diffuse infiltrative type, 2) Nodular type and 3) Tuberculous abscess. Nodular form of involvement can mimic either cirrhosis or carcinoma and may present as either portal hypertension or gastric varices. Even it can mimic Hodgkin's lymphoma. Tuberculoma can also be formed in the liver. Tubercular abscess can be single or multiple.

Though hepatic tuberculosis is not a rare disease entity, tubercular liver abscess is extremely rare even in a country where tuberculosis is an alarming public health problem. It is usually associated with foci of infection either in the lung and/or gastrointestinal tract or with an immunocompromised state.⁵ The diagnosis is difficult in most instances and is frequently confused with hepatoma, pyogenic liver abscess or amoebic liver abscess.⁶⁻⁸ Most of the cases of hepatic TB usually occur in association with miliary tuberculosis, mainly through hematogenous dissemination. The respiratory and GI tracts are the major sources of infection and bacilli traveled there via hepatic artery or the portal vein⁹.

Levine classified hepatic tuberculosis into various forms of presentation such as (i) miliary tuberculosis, (ii) primary pulmonary tuberculosis with liver involvement, (iii) primary liver tuberculosis, (iv) tuberculoma, and (v) tuberculous cholangitis.¹⁰ The radiological findings of hepatic TB have a low specificity¹¹

Fibreoptic bronchoscopy is the most effective procedure for obtaining cultures (bronchoalveolar lavage). The culture yield for transbronchial biopsies is 90%. Though FNA (Fine Needle Aspiration) from the liver is a safe procedure in the expert hand, liver biopsy may cause serious bleeding and is potentially a life-threatening complication estimated to occur in approximately 10% of cases. For

abdominal involvement, laparoscopy is useful to obtain tissue and material for culture.

CT scan of the chest has higher sensitivity and specificity than chest radiography in displaying well-defined randomly distributed nodules. It is useful in the presence of suggestive and inconclusive chest radiographic findings but in no way it is diagnostic of TB when sputum smear or culture is negative.

USG and computed tomography (CT) scan findings usually reflect different stages of disease varying from granulomatous tubercles with or without caseous necrosis to fibrosis and calcification in the healing stage⁹.

USG findings of hepatic tuberculosis usually show hypo-echoic lesions¹², but few studies have demonstrated hyperechoic lesions as well⁸. Therefore, the ultimate diagnosis of hepatic TB depends upon the demonstration of AFB in pus, aspirate or biopsy specimen or the necrotic tissue or upon typical granulomatous lesion with caseation necrosis¹². Ultrasonography may reveal diffuse liver disease, hepatomegaly, splenomegaly, or para-aortic lymph nodes.

CT scanning of head with contrast and/or MRI of the brain is used to assess for suspected TB lesions. Funduscopy may reveal retinal tubercles. Lumbar puncture and CSF analysis is the most frequently used tool for giving confirmatory result in case of TB meningitis. Lumbar puncture should be strongly considered, even with normal brain MRI findings. Hydrocephalus or cerebral mass lesion (tuberculoma) may increase the risk of herniation if lumbar puncture is performed. CT scan of the abdomen may reveal enlarged para-aortic lymph nodes, hepatosplenomegaly, or tuberculous abscess. Echocardiography is the most sensitive test for pericardial effusion.

Nucleic acid amplification through PCR has been found to be a useful diagnostic tool for hepatic tuberculosis as it enables rapid identification of *Mycobacterium tuberculosis* and expedites a treatment decision¹¹. At least 57% of tuberculous hepatic granulomas gave positive PCR results compared to other conventional diagnostic techniques for TB¹³. Nucleic acid amplification techniques may aid in the diagnosis, but negative findings do not rule out TB. But additional

advantage is that PCR analysis can distinguish *M. tuberculosis* from other mycobacterium saving a lot of precious time¹³

Authors' contributions

Jalal M managed the entire exercise of the patient work-up under guidance and supervision and presented the case in weekly seminar. Ganguly K C analyzed and interpreted the patient data regarding the presentation, provided guidance and supervised the entire exercise of the patient work-up, reviewed literatures and prepared the manuscript for publication in journal. Hassan KH coordinated with pathology and imaging department having the procedures done and guided management of the patient and monitored follow-up. All authors were involved in the management of the patient, read and approved the final manuscript.

References:

1. WHO communicable diseases-TB URL: http://www.who.org/communicable_dis_tb.html
2. Chaisson RE, Nachega Jean. Tuberculosis. In: Warrel DA, Cox TM, Firth JD, Benz Jr EJ, editors. Oxford Text book of Medicine. 4th ed. Oxford, NY. Oxford University Press; vol-1: 2003, 561.
3. Raviglione MC, O'Brien RJ. Tuberculosis. In: Braunwald E, Fauci AS, Kasper DL, Hauser SL, Longo DL, Jameson JL, editors. Harrison's Principles of Internal Medicine. 15th edn. New York. McGraw-Hill; vol-1: 2001, pp1025-27
4. Leitch A.G. Pulmonary Tuberculosis Clinical features: In Seaton A, Seaton D, Leitch AG, editors. Crofton and Douglas's Respiratory diseases. Oxford. 5th ed. Blackwell Science Ltd. Part-1, 2000, 512.
5. Akcay MN, Polat KY, Oren D, Ozturk G. Primary tuberculous liver abscess: a case report and review of literature. *Int J Clin Pract.* 2004; **58**(6):625–627. doi: 10.1111/j.1368-5031.2004.00105.x. [PubMed].
6. Balsarkar DD, Joshi MA. Isolated tuberculous hepatic abscess in a non immunocompromised patient. *J Postgrad Med.* 2000; **46**(2):108–109. [PubMed]

7. Roy R, Goyal RK, Gupta N. Tuberculous liver abscess - a case report. *J Assoc Phys Ind.* 2000; 48:241
8. Bangaroo AK, Malhotra AS. Isolated hepatic tuberculosis. *J Ind Assoc Paediatr Surg.* 2005; 10(2):105–107. doi: 10.4103/0971-9261.16474.
9. Hayashi M, Yamasaki Iokajima K, Tomimatsu M, Ohkawa S. Tuberculous liver abscess not associated with lung involvement. *Intern Med.* 2004;43(6):521–523. doi: 10.2169/internal-medicine.43.521.
10. Levine C. Primary macronodular hepatic tuberculosis: US and CT appearances. *Gastrointest Radiol.* 1990; 15:307–309. doi: 10.1007/BF01888805. [PubMed]
11. Polat KY, Aydinli B, Yilmaz O, Aslan S, Gursan N, Ozturk G, Onbas O. Intestinal tuberculosis and secondary liver abscess. *Mount Sinai J Med.* 2006; 73(6):887–890.
12. Jain R, Sawhney S, Gupta RG, Acharya S. Sonographic appearances and percutaneous management of primary tuberculous liver abscess. *J Clin Ultrasound.* 1998; 27:157–163.
13. Diaz ML, Herrera T, Lopez-Vidal Y, Calva JJ, Hernandez R, Ruiz Palacios G, Sada E. Polymerase chain reaction for the detection of *Mycobacterium tuberculosis* DNA in tissue and assessment of its utility in the diagnosis of hepatic granulomas. *J Lab Clin Med.* 1996; 127:359–363. doi: 10.1016/S0022-2143(96):90184-5. [PubMed].