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THE CHEST & HEART JOURNAL

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

Volume 33, Number 2, July 2009

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

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Address of Correspondence : The Editor, Chest and Heart Journal.
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Cancer in South Africa (editorial). *S Afr Med J* 1994; 84-15.
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The Cardiac Society of Australia and New Zealand. Clinical exercise stress training. Safety and performance guideline. *Med J Aust* 1996; 164 : 282-4.

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Tierney LM, -McPhee SJ, Papakadis MA. *Current Medical Diagnosis and Treatment*. Lange Medical books/McGraw Hill 2000.
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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.
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ORIGINAL ARTICLE

Change in Clinical Outcome of Exacerbation of Bronchiectasis on Addition of Nebulized Gentamicin to Systemic Antibiotic

Masum Ahmed¹, Md. Ali Hossain², Mirza Mohammad Hiron³, Mohammad Abdus Shakur Khan⁵, Md. Shahidullah⁴, Md. Abdur Rouf⁶, Biswas Akhter Hossain⁶, Abul Kalam⁷

Abstract:

In this study, we try to demonstrate safety, efficacy of nebulized gentamicin as an adjunctive therapy in treatment of exacerbation of bronchiectasis.

A total 65 patients were taken initially for the study. Randomized into two groups thirty-three in group A received nebulized gentamicin in addition to systemic antibiotic and thirty-two in group B received systemic antibiotic with placebo (normal saline) nebulization. Three from group A and 8 from group B were excluded as they either withdrawn their consent or failed to attend their follow-up visit.

So, finally 30 patients in group A and 24 patients in group B completed the study. Sputum culture and sensitivity was done at baseline, it is not done at follow-up visit because a few comparable studies performed in patients with non-cystic fibrosis bronchiectasis have shown that successful treatment does not depend on the eradication of the organisms responsible for acute exacerbation state (Hill SL, Burnett D, 1988) (F Sauj KW, Chan WM, 1999).

We evaluated the patients for clinical outcome at day 3, 7, 14 and 21 and categorized them as: resolved -

- resolution of S/S of acute exacerbation*
- improved - not fully resolved*
- not improved - if no change or deterioration of S/S.*

At day 3, no significant improvement was observed but sputum viscosity reduced and became frothy in character in group A.

Clinical outcome at different time interval showed that addition of nebulized gentamicin to systemic antibiotic enhance recovery rate compared to systemic antibiotic alone.

At all level of evaluation, the rate of recovery was significantly higher in group A than that in group B ($P=0.05$, $p=0.023$ and $p= 0.020$ respectively) [Table XII] which is consistent with the study of Diana Bilton, MD, Noreer Henij MD, Mark Gtfried MD, FCCP, 2006.

Though new wheeze and chest tightness developed following administration of nebulized gentamicin in 5 cases of group A, it did not affect overall lung function status as revealed by no significant change in FEV₁. (Table XI).

[Chest & Heart Journal 2009; 33(2) : 74-82]

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Introduction:

Bronchiectasis is defined as a permanent dilatation of the airways⁴. It involves medium sized subsegmental bronchi from about 4th to 9th generations.¹ It is estimated that 110,000 people in the United States may be receiving treatment for symptoms of bronchiectasis. Twenty percent of these patients account for nearly 80% of the total resources devoted to bronchiectasis management (approximately \$600 million annually). These costs can be attributed in part to hospital admission for the treatment of acute exacerbations of bacterial infection that cannot be effectively managed in an outpatients setting. This is a particular problem for persons chronically infected with *P aeruginosa* who have become refractory to management with oral antipseudomonal antibiotics such as ciprofloxacin (Cip) and levofloxacin.²

Clinical manifestation of bronchiectasis are recurrent, chronic and refractory infections. The incidence of bronchiectasis has dramatically decreased over the last 60 years in developed countries because of the remarkable advance in ability to prevent and treat many infectious respiratory diseases that caused bronchiectasis. This is due to vaccinations for measles, pertosis, treatment of tuberculosis and antibiotics effective against the usual bacterial pneumonia and acute bronchitis.³

Bronchiectasis is often associated with increased microbial load. This results in persistent inflammatory host response thereby causing progressive lung damage and deterioration in lung functions. Usual organisms in bronchiectasis are *Pseudomonas aeruginosa*, *Haemophylus influenzae*, *Streptococcus pneumoniae*, *Staphylococcus aureus*. Among them *pseudomonas aeruginosa* are a major cause of morbidity and mortality in bronchiectasis Patients infected with *pseudomonas aeruginosa* have frequent acute exacerbations.^{2,3}

Antibiotics therapy is given for infective exacerbations or regular pulsed basis to reduce microbial load.³

The current management paradigm includes the promotion of bronchial hygiene, the reduction of bronchial inflammation, and administration of

courses of directed antibiotic treatment aimed at pathogen reduction rather than eradication. These measures can improve patient quality of life, but neither can reverse bronchial dilation nor cure the underlying pathology.

Because of limited options for the treatment of *pseudomonas aeruginosa* with oral antibiotics, parenteral preparations of aminoglycosides or other antibiotics have been delivered to the lower respiratory tract by aerosol. Though this therapy is established in cystic fibrosis, *nebulized* antibiotics can be given in bronchiectasis and is well tolerated, improves symptoms and preserve lung functions.^{1,3,4}

Rationale

Nebulized antibiotic is an established safe and effective therapy for cystic fibrosis. Bronchiectasis is similar respiratory disease, so this effective therapy can be used in bronchiectasis. Aminoglycosides including gentamicin are considered among the most useful classes of antibiotics for treating *pseudomonas aeruginosa* infections. The major drawback of aminoglycosides is the need for their relatively high dose intravenous administrations which carries the potential systemic toxicity, consequently when gentamicin is given intravenously in maximum safe doses, only relatively low sputum aminoglycoside concentration are achievable. These limitations can be circumvented by direct delivery of aerosolized antibiotic to the airways. Thus inhaled antibiotics have the potential to provide more effective antimicrobial therapy with fewer side effects.⁵

Materials and Methods:

Type of Study : Prospective study.

Period of Study : April 2008 to April 2009

Place of Study : This study was carried out in National Institute of Diseases of Chest and Hospital, Mohakhali, Dhaka.

Study Population:

Men and women aged above 18 years with bronchiectasis confirmed by HRCT of chest were considered.

Initially 65 patients were included according to inclusion and exclusion criteria. One patient from

group A and four patients from group B, withdrawn their consent. Two from group A and four from group B did not complete their follow-up. Finally 54 patients completed the study. By Lottery method patients were divided into two groups. Thirty patients in group A were treated with nebulized gentamicin in addition to systemic antibiotic whereas in group B, 24 patients were treated with placebo (Normal Saline-4ml) nebulization in addition to systemic antibiotic.

In both groups, initial systemic antibiotic was levofloxacin. Sputum of total of 6 patients (group A=2, group B=4) were levofloxacin resistant and then it was changed accordingly.

Among the studied patients the mean ages of the subjects in group A and group B were 41.1 ± 9.7 and 43.6 ± 15.3 years respectively. All are adults. In both groups lower age limit was 21 years. No significant age difference was observed between groups ($p=0.487$). 66.7% of patients in group A and 79.2% in group B were male giving a male to female ratio of 2:1 in the former group and 4:1 in the later group. No significant difference was observed between groups ($p=0.308$).

1) Inclusion criteria:

Patients aged above 18 years with bronchiectasis confirmed by HRCT of the chest was included in this study at acute exacerbation state. Acute exacerbation was defined according to criteria.

Criteria defining an acute exacerbation:

Presence of at least two of the following symptoms:

- Increased cough
- Increased volume of sputum produced
- Increased dyspnoea, increased wheezing

And at least one of the following:

- Fever (temperature $>38^{\circ}\text{C}$)
- Increased WBC count $>10 \times 10^3$ cells/mL
- Increased ESR

And laboratory evidence of purulent sputum.

2) Exclusion criteria:

Patients with following characteristic was excluded from the study.

- Patient having creatinine level $>2\text{mg/dl}$
- Pregnant women also not included in this study

- Patients with cystic fibrosis, allergic bronchopulmonary aspergillosis, active tuberculosis.
- Gentamicin resistant cases.

Sample Size: About 4 to 5 nos. of bronchiectasis patient are admitted in NIDCH in one week admission period and I had follow up them upto 3 to 4 weeks. As my study period was one year, 48 to 60 nos. of patients was expected to be included in this study.

Sampling Method: Consecutive sampling.

Ethical Clearance and Obtaining Consent:

Ethical clearance was taken from Ethical Committee existent in NIDCH, Mohakhali, Dhaka.

Written consent was obtained after elaborate explanation of all drugs use for this study.

Study Design & Material Used:

The study was hospital based clinical trial. Subject fulfilling the inclusion criteria was included in this study. Data was collected through appropriate questionnaire. Acute exacerbation was defined by using criteria. At the time of exacerbation subjects was randomized into two groups (Group A & Group B) by using lottery method. For random allocation of patient into groups there were two cards. One marked with A and other with B. A doctor on duty reshuffled the card and patients were asked to draw a card blindly. If the patient got the card mentioned with either 'A' or 'B', he or she selected for that group. Next patient was assigned to alternate group. In this way total 65 patients were selected: 33 in group A, 32 in group B. Patients of Group A were treated with nebulization of gentamicin. Patients of Group B were treated with nebulization of normal saline. Patient of both groups was given empirical systemic antibiotic as usual dose and frequency.

Dose formulation of *nebulized* gentamicin: one ampoule gentamicin (80mg) dilute with normal saline to a total vol. of 4 ml and was aerosolized through a jet nebulizer 12 hourly

Duration of treatment was upto clinical resolution that is 10 days in 13 nos. of patient (group A=10 & group B= 3), 14 days in 26 nos. of patients (group A=16 and group B=10) and 21 days in 04 nos. of patients (group A=2 and group B=2), rest of 11 nos. patients was given antibiotic more than 21 days as they were not resolved within follow-up period.

Choice of Empirical antibiotic is based on stranded treatment protocol: In this study Levofloxacin was used as empirical systemic antibiotic as it has both gram (+)ve and gram (-)ve coverage including *pseudomonas aeruginosa*.⁴

Before starting antibiotic, sputum was sent for C/S. Sputum collection and transport was done according to standard procedure and C/S was done in ICDDR,B, Dhaka. Sputum of total of 6 patients (group A=2, group B=4) were levofloxacin resistant and then it was changed accordingly.

Patient was encouraged to continue other regular drugs and postural drainage.

Outcome measure: after start of treatment at regular intervals (3rd, 7th, 14th & 21st day) subjects was assessed by the following parameters:

Clinical:

- Character of cough
- Volume of sputum produced
- Sputum purulence
- Changed in dyspnoea and wheezing
- Fever

Laboratory:

- Total WBC count
- ESR
- Sputum microscopy and gram stain

Spirometry was performed before and 30 minutes after nebulization of gentamicin in group A on 3rd & 7th day to assess acute bronchoreactivity.

End points:

- Patients were followed up at regular intervals of 3rd, 7th, 14th and 21st day and was categorized as follows:
- **Resolved:** resolution of sign symptoms of acute exacerbation.
- **Improved-** sign symptoms not fully resolved.
- **Not improved:** if no change or deterioration of the sign symptoms.

We tried to follow-up all patients within the hospital but 2 patients from group A and 4 patients from group B did not agree to stay hospital as they were resolved at day 14. We advise them to come to hospital at day 21. They failed to attend and we excluded them from the study.

Statistical Analysis

Data were processed and analyzed using SPSS (Statistical Package for Social Sciences) version

11.5. The test statistics used to analyse the data were descriptive statistics, Chi-square (χ^2) or Fisher's Exact Probability Test, Student's t-Test and repeated measure ANOVA. Data presented on categorical scale were compared between groups using Chi-square (χ^2) or Fisher's Exact Probability Test, while the data presented on quantitative scale were compared between groups using Student's t-Test and repeated measure ANOVA. For all analytical tests the level of significance was 0.05 and $p < 0.05$ was considered significant.

Observations & Results

In this study, we try to demonstrate safety, efficacy of nebulized gentamicin as an adjunctive therapy in treatment of exacerbation of bronchiectasis.

A total 65 patients were taken initially for the study. Randomized into two groups thirty-three in group A received nebulized gentamicin in addition to systemic antibiotic and thirty-two in group B received systemic antibiotic with placebo (normal saline) nebulization. Three from group A and 8 from group B were excluded as they either withdrawn their consent or failed to attend their follow-up visit.

So, finally 30 patients in group A and 24 patients in group B completed the study.

Analysis was done and the outcome was as below:

At day 3, no significant improvement was observed but sputum viscosity reduced and became frothy in character in group A.

Clinical outcome at different time interval showed that addition of nebulized gentamicin to systemic antibiotic enhance recovery rate compared to systemic antibiotic alone.

At all level of evaluation, the rate of recovery was significantly higher in group A than that in group B ($P=0.05$, $p=0.023$ and $p=0.020$ respectively)

Table-I
Distribution of patients by age (n = 54)

Age (years)	Group		p-value
	Group- A (n = 30)	Group-B (n = 24)	
<40	11(36.7)	10(41.7)	
40 – 50	14(46.7)	3(12.5)	
e"50	5(16.7)	11(45.8)	
Mean \pm SD	41.1 \pm 9.7	43.6 \pm 15.3	0.487

Chi-square (χ^2) Test was employed to analyse the data; Figures in the parenthesis denote corresponding percentage.

Table-II
Causative organisms isolated on culture of sputum (n = 54)

Pathogens	Group A (n = 30)		Group B (n = 24)		Total(%)
	Frequency	Percentage	Frequency	Percentage	
<i>Pseudomonas auruginosa</i>	15	50.0	11	45.8	26(48.1)
<i>Acinetobacter</i>	06	20.0	06	25.0	12(22.2)
<i>Escherichia coli</i>	05	16.7	03	12.5	08(14.8)
<i>Klebseilla</i>	05	16.7	02	8.3	07(12.9)
<i>Haemophilus influenzae</i>	02	6.7	02	8.3	04(7.4)
<i>Beta-hemolytic Streptococcus</i>	01	3.3	03	12.5	04(7.4)
<i>Enterobacter</i>	02	6.7	02	8.3	04(7.4)
<i>No growth</i>	01	3.3	02	8.3	03(5.5)

Table-III
Baseline clinical characteristics of the study population (n = 54)

Baseline clinical variables	Group		p-value
	Group-A (n = 30)	Group-B (n = 24)	
Sputum volume (ml)*	169.0 ± 59.4	173.9 ± 62.4	0.767
Sputum type [#]			
Mucopurulent	28(93.3)	21(87.5)	0.393
Purulent	2(6.7)	3(12.5)	
Dyspnoea [¶]			
Grade-I	4(13.3)	4(16.7)	0.241
Grade-II	18(60.0)	9(37.5)	
Grade-III	8(26.7)	11(45.8)	
Wheeze[¶]	22(73.3)	20(83.3)	0.38
Present	8(26.7)	4(16.7)	
Absent			
Fever [¶]			
Present	11(36.7)	15(62.7)	0.103
Absent	19(63.3)	9(37.5)	

*Student's t test was employed to analyse the data; #Fisher's Exact Test was employed to analyse the data; ¶Chi-square Test was employed to analyse the data

Table-IV
Changes in clinical variables at day 7 (n = 54)

Clinical variables at day 7	Group		p-value
	Group-A (n = 30)	Group-B (n = 24)	
Sputum volume (ml)	111.3 ± 63.7	121.1 ± 49.9	0.543
Sputum type			
Mucopurulent	13(43.3)	20(83.3)	<0.001
Purulent	2(6.7)	4(16.7)	
Froathy	15(50.0)	0	
Dyspnoea			
Grade-I	19(63.3)	8(34.8)	0.113
Grade-II	8(26.7)	10(43.5)	
Grade-III	3(10.0)	5(21.7)	
Wheeze	23(76.7)	20(83.3)	0.546

*Student's t test was employed to analyse the data; ¶Chi-square (c²)Test was employed to analyse the data

Table-V*Changes in laboratory variables at day 7 (n = 54)*

Laboratory variables on day 7	Group		p-value
	Group-A (n = 30)	Group-B (n = 24)	
ESR¶			
<30	15(50.0)	5(20.8)	0.027
e ³ 30	15(50.0)	19(79.2)	
WBC¶			
<10000 × 10 ⁹ /L	24(80.0)	15(62.5)	0.154
e ⁷ 10000 × 10 ⁹ /L	6(20.0)	9(37.5)	
Gram stain¶			
Pus cell plenty	4(13.3)	5(20.8)	
Few pus cells	10(33.3)	16(66.7)	0.027
Pus cell absent	18(53.3)	3(12.5)	

¶Chi-square (c²) Test was employed to analyse the data; Figures in the parentheses denote corresponding percentage.

Table-VI*Changes in clinical variables at day 14 (n = 54)*

Clinical variables at day 14	Group		p-value
	Group-A (n = 30)	Group-B (n = 24)	
Sputum volume (ml)#	61.8 ± 33.5	97.7 ± 53.4	0.004
Sputum type#			
Mucoid	21(70.3)	13(54.2)	
Mucopurulent	6(20.0)	11(45.8)	0.032
Frothy	3(10.0)	0(0.0)	
Dyspnoea¶			
Grade-I	24(80.0)	9(37.5)	
Grade-II	6(20.0)	14(58.3)	0.005
Grade-III	0	1(4.2)	
Wheeze¶	4(13.3)	11(45.8)	0.008

Student's t test was employed to analyse the data; ¶Chi-square (c²)Test was employed to analyse the data; figures in the parentheses denote corresponding percentage.

Table-VII*Changes in laboratory variables at day 14 (n = 54)*

Laboratory variable at day 14	Group		p-value
	Group-A (n = 30)	Group-B (n = 24)	
ESR#			
<30	28(93.3)	18(75.0)	
eH30	2(6.7)	6(25.0)	0.067
WBC#			
<10000	28(93.3)	22(87.5)	
e ⁷ 10000	2(6.7)	3(12.5)	0.393
Gram stain#			
Pus cell plenty	2(6.7)	1(4.2)	
Few pus cells	4(13.3)	13(54.2)	0.006
Pus cell absent	24(80.0)	10(41.7)	

#Fisher's Exact Test was employed to analyse the data; ¶Chi-square (c²)Test was employed to analyse the data; figures in the parentheses denote corresponding percentage.

Table-VIII*Changes in clinical variables at day 21 (n = 54)*

Clinical variables at day 21	Group		p-value
	Group-A (n = 30)	Group-B (n = 24)	
Sputum volume (ml)#	61.3 ± 28.2	92.9 ± 58.4	0.021
Sputum type¶			
Mucoid	25(83.3)	17(70.8)	
Mucopurulent	4(13.4)	5(20.8)	0.517
Frothy	1(3.3)	2(8.4)	
Dyspnoea¶			
Grade-I	27(90.0)	7(29.2)	
Grade-II	3(10.0)	15(62.5)	< 0.001
Grade-III	0	2(8.3)	
Wheeze*	2(6.7)	10(41.7)	0.002

Student's t test was employed to analyse the data; ¶Chi-square (c²) Test was employed to analyse the data.; *Fisher's Exact Test was employed to analyse the data; Figures in the parentheses denote corresponding percentage.

Table-IX*Changes in laboratory variable at day 21 (n = 54)*

Outcome variables	Group		p-value
	Group-A (n = 30)	Group-B (n = 24)	
ESR#			
< 30	27(90.0)	19(79.2)	
eH 30	3(10.0)	5(20.8)	0.233
WBC#			
<10000	28(93.3)	22(91.7)	
>10000	2(6.7)	2(8.3)	0.605
Gram stain¶			
Pus cell plenty	2(6.7)	0(0.0)	
Few pus cells	2(6.7)	8(33.3)	0.025
Pus cell absent	26(86.7)	16(66.7)	

#Fisher's Exact Test was employed to analyse the data; ¶Chi-square (c²) Test was employed to analyse the data; Figures in the parentheses denote corresponding percentage.

Table-X
Changes in sputum volume at different time interval

Sputum volume (ml)	Evaluation at					p-value
	Baseline	Day 3	Day 7	Day 14	Day 21	
Group-A	169.0±59.4	176.8±78.1	111.3±63.7	61.8±33.4	61.3±28.2	< 0.001
Group-B	173.9±62.4	160.4±56.9	121.1±49.9	97.7±53.4	92.9±58.4	

Repeated measure ANOVA statistics was employed to analyse the data and '**p**' refers to overall difference between the two treatment groups.

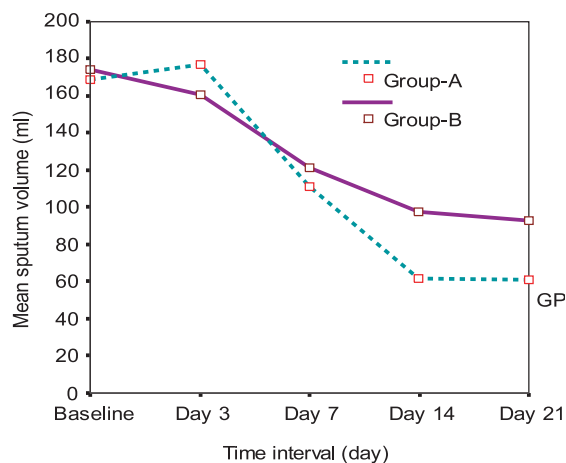


Fig. 3: *Changes in sputum volume at different time interval (n = 54)*

Table-XII
Evaluation of clinical outcome at different time interval

Outcome	Evaluation of outcome					
	Day 7		Day 14		Day 21	
	Group-A	Group-B	Group-A	Group-B	Group-A	Group-B
Resolved	10(33.3)	3(12.5)	26(86.7)	13(54.2)	28(93.3)	15(62.5)
Improved	17(56.7)	13(54.2)	2(6.7)	8(33.3)	1(3.3)	5(20.8)
Not improved	3(10.0)	8(33.3)	2(6.7)	3(12.5)	1(3.3)	4(16.7)
p-value	0.050	0.023	0.020			

Discussion:

Initially 65 patients were included according to inclusion and exclusion criteria. One patient from group A and four patients from group B, withdrawn their consent. Two from group A and four from group B did not complete their follow-up. Finally 54 patients completed the study. By Lottery method patients were divided into two groups. Thirty patients in group A were treated with nebulized gentamicin in addition to systemic

Table-XI
Safety analysis of the study population (n = 30)

Day of evaluation	Group		p-value
	Before drug (n = 30)	After drug (n = 24)	
Day 3	46.6 ± 10.1	47.1 ± 6.6	0.684
Day 7	49.1 ± 6.7	48.6 ± 7.3	0.142

Student's t test was employed to analyse the data and data were presented as **mean ± SD**.

antibiotic whereas in group B, 24 patients were treated with placebo nebulization in addition to systemic antibiotic. In both groups, initial systemic antibiotic was levofloxacin. Sputum of total of 6 patients (group A=2, group B=4) were levofloxacin resistant and then it was changed accordingly. Our main outcome measures were change in cough, sputum volume and purulence, change in grading of dyspnoea, change in wheezing, presence or absence of fever and change in laboratory

inflammatory markers, which included total count of WBC, ESR, microscopic examination of sputum including gram-stain. Sputum culture and sensitivity was done at baseline and not done at follow-up visit because a few comparable studies performed in patients with non-cystic fibrosis bronchiectasis have shown that successful treatment does not depend on the eradication of the organisms responsible for acute exacerbation state.⁶ The commonest organism isolated was *Pseudomonas aeruginosa* (48.1%), followed by *Acinetobacter* (22.2%), *E.coli* (14.8%), *Klebsiella* (12.9%), *Haemophilus influenzae* (not group A) (7.4%), *beta-haemolytic beptococcus* (not group B) (7.4), *Enterobactor* (7.4%) and no organism was cultured in 5.5% cases. Different studies of UK, Spain, Texas-USA, had shown that *H. influenzae* (35-55%) and *P. aeruginosa* (26-31%) were most frequently isolated organisms.⁷ In this study, *pseudomonas aeruginose* was most commonly isolated organism.

Chance of laboratory contamination is less as sputum culture was done in a reference laboratory. In both groups, baseline characteristics were almost similar (Table-VI-A & VI-B), which includes sputum volume, sputum type, grading of dyspnea, presence or absence of fever, ESR, total WBC count, spirometry (FEV₁) and sputum microscopy and gram-stain. Clinical success in treating bronchiectasis is usually defined in terms of reduction in 24h sputum volume, an improvement in cough and dyspnea.⁶ That's why we evaluate the patient mostly clinically. This study was conducted with an intension to establish the efficacy of gentamicin as an adjuvant for the treatment of exacerbation bronchiectasis. Stated that gentamicin has activity against *pseudomonas aeruginosa*, *H. influenzae*, *Acinotabacter*, *Klebsiella*, *Streptococcus*, *Staphylococcus*, *E. coli*, *Serratia*.⁸ In this study, most of the organism was *pseudemonas aeruginosa*. Antibiotics were used according to culture & sensitivity report. In the majority of cases levofloxacin was used as systemic antibiotic as it was sensitive. So addition of nebulized gentamicin to systemic antibiotic would achieve more clinical efficacy.

The results of this study showed that addition of nebulized gentamicin to systemic antibiotic improves clinical outcome faster than use of systemic antibiotic alone. Fever Volume of sputum,

character of sputum, improves earlier than change in dyspnoea and wheeze. So these therapies decreased the hospital stay and decrease treatment costs. These findings are consistent with study done by Orriols, et al.⁹, though their aim of study was to see the long-term efficacy of inhaled antibiotic. But our duration of antibiotic use was less than one month. Bilton, et al.¹⁰ had done similar type of study, but they use tobramycin instead of gentamicin and conclude that addition of inhaled tobramycin solution to systemic antibiotic improve microbiological outcome and concordant with clinical outcome. In their study, they failed to demonstrate an additional clinical benefit. That might be due to emergent wheeze resulting from treatment. In this study, though 5 patients in group A, developed new wheeze and chest tightness following administration of nebulized gentamicin, no significant change in FEV₁ was observed before and after administration of nebulized gentamicin (Table XI). Chest tightness and wheeze as side effects was found in all studies of Tobramycin inhalation in non-cystic fibrosis bronchiectasis.¹¹ Similar side-effects also observed in this study and were resolved after nebulization of salbutamol. In this study, these side-effects were resolved after nebulization of salbutamol. Study populations were evaluated for clinical outcome at day 3,7,14 & day 21 and categorized as 'resolved', 'improved', 'not improved.' The few comparable studies performed in patients with non-CF bronchiectasis have shown that successful treatment does not depend on the eradication of organisms,² so in this study microbiological response was not observed. For a successful research it is needed to see the concordance of clinical and microbiological response simultaneously. So, large scale study needed to see concordance of clinical and microbiological efficacy.

Though spirometry was done in study population, that parameter was not chosen as major end point, because study⁶ shown that patients with bronchiectasis have a significant improvement in clinical symptoms without a significant change in FEV₁. As FEV₁ represent an important safety parameter, FEV₁ was measured before and 30 minutes after nebulization of gentamicin in group A patients at day 3 and at day 7 to assess acute bronchoreactivity as it was done in the study by

Diana Bilton et al². Several peer-reviewed reports in cystic fibrosis have found improvement in lung function after aerosolized antibiotics.⁹ Contrary to these studies, in my study, lung function was not assessed as end points parameters, as explained earlier.

As other study, we use inhaled gentamicin for a short period. There are few studies regarding use of nebulized antibiotic for long-term in non-cystic fibrosis bronchiectasis. A study done by Orriols, et al.⁹ is one of the studies where long-term efficacy and safety of inhaled antibiotic was assessed and suggests long-term inhaled antibiotic therapy may be safe and lesser the severity of diseases in non-cystic fibrosis bronchiectasis. But this was an uncontrolled trial. However, the time scale and frequency of treatment as well as the type, dose and amount of antibiotics, cannot be definitely recommended in this time.⁹

This study concludes that

1. Addition of nebulized gentamicin to systemic antibiotic improve clinical efficacy compared to only systemic antibiotic.
2. It can reduce hospital stay when used as adjuvant with systemic antibiotic for the treatment of exacerbation of bronchiectasis.
3. Though nebulized gentamicin leads to development of chest tightness and wheeze in some case that can be overcome with concomitant use of salbutamol nebulization.

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ORIGINAL ARTICLE

Anti Tuberculosis Drug resistance Patterns among Category 2 Failure Patients in Bangladesh

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Abstract

Aim: To determine the pattern of anti tuberculosis drug resistance among category 2 failure TB patients in Bangladesh, a drug resistance survey of category 2 failure patients was undertaken in Bangladesh.

[Chest & Heart Journal 2009; 33(2) : 118-121]

Introduction:

The magnitude of drug resistance is not yet known in many areas of the world including high TB and MDR TB burden countries. Nevertheless, evidence from half the world's nations confirms that drug resistance is a serious problem worldwide. WHO estimates that the number of incident cases of MDR (including new and re-treatment cases) occurring worldwide in 2003 were 458000 (95% confidence limits, 321000-689000)¹. Prevalent cases worldwide could be two or three times higher than the number of incident cases.

There are no representative data on drug resistance in Bangladesh. However, in collaboration with the Shymoli Chest Disease Clinic, the International Center for Diarrheal Diseases and Research (ICDDR,B) have conducted DST among 657 patients showing 3% and 15% MDR-TB among new and previously treated TB patients respectively². The Damien Foundation has also conducted two drug resistance studies in 1995 and 2001 comprising 645 and 1041 patients. Where they have found that the over all MDR-TB prevalence has fallen from 0.7% to 0.4% in new and from 6.8% to 3.0% in retreatment cases.³. Bangladesh is the world's most densely populated country with population of 140 millions. Extreme poverty, overcrowding and malnutrition make people more prone to infection with *M. tuberculosis*. Bangladesh ranks 6th and 9th in the

world in terms of burden TB and MDR-TB respectively⁴.

Although the rates of MDR-TB in Bangladesh do not appear to be high according to present data, the absolute number of new MDR-TB cases is high considering the high TB burden.

According to 2004 cohort of NTP registered TB cases, among the retreatment cases (4956) 3% failed and 7% defaulted. We carried this survey to assess the pattern of anti tuberculosis drug resistance among retreatment failure cases⁵.

Design: All Chest Disease Clinics (CDC) were requested to send category 2 failure patients (smear positive at the end of 5 months of cat 2 treatment) to National Institute of Disease of Chest and hospital, Dhaka. From July 2005 to December 2005, 63 patients were referred from different areas of Bangladesh. Sputum was collected and AFB microscopy was done at NIDCH and sputum was sent to Supra National Reference Laboratory at Antwerp, Belgium where susceptibility testing with 4 first line drugs and 4 second line drugs was done.

Methods:

There are 44 CDCs in the country, on average thus covering 1.5 districts each. They are staffed by a Junior consultant, medical officer and supporting paramedical and clerical staff of the chest diseases clinics. Besides their limited catchment area, CDCs

1. National Institute of Diseases of Chest and Hospital.
2. World Health Organization, HQ.
3. International Union Against Tuberculosis & Lung Diseases.

are oriented to providing referral services for the entire district in which they are located. Most of the retreatment cases (except private practitioner's cases) are treated in CDCs as they have chest specialist doctors. All CDCs were requested by Director MBDC and Line Director TB-Leprosy to send category 2 failure patients to National Institute of Disease of Chest and Hospital (NIDCH), Dhaka. NIDCH is the only tertiary referral hospital for chest diseases and Tuberculosis in Bangladesh. At NIDCH, Personal history of the patients, and sputum samples were collected. All sputum specimens were examined for AFB smear microscopy by Z-N staining method. Sputum samples with CPC powder (Cytyl Pyrimidinium Chloride) in falcon tubes were sent regularly to Supra National Reference Laboratory at Antwerp Belgium.

From July to December 2005, 63 patients of retreatment failure were referred from different areas of Bangladesh and accordingly 63 sputum samples were sent to Antwerp. These samples were cultured on Lowenstein-Jensen medium and drug susceptibility test were performed using standard techniques. Susceptibility testing with 4 first line drugs (Rifampicin, Isoniazid, Ethambutol and Streptomycin) and 4 second line drugs (Kanamycin, Ofloxacin, Ethionamide and PAS) was done.

Results:

Among 42 positive cultures 36 (86%) had Resistance to Isoniazid, 36 (86%) to Rifampicin and 35 (83%) to both MDR. Of all MDR TB cases, 46% were also resistant to any of the 2nd line drugs.

Among 63 patients, 79% were male and 21% were female. Most of the patients (88%) came from urban areas, 51% were less than 30 years of age and 76% were less than 50 years of age.(Table 1)

Table-I

Distribution of referred cases by age and gender

Age	Male n (%)	Female n(%)	Total n
10-19	7 (70%)	3 (30%)	10
20-29	19 (86%)	3 (14%)	22
30-39	6 (67%)	3 (23%)	9
40-49	5 (71%)	2 (29%)	7
50-59	9 (90%)	1 (10%)	10
60-69	3 (75%)	1 (25%)	4
>70	1 (100%)		1

Of the 63 samples , One was contaminated, two had leaked and the result of one sample had not been completed. Of the remaining 59, 16 (27%) were culture negative and of 42 (71%) were culture positive for Mycobacterial growth. Of the 42 isolates, 41 were *M. tuberculosis* and 1 was *Mycobacterium Intracellulare*.(Table II).

Among 42 positive cultures, 36 (86%) had resistance to Isoniazid, 36 (86%) to rifampicin and 35 (83%) to both (MDR). 9 (21%) to Ethambutol and 4 (10%) to PAS. No resistance was found to Kanamycin. 7 (17%) had resistance to Ofloxacin. (Table III).

Among 42 culture positive category 2 failure cases, 83% are MDR (Multi drug resistant to Rifampicin and Isoniazid), 60% of MDR had only resistance to 1st line drugs but 40% had resistance to any of the 2nd line drugs. 20% of MDR are resistance to ofloxacin, 26% of MDR to Ethionamide and 11% MDR to PAS. (Table-IV).

Table-II

Culture results

Total Specimen	Growth Positive n=%	Growth Negative n=%	Specimen Excluded n=%	<i>M.tuberculosis</i>	<i>M. intracellulare</i>
63	42 (71%)	16 (27%)	4 (2%)	41	1

Table-III
Distribution of antimicrobial resistance pattern of isolates

Drug	Number	Percentage
First line drug (n=42)		
Rifampicin	36	86
Isoniazid	36	86
Ethambutal	29	69
Streptomycin	28	67
Rifampicin+ Isoniazid	35	83
Second line drug (n=42)		
Kanamycin	0	0
Ofloxacin	7	17
Ethionamide	9	21
PAS	4	10

Table-IV
Summary of drug resistance to both 1st and 2nd line anti TB drug

Drug history	Number (n)	%
Total Category 2 failure	42	100
Non MDR	7	17%
MDR	35	83%
MDR 1 st line only	21	60% of MDR
MDR + 2 nd line resistance	14	40% of MDR
Ofloxacin resistance to MDR	7	20%
Prothienomide resistance of MDR	9	26%
PAS resistance of MDR	4	11%

Discussion:

The result showed that MDR occurs in a high proportion (83%) of category 2 failure cases. This is concordant with the MDR-TB rates reported in Peru (87%)⁶ and Nicaragua (89%)⁶. However lower rates have also been reported from Brazil (65%)⁶. NTP 2004 data showed that 3% of retreatment cases failed and 7% defaulted. So, there is an urgent need to detect and isolate MDR TB cases in order to prevent transmission and mortality. MDR TB treatment strategy is needed to address the challenge of MDR TB cases in Bangladesh urgently.

We observed that 40% of MDR cases are also resistant to any of the 2nd line drugs. Resistance to Ethionamide is surprisingly high. Ethionamide is available in only a few pharmacies in Dhaka and is very expensive. In addition the Supra National Reference Laboratory have in a previous

study in Damien Foundation areas indicated uncertainty in Eth results due to large fluctuations possibly due to variations in the laboratory.

The only second line drugs produced in the country are Amikacine, Levofloxacin, Ciprofloxacin, Ofloxacin and Sparfloxacin. Gatifloxacin started to be available 3-6 months ago but Moxifloxacin use is limited and very expensive. Private practitioners would be more rationale to use the quinolone derivatives. PAS is not sold in Dhaka but could be purchased in neigbory India. Resistance to some of 2nd line drugs indicates irrational use of 2nd line drugs by the private sectors.

Several limitations of the survey should be noted. The number of samples was limited. It was a pilot study. The findings may not be generalizable since specimens were collected only from referred patients.

In view of the considerably large number of MDR-TB patients estimated by WHO, there is an urgent need to identify and treat MDR-TB patients, as raid out in the stop TB strategy. This study has provided important data in the designing of the standardized treatment regimen for MDR TB patients enrolled in the DOTS-Plus Pilot Project.

Due to relativity high resistance to Ethhambutal (69%)⁷, it has been omitted from the regimen which now consist of intensive phase 6 months Kanamycin, Ofloxacin, Ethambutal, Cycloerine, Pyrazinamide

The National Tuberculosis Reference Laboratory (NTRL) was established in NIDCH provides by the National TB control Program (NTP) started functioning in June 2007 and is presently providing complete laboratory support for the diagnosis and follow up of MDR TB patients in DOTS plus pilot project.

Having received recognition from supranational laboratory, the NTRL is preparing to conduct a nationwide drug resistance surveillance study which is imperative for appropriate management of the MDR-TB menace.

Conclusions:

There is a high proportion of MDR-TB among patients who fail to convert often receiving 5 months of Cat II. In order to diagnose these large number of cases entranced capacity of the NTRL

is imperative. Treatment facilities for MDR-TB patients shorted receive due emphasis. This will not only save lives but save us from the deadly menace of Extremely drug resistance TB (XDR-TB)

Acknowledgements:

We acknowledge the contribution of Institute of Tropical Medicine, Antwerp, Belgium for its support in conducting this study.

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ORIGINAL ARTICLE

Immediate Outcome of Congenital Pulmonary Stenosis Patients undergoing Pulmonary Valve Balloon Dilatation

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Abstract:

Aims and objectives: To assess the immediate results of pulmonary valve balloon dilatation (PVBD) in patients with congenital pulmonary stenosis.

Methods: 56 patients with congenital pulmonary stenosis undergoing pulmonary valve balloon dilatation were studied from August 2003 to July 2009

Results: 56 patients with congenital pulmonary stenosis admitted in NICVD and Al-Helal Heart Institute, Mirpur were included during this period. Age group ranged from 14 years to 48 years (Men age 20+06.23 years). Amongst whom male were 36 and female were 20. PVBD was done by femoral vein routes. The mean pulmonary valve annulus to balloon size ratio was 1.2. The pre PVBD echo pulmonary stenosis gradient was 114 ± 32 mmHg, Post PVBD echo was 28 ± 11 mmHg, Pre PVBD cath PS gradient was 119 ± 29 mm Hg, post PVBD cath PS gradient was 44 ± 12 mmHg. One patient had ventricular fibrillation one patient had a systole, who were resuscitated successfully. There were no mortalities.

Conclusion: Pulmonary valve balloon dilatation is a therapeutic procedure of choice for pulmonary stenosis patients. It yields excellent immediate results.

Key Words: Immediate Outcome, Pulmonary Stenosis, Pulmonary Valve Balloon Dilatation.

[Chest & Heart Journal 2009; 33(2) : 83-86]

Introduction

Congenital pulmonary valve stenosis comprises 7.5% to 9% of all congenital heart defects. The pathologic features of the stenotic pulmonary valve vary; the most commonly observed pathology is what is described as a “dome-shaped” pulmonary valve. The fused pulmonary valve leaflets protrude from their attachment into the The size of the pulmonary valve orifice varies from a pinhole to several millimeters, most usually central in location, but can be eccentric. Raphae presumably fused valve commissures extending from the

stenotic orifice to a variable distance down into the base of the dome-shaped valve. pulmonary artery as a conical, windsock-like structure. The number of the raphae may vary from zero to seven. Less common variants are unicommissural, bicuspid and tricuspid valves. Pulmonary valve ring hypoplasia and dysplastic pulmonary valves may be present in a small percentage of patients.

In the past, surgical valvotomy was the treatment of choice; however, now, balloon valvuloplasty has gained acceptance as the first option in the management of congenital pulmonary valve

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stenosis. The first attempt to relieve pulmonary valve obstruction by transcatheter methodology, was in the early 1950s by Rubio-Alvarez et al.^{1,2,6} They used a ureteral catheter with a wire to cut open the stenotic pulmonary valve.

In 1979, Semb and associates employed a balloon-tipped angiographic (Berman) catheter to produce rupture of pulmonary valve commissures by rapidly withdrawing the inflated balloon across the pulmonary valve³.

Kan and her associates^{4,5} applied the technique to relieve pulmonary valve obstruction by the radial forces of balloon inflation of a balloon catheter positioned across the pulmonic valve.

This static balloon dilatation technique is currently employed throughout the world to relieve pulmonary valve obstruction. Subsequent to Kan's report, a large number of cardiologists have adopted this technique and reported immediate and intermediate-term results of this procedure.

Materials and Methods

56 patients with congenital pulmonary stenosis admitted in NICVD, Dhaka and AL Helal Heart Institute, Mirpur, undergoing pulmonary valve balloon dilatation were studied from August, 2003 to July, 2009. PVBD was done by femoral vein routes. The mean pulmonary valve annulus to balloon size ratio was 1.2.

The procedure was performed under local anaesthesia. Full diagnostic catheterization was performed to confirm the diagnosis and to exclude any additional malformations. Only patient with right ventricular systolic pressure gradient greater than 50 mmHg at rest were considered for Pulmonary valvuloplasty. The right ventriculography was performed in antero-posterior and Lateral projections. Diagnosis of pulmonary valve stenosis was confirmed and size of the pulmonary valve annulus was measured. We used balloon catheter with diameter of 20-24 mm.

An end-hole catheter was manipulated into left pulmonary artery and through it a 0.035 inch (0.89mm) exchange guide wire was advanced into the left lower lobe pulmonary artery. The catheter was withdrawn, care being taken to maintain the position of the guide wire. The catheter and sheath

were removed. Entry site was dilated with a dilator.

The balloon was advanced until the pulmonary valve was at the centre of the balloon. the balloon was then inflated to its maximum pressure with diluted contrast medium. When balloon was inflated, indentation seen at the site of pulmonary valve (Fig-2). Indentation was abolished when full inflation was achieved (Fig-3). Single to several times performed to achieve optimum goal.

Results

Total 56 patients were studied in National Institute of Cardiovascular Diseases, Dhaka and Al-Helal Heart Institute, Mirpur. All patients had congenital pulmonary valvular stenosis with severe pulmonary hypertension. All were symptomatic but without any sign of heart failure. Age Group was 14 years to 48 years and Mean age was 20 ± 06.23 years. 64% were male and 36% were female (Fig-1).

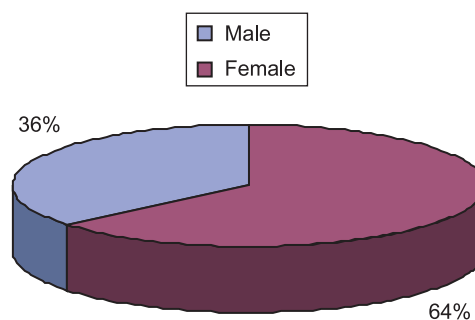


Fig-1: Sex distribution of the patients:

Before Pulmonary valve balloon dilatation mean pulmonary valve gradient in Echo Doppler Study was 114 ±32 mm Hg and after Pulmonary valve balloon dilatation mean pulmonary valve gradient in Echo Doppler Study was 28 ±11 mm Hg (Table-1).

Table-I
Echo Doppler Gradient of pulmonary valve

	Pulmonary valve gradient (Mean)
Pre PVBD	114 ±32 mm Hg
Post PVBD	28 ± 11 mm Hg

Before Pulmonary valve balloon dilatation mean pulmonary valve gradient in Cardiac Catheterization was 119 ±29 mm Hg and after

Pulmonary valve balloon dilatation mean pulmonary valve gradient was 44 ± 12 mm Hg (Table-2).

Table-2: Cardiac Catheter Gradient of pulmonary valve.

	Pulmonary valve gradient (Mean)
Pre PVBD	119 ± 29 mm Hg
Post PVBD	44 ± 12 mm Hg

There were no death. One patient had ventricular fibrillation and one patient had asystole during the procedure, who were resuscitated successfully. Few patients had small hematoma at puncture site.

Table-III
Periprocedural complications

Complication	No. of patients	Percentage of patients
Hematoma at puncture site	05	8.9%
Ventricular fibrillations	01	1.8%
Ventricular asystole	01	1.8%

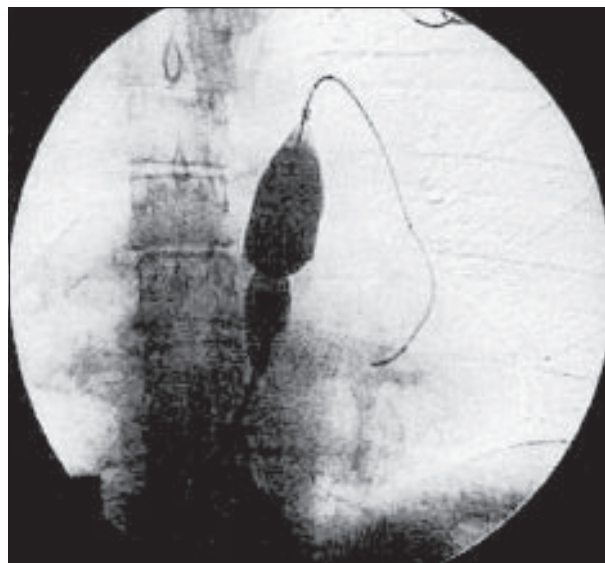


Fig-2: *Indentation seen at the site of pulmonary valve*

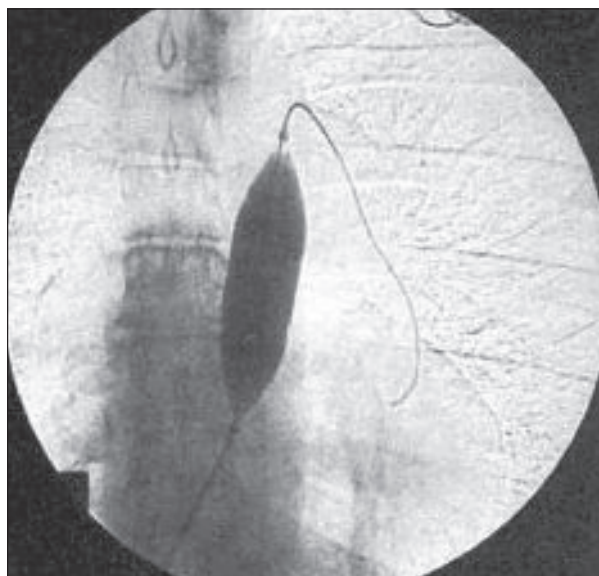


Fig-3: *Full Inflation of Balloon Catheter.*

Discussion:

Valvular PS is usually an isolated lesion, occurs in approximately 7% to 12% of all CHD, and accounts for 80% to 90% of all lesions that cause RVOT obstruction⁷. Its inheritance rate is low, ranging from 1.7% to 3.6%^{8,9}. Approximately 20% of patients with valvular PS have a dysplastic valve^{10,11} and if part of Noonan syndrome, these patients have an autosomal dominant trait with variable penetrance that has been mapped to chromosome 12^{12,13}.

Since the initial successful report of percutaneous balloon valvotomy for pulmonary valve stenosis in 1982⁴, the procedure has evolved to become the treatment of choice for patients with classic domed valvular PS. Balloon valvotomy produces relief of the gradient by commissural splitting. As might be expected from the morphology, results in patients with a dysplastic pulmonary valve are less impressive. In the Valvuloplasty and Angioplasty of Congenital Anomalies (VACA) registry, in 784 cases, the mean transvalvular gradient declined from 71 to 28 mm Hg in patients with typical PS and from 79 to 49 mm Hg in patients with a dysplastic valve¹⁴.

Because of the elasticity of the pulmonary annulus, it has been found that oversizing the balloons up to 1.4 times the measured pulmonary annulus is more effective in achieving

a successful result (usually defined by a final valvular gradient of less than 20 mm Hg). To accomplish this oversizing in adults, a double-balloon procedure is frequently used. In general, acute complications from the procedure have been minimal. During the acute performance of the valvotomy, vagal symptoms predominate, along with catheter-induced ventricular ectopy and occasionally right bundle-branch block. Other complications include pulmonary valve regurgitation, pulmonary edema (presumably from increasing pulmonary blood flow to previously underperfused lungs), cardiac perforation and tamponade, high-grade AV nodal block, and transient RVOT obstruction. The latter is sometimes referred to as a “suicidal right ventricle” and is due to abrupt infundibular obstruction once the pulmonary valve obstruction has been relieved¹⁵. This may be alleviated by volume expansion and beta blockade. This post procedural infundibular obstruction tends to regress over time.

Conclusion:

Pulmonary valve balloon dilatation is a therapeutic procedure of choice for pulmonary stenosis patients and it yields excellent immediate results.

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ORIGINAL ARTICLE

Influence of Asthma in Pregnancy on Labor and the Neonates

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Abstract:

Asthma is the most common potentially serious medical problem to complicate pregnancy. A study was designed to investigate whether asthma is associated with an increased risk of complications in connections in pregnancy. This study as carried out in Maternal and Child Health Training Institute (MCHTI) Azimpur during mid 2008 to mid 2009 Ninety-eight asthmatic women were monitored during their pregnancy and perinatal periods. A control group of ninety-eight non-asthmatic pregnant women were matched for age and height in categorized group wise from the indoor pregnant. Asthmatic mother had a greater risk of abortion, higher rates of UTIs. There were also significantly more occurrences of pregnancy-induced hypertension, pre-eclampsia, pre-term labor, and caesarian section among the asthmatic mother. Further more low birth weight, less Apgar score and hypoglycemia were occurred more considerably in infants of mothers with asthma. No significant difference among the groups by IUGR was seen. Besides, no maternal as well as neonatal mortality was observed in study population. This finding suggest that careful supervision and necessary appropriate treatment of asthma during pregnancy and labor should be given, so that to prevent the adverse occurrence among our beloved and valuable mother as well as our upcoming children.

[Chest & Heart Journal 2009; 33(2) : 122-126]

Introduction:

Asthma is defined as a chronic inflammatory disorder of the airway that extends beyond the central airways to the distal airways and lungs parenchyma in response to a wide variety of provoking stimuli, characteristic clinical symptoms of asthma are bronchial hyperactivity, reversible airway obstruction, wheezing and dyspnea¹.

It affects people of all ages. According to the European Community Respiratory Health Survey (ECRHS), prevalence of adult asthma across 22 countries ranged from 2% to 12%.² In Australia,

the prevalence of current adult asthma was estimated to be 10.2%.³ According to the First National Asthma prevalence Study (NAPS) 1999, in Bangladesh about 7 million people (5.2% of the population) are suffering from current asthma (at least three episodes of asthma attack at least in last 12 months).⁴

Asthma is the most common pre-existing medical disorder encountered in pregnancy.⁵ It affects between 3% and 12% of pregnant women world wide. The prevalence of asthma among pregnant females is increasing. In a estimates in the USA

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suggest that 3.7-8.4% of pregnant females had asthma in 1997-2001, an increase from 3.2% from 1988-1994. In Australia the prevalence is 12.4% among the pregnant women.⁶

More over Asthma is the most common potentially serious medical problem to complicate pregnancy⁷⁻⁸. Epidemiological studies have shown that approximately 1-4% of pregnancies are complicated by bronchial asthma, but these percentages are likely to be substantially underestimated because, in many cases, the condition will be undiagnosed, just as in the non pregnant population⁹.

The natural history of asthma is extremely variable among the pregnant women: symptoms severity may improve, worsen or remain unchanged in equal proportions as compared to with the pregravid state¹⁰. Patient with asthma are thought to be at high risk to develop a lots of complication that may lead to severe maternal morbidity latter on¹¹. It is often underrecognized and suboptimally treated.¹² and undertreatment or uncontrolled of pregnant asthmatics especially owing to unfounded fears of adverse pharmacological effects on the developing foetus, remains the major problem. Several studies have demonstrated that severe, uncontrolled asthma may produce serious maternal and foetal complications; consequently pregnant females with severe asthma must be considered at a particularly high risk¹³⁻¹⁴.

Asthma presents a major public health problem and it effects vary between gender, ethnic groups and countries. There has been little attention paid to asthma complication pregnancy in our country. We also do not know the real scenarios of influence of asthma in pregnancy and its outcome.

Objective: The aim of this study to examine the relationship between asthmatic pregnancies and selected maternal and neonatal outcome.

Methodology:

This prospective study was conducted in the Maternal and Child Health Training Institute (MCHTI), Azimpur, Dhaka, during the period of mid 2008 to mid of 2009 in the department of Gynaecology and Obstetrics and Anaesthesiology.

A total 98 patients who suffered from asthma, as diagnosed by the pulmonologist during ANC visit, were included in this study and another 98 patients who were randomly selected from the all patients who attended in ANC and came to this institute

for delivery or other end results of pregnancy. Both the asthmatic or non asthmatic patients were matched carefully according to the age and heights (after categorizing them into equal number of groups). Both the subject and control group were non smokers and no serious illness except asthma.

Results:

The desired maternal outcomes were (i) Hospital admission, (ii) past history abortion or still birth, (iii) Presence of UTI (iv) Pre-term labor (v) Pre-eclampsia (vi) IUGR (vii) Hypertension and (viii) vaginal haemorrhage (APH & PPH), (ix) maternal mortality and the fetal outcomes were (i) low birth weight (ii) pre term baby, (iii) APGAR score and (iv) fetal or neonatal mortality.

The frequency of getting admission into the hospital was more in asthmatic patient than that in the non asthmatic patients (6.11% vs 2.0%) and no significant relationship was observed in between them.

The frequency of occurrence of UTI episode during pregnancy was more in asthmatic patients (30.6%) than that of non asthmatic patients (8.2%) and had a significant relationship ($p < .000$).

The average mean parity of asthmatic women was 1.04 ± 0.98 while that in non-asthmatic group was 1.09 ± 0.17 had no association ($p > .702$).

The episode of abortion in past with asthmatic pregnant women (10.2%) was found more in comparison to the non asthmatic pregnant women (3.1%) which had a statistical significance ($p < .045$).

About twenty three percent of asthmatic pregnant women suffered from pregnancy-induced hypertension (PIH) during the period of pregnancy. On the other hand occurrence of pregnancy induced hypertension in non asthmatic patients was about seven percent and found a significant association between this two groups of pregnant women ($p < .000$). Further more, about sixteen percent asthmatic pregnant women had pre-eclampsia and in non asthmatic that was only about six percent. There was also a positive relationship in between them ($p < .024$). Besides, vaginal haemorrhage (APH & PPH) was taken place more significantly among the asthmatic group than that in non asthmatic group ($p < .047$).

Table-I
Distribution of the respondents by maternal pregnancy outcome

Name of the Characteristics	Asthmatic group	Non asthmatic group	p value
Past history of abortion	10(10.2%)	03(3.1%)	0.045
Occurrence of UTI episode	30(30.6%)	08(8.2%)	0.000
Frequency of hospital admission	06(6.1%)	02(2.0%)	0.149

Table-II
Distribution of the respondents by maternal pregnancy outcome

Name of the Characteristics	Asthmatic group	Non asthmatic group	p value
Pregnancy induced Hypertension	23(23.5%)	07(7.1%)	0.002
Pre Eclampsia	16(16.3%)	06(6.1%)	0.024
Vaginal Haemorrhage	20(20.4%)	10(10.2%)	0.047

Happening of Intra uterine growth retardation (IUGR) in asthmatic mother and non asthmatic mother were twice and nil respectively and had no significant relationship ($p>.155$).

In addition to that pre term labor occurred more in asthmatic group (16.3%) than non asthmatic group (7.1%) and had statistical difference ($p<.046$). Further more asthmatic mother (23.5%) had to face more caesarian section operation in delivery their baby than the non asthmatic mother (11.2%) and there was a statically difference ($p<0.024$).

No case maternal mortality was seen in the both asthmatic and non asthmatic group of study population.

In the fetal outcome, it was found that about forty five percent (44.9%) asthmatic mother delivered baby who had low birth weight (<2.5kg wt) and the occurrence of low birth weight in non-asthmatic mother was eighteen percent (18.4%) and there was a affirmative relationship ($p<0.000$). The mean Apgar score of the baby of asthmatic mother was 7.65 with standard deviation (\pm) 1.01 and that in the baby of non-asthmatic mother was 8.36 with standard deviation (\pm) 0.502 and had a statistical association ($p<0.000$). The occurrence of hypoglycemia in neonates was found more in asthmatic mother (14.3%) than that of the non-asthmatic mother (5.1%) having a significant difference ($p<0.030$). Like maternal case, there was no fetal as well as neonatal mortality was occurred here also.

Table-III
Distribution of the respondents by maternal pregnancy outcome

Name of the Characteristics	Asthmatic group	Non asthmatic group	p value
Pre term labor	16(16.3%)	7(11.7%)	0.046
IUGR	02(2.0%)	00(0%)	0.155
Caesarian section	23(23.5%)	11(11.2%)	0.024

Table-IV
Distribution of the respondents by maternal pregnancy outcome

Name of the Characteristics	Asthmatic group	Non asthmatic group	p value
Low birth weight (LBW)	44(44.9%)	18(18.4%)	0
Hypoglycemia	14(14.3%)	5(5.1%)	0.03

Discussion:

Although this study had limitations like area specific data and sample size was so small that the result did not reflect the overall situation of asthmatic mother and their pregnancy outcomes. In this prospective study, we did try to find out some selected maternal as well as neonatal outcomes of the asthmatic mother.

Asthmatic mothers had a greater risk of abortions and had higher rates of UTIs were seen in this study that had likeness to many studies^{6,11,15,16}. and frequency of attack was the only difference there. The history of admission by the asthmatic women was found no significantly more in comparison to non asthmatic women of this study which differed from above mentioned studies^{6,11,15-16}.

In this study, we had also noticed that asthma considerably affects pregnancy and its outcome like pregnancy-induced hypertension, pre-eclampsia, and vaginal haemorrhage, pre term labor, mode of delivery like caesarian section, low birth weight, less APGAR score and hypoglycemia in neonates. We also observed that no occurrence of significant intra uterine growth retardation and no maternal or neonatal death happened here.

Some studies had resemblance to the findings of current study and some had not. A number of studies have suggested an increase in the risk of pre-term labour¹⁸⁻²² or low birth weight,^{19,22-24} although two prospective case control studies have not confirmed these findings.^{9,11} Similarly, higher rates of pregnancy induced hypertension or pre-eclampsia^{11,22,25} and caesarean section^{11,21, 22,26} have been reported in some studies, but this may be a consequence of increased surveillance of asthmatic pregnancies rather than a result of maternal asthma. Vaginal bleeding, both APH & PPH, had been reported in some studies^{9,14,28} and no occurrence of Intra Uterine Growth Retardation (IUGR)⁹ There have been reports of increased incidence of neonatal hypoglycaemia,¹¹ and less APGAR Score^{28,29}

On the other hand a lot of study where asthma was found no effect on pre-eclampsia^{9,31}, pre term labor^{9,27,28}, birth weight^{9,27,28}, Apgar score⁹ no maternal or neonatal mortality^{9,30} but have influence over IUGR^{9,27}

Conclusion:

The evidence from this study supports that pregnant asthmatic women may have an increased risk of adverse perinatal outcomes. So special attention should be given to the asthmatic pregnant women. Besides, a wide range of field based longitudinal study should be carried to evaluate the actual influence of the asthma affecting the pregnancy, labor as well as its all outcomes.

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CASE REPORT

Kartagener's Syndrome in a 18 Years Male Patient - A Case Report

Samir C Majumder¹, Md.Hafizur Rahman², Md.Azraf Hossain Khan³

Abstract :

Lower Respiratory Tract Infections (LRTI) are common problem in our country.In recurrent LRTI the cause may be either general impairment of immune mechanism,abnormalities of mucus or abnormalities of cilia.

Rony,16 years old male patient hailing from Puthia,Rajshahi presented with complain of recurrent cough with sputum,breathlessness,fever, headache and running nose since childhood.On examination,clubbing(+),breath sound vesicular with prolong expiration,bilateral basal coarse crepitations,heart sounds best heard on right side of chest.CxR shows dextrocardia and bilateral bronchiectatic changes in both lower zones,more on right side.HRCT scan of chest revealed bilateral bronchiectatic changes & situs inversus.CT scan of PNS consistent with bilateral maxillary sinusitis.Earlier he was treated with different antibiotics and a course of anti -TB drugs(Cat-1}but the response was only partial and temporary.From clinical picture,sinusitis,bronchiectasis and situs inversus the patient was diagnosed as Kartagener's Syndrome.

[Chest & Heart Journal 2009; 33(2) : 138-139]

Introduction:

Kartagener's Syndrome is an autosomal recessive disorder characterized by dextrocardia ,bronchiectasis,sinusitis¹.The condition was described for the first time by Siewert in 1904.but the details of the condition was given by Manes Kartagener in 1933 and thus known as Kartagener's Syndrome.The basic problem is defective movement of cilia .Males are generally infertile because of immotile sperms^{2,3}, however some males have completely normal spermatozoa⁴.

Case History:

A 16 years old male patient presented with productive cough,running nose,headache with episodic fever and worsening of symptoms since childhood.On examination, digital clubbing present,febrile,wheezy chest and bilateral basal coarse crepitations;heart sounds best heard on right side of chest.Investigations showed neutrophilic leucocytosis;ESR-73 mm in 1st hour;no AFB in sputum samples;right lobe of liver in left side &

spleen in right side of abdomen in abdominal ultrasound;dextrocardia with bronchiectatic changes in lower zones of both lung fields and fundal gas in right subdiaphragmatic area in CxR;mucosal thickening with opacified maxillary sinuses in X-ray PNS. HRCT scan of chest revealed bilateral bronchiectasis in both lower zones.

All routine investigations were done except semen analysis for sperm motility as the patient was unmarried and unwilling to do so.

Treatment history revealed that he received several courses different antibiotics, antihistamin, bronchodilators and 6 month course of Anti-TB drugs even,but the response was partial and temporary.

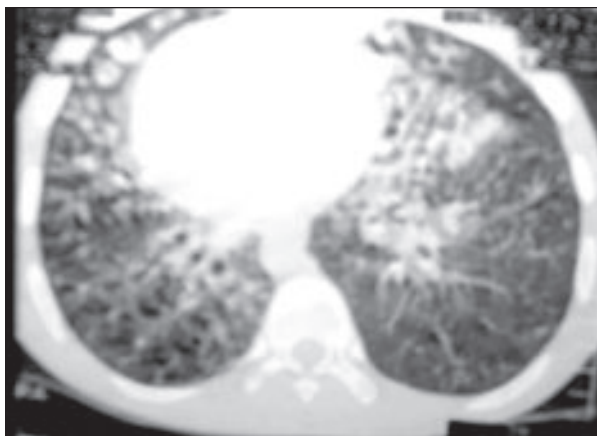
The case was discussed radiologist.Considering the clinical scenario, sinusitis, bronchiectasis and situs inversus the patient was diagnosed as Kartagener's Syndrome.The condition was explained to patient and his father and given management accordingly.

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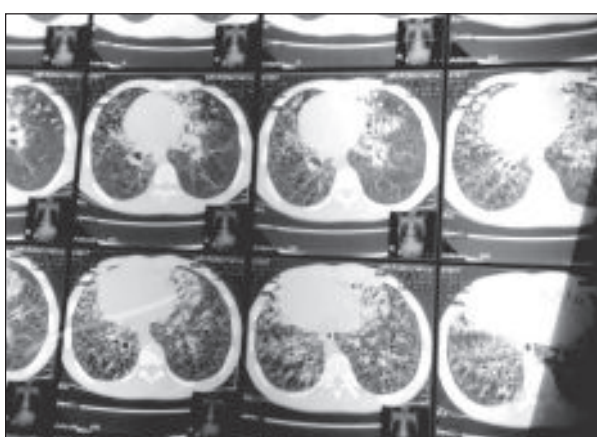
X-Ray Chest P/A view



HRCT scan of Chest(close view)



X-Ray PNS



HRCT scan of Chest (series)

Discussion:

Kartagener's Syndrome or Immotile Cilia Syndrome, a variant of Primary Ciliary Dyskinesia (PCD) is a rare autosomal recessive genetic disorder caused by defect in the lining the respiratory tract, sinuses, Eustachian tubes, middle ears and fallopian tubes. Electron microscopy shows abnormal arrangement of ciliary tubules and absence of dynein arms at the base of the cilia².

Abnormal ciliary motility results in inadequate clearance of bacteria from the air passages resulting an increased risk of infection and causing bronchiectasis. Patients with Kartagener's Syndrome may have either situs solitus i.e, dextrocardia only or situs inversus totalis where all the viscera are on the opposite side⁵ including left sided appendix .

The patient in this case was having situs inversus totalis. Demonstration of abnormal ciliary movement needs electron microscope studies of biopsies obtained from nasal mucosa or trachea. However these procedures are invasive

and available in specialized centres, therefore, the diagnosis of Kartagener's Syndrome in this case was clinical supported by imaging studies.

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ORIGINAL ARTICLE

Outcome of the Capitonage and non-Capitonage Procedure for Pulmonary Hydatid Cyst Surgery

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[*Chest & Heart Journal 2009; 33(2) : 87-93*]

Introduction:

Pulmonary hydatid cyst is a zoonotic disease with worldwide distribution. Most individuals who contract this parasite are young and majority of patients are less than 40 years of age¹. In man, hydatid disease affects the liver in 50 to 60% the lung in 18 to 35% of cases. The Pulmonary hydatid disease affects the rightlung in 60% of cases, 30% exhibit multiple pulmonary cysts, 20% bilateral cysts and 60% are located in the lower lobes².

Small simple cyst located peripherally usually remains asymptomatic. Symptomatic patients may present with chest pain, cough, haemoptysis, dyspnea, fever and respiratory distress¹.

Surgical methods for dealing with pulmonary hydatid cysts include enucleation of intact cysts. Closure of the bronchial opening done by muscle pledgeted suture or by simple 3-0 silk. After bronchial opening closure the remaining cavity can be obliterated by capitonnage. Capitonnage is the procedure by which residual cavity is obliterated by imbricating sutures form with in (separate purse String sutures that is places into the cavity from deepest level to the surface). The impact of capitonnage on surgical out come is unknown and the technique continues to be performed at the choice of the surgeon³. Some surgeons preferred to keep the cavity open after closing of the bronchial opening. Post-operative complication are

pronged air leak (air leak>7 days), empyema and wound infection³.

Hypothesis

Enucleation of pulmonary hydatid cyst without capitonnage yields better surgical outcome.

Aims and objectives

To compare the outcome of the capitonnage and non-capitonage procedure for pulmonary hydatid cyst surgery.

Surgical treatment of pulmonary hydatid cyst:

The current treatment of hydatid disease of the lung is complete excision of the disease process with maximum preservation of lung tissue⁴.

Hucubrahimoglu et al⁵ in his series of 91 patients, enucleation plus capitonnage was the most frequently performed operative technique followed by enucleation plus closure of bronchial openings, pericystectomy plus capitonnage, decortication, lobectomy and segmentectomy. There was no mortality among the patients but only 5 developed early postoperative complications (1 haemorrhage, 1 prolonged air leakage and 3 patients with atelectasis).

Ahsan et al⁶ in his 110 cases, all of the patients underwent enucleation of the cyst along with closure of the feeding bronchus either with Teflon, free muscle flap or direct closure without capitonnage. Postoperative morbidity was detected

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in 9 patients (6%). There was no mortality in that series.

Turna et al.⁴ in his series of 71 patients with pulmonary hydatid cyst, enucleation with capitonage were performed in 39 patients and 32 patients were performed only enucleation with closure of bronchial openings without capitonage. There was no significant difference between groups in the development of empyema and prolonged air leakage. There was also no significant difference in the rate of recurrence.

A lack of improvement in the radiologic lesion with time and a patient coming from an endemic area were other supporting factor¹. Pre operative evaluation is done by means of physical examination, hematological and biochemical examination, chest Xray, ECG, Spirometry, CT Scan of the chest and upper abdomen⁷. For anesthetic management single lung ventilation is essential and is best provided with the use of a standard disposable Robert Shaw double lumen endotracheal tube⁵. A posterolateral thoracotomy incision the fifth or sixth inter costal space is accomplished. After the cyst is identified it is surrounded by 1% povidone iodine impregnated gauze to prevent seeding of possible daughter cysts. Intact cysts are enucleated and bronchial opening is closed with 3-0 polyglactin. Some patient underwent enucleation of the cyst with obliteration of cavity by capitonage⁴. Serious post operative complication of perforated hydatid cyst are extended air leak, empyema, bronchopleural fistula, atelectasis and pneumonia³.

Materials and Methods

The study was done in the Department of Thoracic surgery, NIDCH Mohakhali, Dhaka from July 2004 to June 2006.

This was a prospective non randomized consecutive cross sectional study.

A total number of 43 patients were selected for this study having

Group-I = 23 (Enucleation of cyst with closure of bronchial opening).

Group-II = 20 (Enucleation of cyst with capitonage).

The following variables were studied.

Demographic variables: Age, Sex.

Clinical variables: Cough with sputum, Cough without sputum, Chest pain

Haemoptysis, Respiratory distress

Preoperative variables: Side of lungs affected, Lobe affected, Number of cyst, Condition of the cysts, Type of operation.

Post Operative variables: Haemorrhage, Prolonged air leakage, Empyema, Wound infection, Bronchopleural fistula, Hospital stay (>15 days), Complication at 6 months follow up

Operative management

All the patients were carefully assessed preoperatively. Sputum was cultured and treated with appropriate antibiotics when needed. All patients undergone chest physiotherapy with incentive spirometer before operation. Blood transfusion and nutritional supplement were given when required. Systemic antibiotic was started at the time of induction of anaesthesia and continued postoperatively for 10 days.

Follow up

All patients were followed up for six months at monthly interval. In every follow up patients were evaluated clinically and radiologically. Clinically any morbidity such as cough, sputum production, haemoptysis, febrile episodes were noted. Radiologically any evidence of space infection, any suspected lesion or recurrence of pulmonary hydatid cyst was noted. However all information of the patient were recorded in an individual patient data collection sheet.

Data Collection

All relevant data were collected from each participant using predesigned individual data sheet. A major data sheet was compiled and prepared form information gathered through individual data sheet for complete evaluation.

Data Analysis

Collected data were expressed as mean+SD. Statistical analysis was done using computer based programme SPSS for windows version 10.0. Unpaired students 't' test, chi-square test and proportionate 'z' test were used for statistical

analysis. The p-value of less than 0.05 was considered statistically significant.

Results

A total of 43 patients of pulmonary hydatid cysts cases were taken in our study. The findings of the study derived from data analysis are presented below.

It has been shown that 41.8% of the patients were between 20-30 years of age followed by 23.3% between 10-20 years 18.6% between 30-40 years, 9.3% below 10 years and 7% was above 40 years of age. The mean age was 25+1.4 years with the lowest and the highest ages being 7 and 45 years respectively (Table I).

Table-I
Distribution of patients by age (n = 43)

Age in years	No	%
< 10	4	9.3
20-Oct	10	23.3
20-30	18	41.8
30-40	8	18.6
>40	3	7

* Mean age was 25.0+1.40 years: range : (7-45) years.

65% of the patients were female and the rest 35% were male (Fig. I).

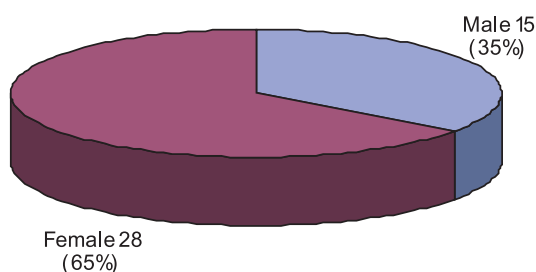


Fig.-1: *Distribution of patients by sex (n = 43).*

We observed that distribution of patients by clinical features. Nearly one quarter 23.2% of the patients were asymptomatic. The most predominant complaints of the patients were chest pain 76.7% followed by cough without sputum 46.5%, haemoptysis 30.2% and respiratory distress 27.9% Cough with sputum 11.6% (Table II).

Table-II

Distribution of patients by clinical presentation (n = 43)

Clinical presentation	No	%
Asymptomatic	10	23.2
Cough with sputum	5	11.6
Cough without sputum	20	46.5
Chest pain	33	76.7
Haemoptysis	13	30.2
Respiratory distress	12	27.9

* Mean age was 25.0+1.40 years: range : (7-45) years.

Of the 43 patients 63% were diagnosed by X-ray chest, 28% by CT Scan of chest and the rest 9% by intraoperatively (Fig 2).

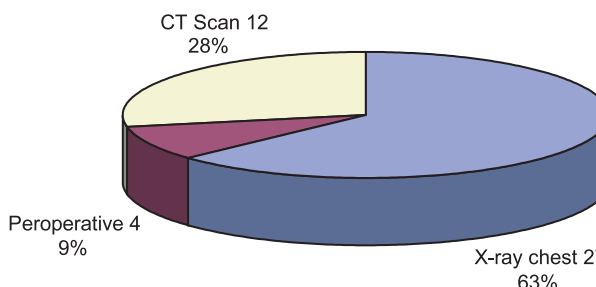


Fig 2: *Distribution of patients by diagnostic work up.*

We found that 65.1% patients had right lung involvement, 23.3% left lung involvement and the rest 11.6% both lungs involvement (Table III).

Table III

Distribution of patients side of lung affected (n = 43)*

Side of lung	No	%
Right	28	65.1
Left	10	23.3
Both	5	11.6

It is observed that in the right lung 6 (18.2%) had upper lobe affected, 5 (15.1%) had middle lobe affected and 22(66.7) lower lobe affected. In the left lung 11(73.3%) had lower lobe involvement, while the rest 4(26.7%) had upper lobe involvement (Table IV).

Table-IV

Distribution of patients side of lung and lobe affected.

Side of lung	Lobe of lung		
	Upper n(%)	Middle n (%)	Lower n (%)
Right	6(18.2)	5(15.1)	22(66.7)
Left	4(26.7)	-	11(73.3)

It is observed overwhelming majority 95.3% of the patients had single cyst and the rest 4.7% had 2 cysts (Table V).

Table-V
Distribution of patients by number of cysts found (n = 43)

Number of cysts	No	%
1	41	95.3
2	2	4.7

It demonstrates that 58% of the patients had intact cysts and the rest 41.9% exhibited ruptured cysts (Fig. 3).

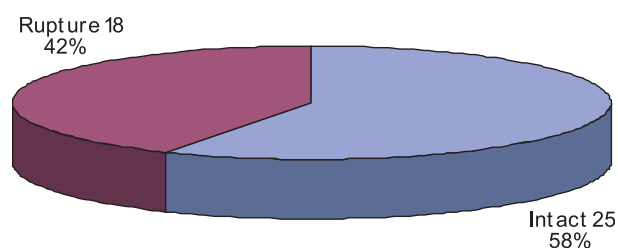


Fig.-3: *Distribution of patients by condition of cysts.*

We observed that 53.4% of the patients underwent enucleation of the cysts with closure of the bronchial opening, and the rest 46.6% enucleation of cysts with capitonnage (Table VI).

Table-VI
Distribution of patients by types of operation (n = 43)

Type of operation	No	%
Enucleation of cysts with closure of bronchial opening	23	53.4
Enucleation of cyst with capitonnage	20	46.6

It has been shown that out of 43 patients 16.3% developed prolonged air-leakage, 4.5% had to stay in the hospital for a prolonged time, empyema, bronchopleural fistula and wound infection each was 2.3% (Fig. 4).

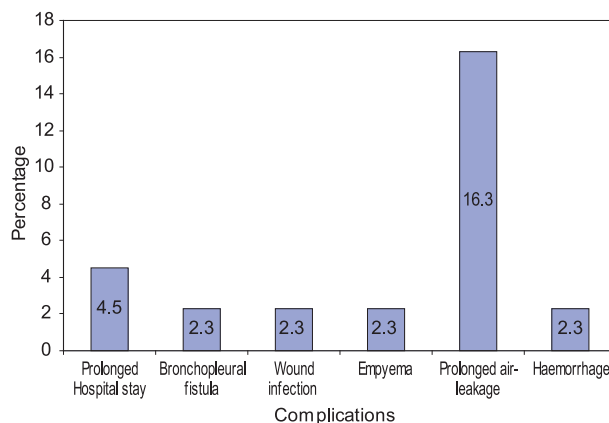


Fig.-4: *Distribution of patients by complications.*

It has been found that postoperative complications, hemorrhage occurs in one patient where Enucleation of cyst with capitonnage done. But in Enucleation of cyst with closure of bronchial opening no haemorrhage occurs. It was statistically not significant between the groups ($p > 0.05$) (Table VII).

Table-VII
Postoperative complication (haemorrhage) between groups (n = 43).

Groups	Number	Percentage
Enucleation of cyst with closure of bronchial opening (n = 23)	0	00
Enucleation of cyst with capitonnage (n = 20)	1	5.0

It has been found that postoperative complications, prolonged air leakage occurs in 4 patient where Enucleation of cyst with capitonnage done. But in Enucleation of cyst with closure of bronchial opening prolonged air leakage occurs in 3 patients. It was statistically not significant between the groups ($p > 0.05$) (Table VIII).

Table VIII
Postoperative complications (Prolonged air leakage) between groups (n = 43).

Type of operation	Number	Percentage
Enucleation of cysts with closure of bronchial opening (n = 23)	3	12.9
Enucleation of cyst with capitonnage (n = 20)	4	20.0

It has been found that postoperative complications, Empyema occurs in one patient where Enucleation of cyst with capitonnage done. But in Enucleation of cyst with closure of bronchial opening no empyema occurs. It was statistically not significant between the groups ($p>0.05$) (Table IX).

Table IX
Postoperative complications (Empyema) between groups.

Groups	Number	Percentage
Enucleation of cysts with closure of bronchial opening (n = 23)	0	00
Enucleation of cyst with capitonnage (n = 20)	1	5

It has been found that postoperative complications, no wound infection occurs in the patients where Enucleation of cyst with capitonnage done. But in Enucleation of cyst with closure of bronchial opening wound infection occurs in one patient. It was statistically not significant between the groups ($p>0.05$) (Table X).

Table-X
Postoperative complications (Wound infection) between groups.

Groups	Number	Percentage
Enucleation of cysts with closure of bronchial opening (n = 23)	1	5
Enucleation of cyst with capitonnage (n = 20)	0	0

It has been found that postoperative complications, bronchopleural fistula occurs in one patient where Enucleation of cyst with capitonnage done. But in Enucleation of cyst with closure of bronchial opening no bronchopleural fistula occurs. It was statistically not significant between the groups ($p>0.05$) (Table XI).

Table-XIII
Comparison of complications between groups (n = 43)

Postoperative Complications	Type of operations		P- value
	Enucleation of cyst with closure of bronchial opening (n = 23)	Enucleation of cyst with capitonnage (n = 20)	
Haemorrhage	0	1 (5.0)	0.059
Prolonged air leakage	3 (12.9)*	4 (20.0)	0.614
Empyema	0	1 (5.0)	0.059
Wound infection	1 (4.3)	0	0.121
Bronchopleural fistula	0	1 (5.0)	0.059
Hospital stay (>15 days)	0	2 (20.0)	0.030 ^s

* Figures in the parentheses denote corresponding %.

Chi-square (X^2) Test was done to analyze the data: ¶ Student' t-test was done to analyze the data and the level of significance was 0.05.

Table-XI

Postoperative complications (Bronchopleural fistula) between groups.

Groups	Number	Percentage
Enucleation of cysts with closure of bronchial opening (n = 23)	0	0
Enucleation of cyst with capitonnage (n = 20)	1	5

It has been found that postoperative complications, Hospital stay (>15 days) observed in two patients where Enucleation of cyst with capitonnage done. But in Enucleation of cyst with closure of bronchial opening no hospital stay (>15 days) observed. It was statistically significant between the groups ($p>0.05$) (Table XII).

Table XII
Postoperative complications (Hospital stay)]>15 days] between groups (n = 43).

Groups	Number	Percentage
Enucleation of cysts with closure of bronchial opening (n = 23)	0	0
Enucleation of cyst with capitonnage (n = 20)	2	10

It has been found that out of 23 patients who were enucleated with closure of bronchial opening 12.9% of them developed air-leakage and 4.3% developed wound infection during postoperative period. Of the 20 patients who were subjected to enucleation of cyst with capitonnage, 20% of them developed air-leakage followed 5% haemorrhage and 5% empyema. None of the patient in the former group had to stay in the hospital for >15 days, where as 10% of the latter group had to stay in hospital for >15 days. The hospital stay was found to be significantly higher in the later group compared to the former group ($p<0.05$) (Table XIII).

It has been found that out of outcome after 6 months of follow up between enucleation of cyst with closure of bronchial opening and capitonnage group. Of the total 43 patients 12 patients were lost during follow up. From the remaining 31 patients none but a single case of capitonnage group developed recurrence of cyst (Table XIV).

Table-XIV

Comparison of outcome after 6 months of follow up between enucleation of cyst with closure of bronchial opening and capitonnage group (n = 31)

Postoperative Complications	Groups		P- value
	Enucleation of cyst with closure of bronchial opening (n = 17)	Enucleation of cyst with capitonnage (n = 14)	
Cough	00	00	-
Haemoptysis	00	00	-
Empyema	00	00	-
Recurrence	00	1 (7.14)	0.21

* Figures in the parentheses denote corresponding %.

Chi-square (X^2) Test was done to analyze the data: and the level of significance was 0.05.

Discussion:

In our series, 43 patient having pulmonary hydatid cyst were studied, with the mean age of 25+1.4 years. Turna et al.⁴ (2002) reviewed 75 patients and showed average age 30.2+17.4 years, in his observation. Age of our study group was consistent with that series.

In our study among 43 cases, 65% of the patients were female and 35% was male. Hacubrahimoglu et al. (2003) in his series shown 93 patient, 48 was male and 43 was female. Ahsan et al. (1997) reviewed 137 patients and showed in male incidence 57% and female 43% respectively. The higher incidence in female in our study had been found but above studies suggest male predominance, so further long term study with adequate sample size is required to comment female predominance in our study.

The most predominant complaints of the patients were chest pain 76.7% followed by cough without sputum 46.5%, haemoptysis 30.2%, respiratory distress 27.9%, fever 23.2% and cough with sputum 11.6%. Dakak et al. (2002) in his study of 422 patients showed the presenting complaints of chest pain 52% fever 34%, cough without sputum 56%, cough with

sputum 6% haemoptysis 14% respiratory distress 11% and 20% were asymptomatic. Our observation was more or less similar to his series.

We used standard posterolateral thoracotomy in cases of pulmonary hydatid cyst surgery. In our series 65.1% patients had right lung involvement, 23.3% left lung involvement and the rest 11.6% both lungs involvement. Ahsan et al.⁶ showed in his series of 137 patients, cyst located in the right lung in 57.06% left lung 31.06% and bilaterally 6.05% Morar and Feldman (2003) in his study shown pulmonary hydatid cyst affects right lung in 60% of the cases. Our study was similar to the above series.

In our study in the right lung 18.2% had upper lobe affected, 15.3% had middle lobe affected and 66.7% lower lobe affected. In the left lung 73.3% had lower lobe involvement, while the rest 26.7% had upper lobe involvement. Dakak et al. (2002) in his series 422 patients cyst located in right upper lobe 58, middle 46 and right lower lobe 105 cases and left upper lobe 66, left lower lobe 87. Hacubrahimoglu et al. (2003) in his series 96 patients, right upper lobe 19, middle lobe 11, lower lobe 24 and left upper lobe 21, left lower lobe 21. The location of the pulmonary hydatid cyst predominance of right lower lobe involvement had been shown in above series. We had also observed same trend of the disease.

It has been shown that majority 95.3% of the patients had single cyst and rest 4.7% had 2 cyst. Dakak et al.⁷ in his 422 patients 296 cases presented solitary pulmonary cyst and other cases had multiple cyst in 1 or 2 lobes. In our series we did not find >2 cyst in 1 or 2 lobes.

In this study 53.4% underwent enucleation of the cyst with closure of the bronchial opening without capitonnage and rest 46.6% underwent enucleation of cyst with capitonnage. The operation was done by almost same quality of surgeons. Almost 100% of the patients had immediate cure. The survival rate was 100% Among the 23 patients who were enucleated with closure of bronchial opening, 3 of them developed air leakage, 1 developed wound infection and none of the patient in this group had to stay in the hospital >15 days. Of the 20 patients who were subjected to enucleation of cyst with capitonnage, 4 of them developed air leakage followed by 1 haemorrhage, 1 empyema, 2 of this group had to stay in hospital for >15 days and 1 developed recurrence. Turna et al.³ showed in his 71 patients 32 were performed enucleation of the cyst and closure of bronchial openings without capitonnage and 39 patients were performed enucleation with

capitonnage. Of the 32 patients who were subjected to enucleation without capitonnage 4 of them develop air leakage, 1 empyema and non of them developed haemorrhage. Of the 39 patients, who were subjected to enucleation of the cyst with capitonnage, 5 of them developed air leakage and 3 of them developed recurrence. Our complication rates were similar to this above series. Ahsan et al.⁶ and Turna et al.⁴ reported best operative method is enucleation of cyst without capitonnage. The above procedure were adopted in 23 cases of our group and the results are satisfactory.

Turna et al.⁴ stated that approximating and suturing cavity edges is not necessary because the pulmonary parenchyma obliterates the space and the surface of the lung at the site of cavity is covered by pleura. Capitonnage provides complete of obliteration of the pericystic cavity to prevent air leak from residual bronchial openings. Without capitonnage, the wall the pericystic cavity is supposed to be covered by epithelial cells for an uncertain length of time. Capitonnage prolongs the operation time and increases the risk of haemorrhage. Enucleation is the preferred method in our institution but is not favoured by others.

Summary and Conclusion

In our study of the 43 patients male 15 and female was 28. Most of the patients were presented with chest pain 76.7% followed by cough without sputum 46.5%, haemoptysis 30.2% and respiratory distress 27.9% cough with sputum 11.6% and 23.2% were asymptomatic. The right lung 65.11% affected more than left lung 23.3% and bilateral pulmonary hydatid cyst was found in 11%.

After preparation of surgery, all patients underwent standard posterolateral thrototomy where enucleation of the cyst with closure of the bronchial opening was done in 53.4%, enucleation of the cyst with capitonnage in 46.6% patients. Postoperative patients were managed accordingly and operative outcome was observed. Patients with satisfactory outcome were discharge on 12th postoperative day after removing stitches. All patients were followed up period of 6 months. On each follow up, patients were reviewed for their previous symptoms, cough, haemoptysis and radiologically any empyema or any recurrence of pulmonary hydatid cyst.

Postoperatively 23 patients who were enucleated with closure of bronchial opening 12.9% of them developed air leakage and 4.3% developed wound

infection and non of this group had to stay in the hospital for >15 days. Of 20 patients who were subjected to enucleation of cyst with capitonnage, 20% of them developed air leakage followed by 5% haemorrhage and 5% empyema and 10% of this group had to stay in hospital >15 days. In our study hospital stay was found to be significantly higher in the enucleation of cyst with capitonnage. There was no significant difference between groups in the development of haemorrhage, empyema, wound infection and bronchopleural fistula. There was also no significant difference in the rate of recurrence.

In conclusion, although surgical treatment is effective in patients with ruptured as well as intact cyst for treatment of pulmonary hydatidosis, surgical intervention before rupture of the cyst is essential. Regardless of whether symptoms are present, all pulmonary hydatid cysts should be surgically treated as soon as they are diagnosed in order to avoid complication.

Recommendation: Enucleation of pulmonary hydatid cyst with closure of bronchial opening should become standard surgical technique for management of pulmonary hydatid cyst.

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ORIGINAL ARTICLE

Renal Revascularization by Percutaneous Renal Intervention with Stenting for Atherosclerotic Renal Artery Stenosis: a Retrospective study and its out come

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Abstract

Objective: Renal artery stenosis is an established cause of hypertension and renal insufficiency. Renal intervention with stenting has been shown to improve blood pressure and renal function of patients with atherosclerotic renal artery stenosis. The aim of this study was to see the extent of effectiveness of renal artery stenting on renovascular hypertension and renal impairment. Patients and Methods: This was a retrospective observational study and data were collected from hospital records of National Heart Foundation Hospital and Research Institute, a tertiary hospital in Dhaka, Bangladesh .Between the period January 2003 and August 2009, total 136 patients who had atherosclerotic renal artery disease were offered renal angioplasty and stenting .Of this patients, 88 (64.7%) were male and 48 (35.3%) were female. Traditional risk factors were analyzed accordingly. Blood pressure, renal function and antihypertensive medication were documented prior to procedure and at regular follow up of a number of patients. Results: Of the 136 patients, 106 (78 %) had ostial and 30 (22 %) had nonostial lesion; besides, 124 patients had severe disease and 12 patients had moderate disease. Out of 136 hypertensive patients, 60 patients were followed up for hypertension and blood pressure were taken at 1, 3 and 6 months after the procedure.40 (66.67%) patients showed improvement in blood pressure while 20 (33.33%) patients remain unchanged and none of the patients showed deterioration in blood pressure ;15 patients having hypertension with renal impairment(serum creatinine level >1.3 mg/dl) were evaluated for renal function response after 1 month and between 3 and 6 months of procedure;5 (33.33%) patients showed improvement,7patients (46.67%)remain unchanged and 3 patients(20 %) had worsening of renal function.

Conclusions: Renal intervention is effective and safe for controlling renovascular hypertension and this approach may also be of value in preventing further deterioration of renal impairment.

Key Words: Renal angioplasty. Renal artery stenting, Atherosclerotic renal artery stenosis

[Chest & Heart Journal 2009; 33(2) : 94-101]

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Introduction:

Considerable attention has been devoted during the last two decades to the topic of renal artery stenosis due to atherosclerosis. Renal artery stenosis accounts for approximately 5% of all cases of hypertension^{1,2,3} and has been implicated as a key factor in the decline of renal function⁴⁻⁶. Restoration of vessel patency reduces the need for antihypertensive medication^{7,8} and may slow the progression of renal failure^{9,10}.

Traditional therapeutic modalities that include drug therapy and surgical revascularization have too many shortcomings. Medicines frequently fail to control the patient's blood pressure adequately despite polypharmacy rather it may cause adverse effects and patients may be non compliant. Moreover lowering the blood pressure in presence of severe renal artery stenosis may lead to ischaemic renal atrophy^{2, 11,12}.

Surgery imparts considerable morbidity and results vary. The associated need for general anaesthesia may cause complications in patients who are often poor candidates because of diffuse atherosclerosis or renal insufficiency. Nonetheless, the correction of renal artery stenosis is considered the treatment of choice whenever feasible^{2, 11-12}.

Catheter- based procedures began in 1964 when Charles Dotter initially developed PTA for treating peripheral vascular atherosclerosis^{13,14}. Since its introduction in 1978, percutaneous trans-luminal renal angioplasty (PTRA) has emerged as a highly effective technique for the correction of renal artery stenosis. Renal angioplasty has notable physiologic, psychologic and economic advantages over other treatment modalities, and it should now be considered the therapy of choice for renovascular hypertension^{13,14}

PTRA since rapidly evolved into a widely used, versatile, and dependable vascular interventional technique. Excellent result can now be achieved in the renal arteries if patient are well selected and if experienced operator perform the procedure^{13,14}.

Patients and Methods

This was a retrospective observational study. Data were collected from hospital records of National Heart Foundation Hospital and Research Institute, a tertiary hospital in Dhaka Bangladesh. 136 patients had atherosclerotic renal artery disease with hypertension and offered renal angioplasty

and stenting during the period January 2003 and August 2009. 88 (64.7%) patients were male and 48 patients (35.3%) were female. Traditional risk factors were analyzed accordingly. No patient had fibromuscular dysplasia.

The patients with haemodynamically significant renal artery stenosis was defined as moderate (50 to 69 %) stenosis with > 20 mm Hg systolic trans-lesional gradient, or a severe stenosis with a visually estimated diameter stenosis of > 70%¹⁵.

Measurement of stenosis involved comparison of minimal luminal diameter within the stenosis to a normal reference segment. For ostial stenotic lesions the reference segment was considered to be a normal appearing distal segment unaffected by post stenotic dilatation. For nonostial disease the reference segment was measured proximal or distal to the stenosis in a normal appearing portion of the blood vessel¹⁶.

Ostial lesions were defined as stenosis located within 5 mm of the aortic lumen and caused by atherosclerotic disease of the aorta¹⁷. The pressure gradient was determined through placing a 4F end hole catheter into the renal artery distal to the stenosis to compare that pressure with the simultaneously measured aortic pressure obtained through an 8F guiding catheter¹⁶. 60 patients for hypertension and 15 patients for hypertension and renal impairment (serum creatinine level >1.3 mg/dl) reported were followed up at 1 and between 3 and 6 months after the procedure.

Procedural Protocol

After standard retrograde femoral access and systemic heparinization (5000 U) a soft 0.035 inch hydrophilic guide wire was advanced across the

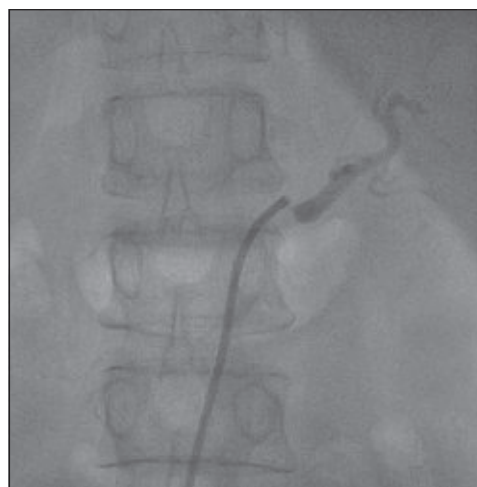


Fig.-1: Critical Ostial Lesion Renal Artery)

lesions through the 7 French guiding catheter and catheter was then pushed forward over the stenosis, the soft guide wire was then replaced with a 0.014 inch guide wire for better support.

A balloon dilation catheter was advanced over the wire and across the stenosis; the selected balloon diameter was equal to or slightly larger than the estimated diameter of the normal renal artery. Balloon-expandable stent (Genesis Cordis, Nefro Balton etc) was placed stent exactly the same as the caliber of the renal artery.

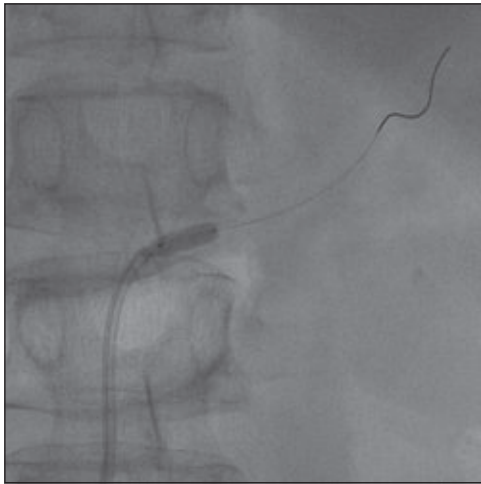


Fig.-2: *Balloon dilatation after wiring*

For ostial lesions, we attempted to have approximately 1.0 to 1.5 mm of the stent protruding into the aorta to reduce the incidence of recurrence of stenosis⁹.

Complete technical success after PTRAs and stent placement was defined as an estimated residual stenosis of less than 30% according to angiographic results and a trans-stenotic pressure gradient lower than 10 mm¹⁷.



Fig.-3: *Stent deployment in progress*

Continuous monitoring of patients was limited to electrocardiogram, arterial oxygen percent saturation (Sao₂) via oximetry, and arterial pressure measurements during the interventional procedure and up to 24 hrs after the procedure. Patients were managed with bed rest and continued anticoagulant therapy for 12 hours after the procedure and were discharged on the following day with standard antiplatelet Fig:4- Stent deployment in progress regimen, in addition to other medication.

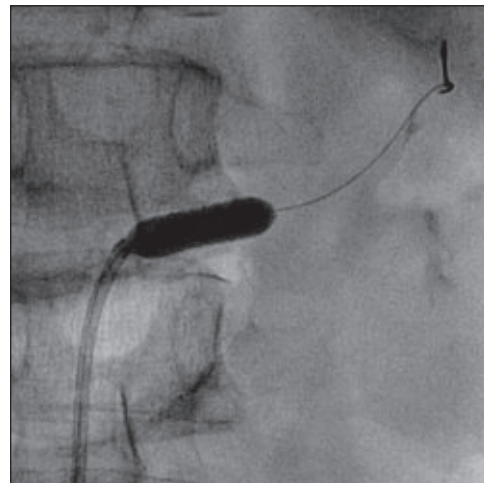


Fig.-4: *Stent deployment in progress*

Criteria for evaluating the effectiveness of the procedures

A patient was considered cured (diastolic pressure < 90 mm Hg without medication), improved (decrease



Fig.-5: *Angiogram after stent deployment*



Fig.-6: Critical Lesion in body (L. Renal Artery)

of 20 mm Hg in systolic/diastolic blood pressure while the patient was taking the same or less medication), unchanged (this did not apply), or worse (systolic blood pressure became uncontrolled or another medication was added¹⁷. Patients were evaluated for renal function response after 1 month and between 3 and 6 months if their serum creatinine level was 130 micro mol/L or more before the intervention. Responses was classified as improved renal function (decrease in serum creatinine level of 15% or more) no change (serum creatinine + 14 %), or deterioration of renal function (increase in serum creatinine level of 15 % or more). Patients' blood pressure were measured at 1 and between 3 and 6 months after the procedure.¹⁷.



Fig.-7: Balloon dilatation after wiring



Fig.-8: Stent deployment in progress

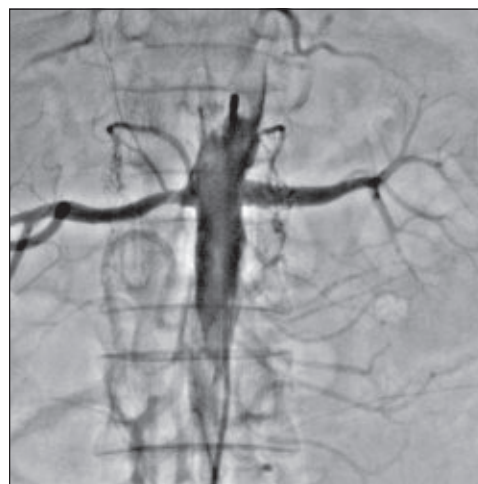


Fig.-9: Angiogram after Stent deployment

Table I

Background characteristics of the patients:

	Male	Female
	Mean ±SD	
Age	59.28±11.81	57.52±9.17
Range	25-80	25-71
BMI	23.45±2.93	25.03±3.68
Range	16.79- 33.30	

Table-II

Sex distribution of the patients

Sex	Male		Female	
	N	%	N	%
	88	64.7	48	35.3

Results

Among 136 patients, age range were 25 to 80 years in male and 25 to 71 years in female, mean body mass index was 23.45 ± 2.93 for male and 25.03 ± 3.68 for female and range were 16.79 to 33.30 (Table-I & Table –II). 122 patients had unilateral, 58 (42.6 %) left, 64 (47.1%) right and 14 patients (10.3%) had bilateral renal artery stenosis (Table–III). Considering the risk factors, 49 patients (36%) were diabetic, 14 patients (10.13%) were smoker and 2 patients had positive family history of hypertension (Table –IV).

Table III
Distribution of stenosis in the artery

	N	%
Left renal artery	58	42.6
Right renal artery	64	47.1
Bilateral	14	10.3

Table-IV
Risk factors among the patients

Risk factors	N	%
Hypertension	136	100
Diabetes mellitus	49	36
Dyslipidaemia	9	6.6
Obesity	7	5.1
Current Smoker	13	9.6
Ex smoker	1	0.7
Family history	2	1.5

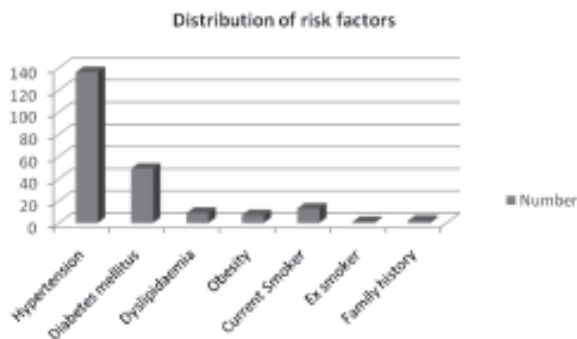


Fig.-2: *Distribution of risk factor among the patients*

Of the 136 patients, 106 (78 %) had ostial and 30 (22 %) had nonostial lesion; besides, 124 patients had severe disease and 12 patients had moderate disease (Table-V&VI).

Table-V
Site of lesion in the artery

Site of lesion	N	%
Ostial	106	78
Non ostial	30	22

Table-VI
Distribution of Stenosis in the renal artery

Stenosis	Right renal	Left renal	Bilateral
Moderate (<70)	11	1	-
Severe (e"70)	53	57	14

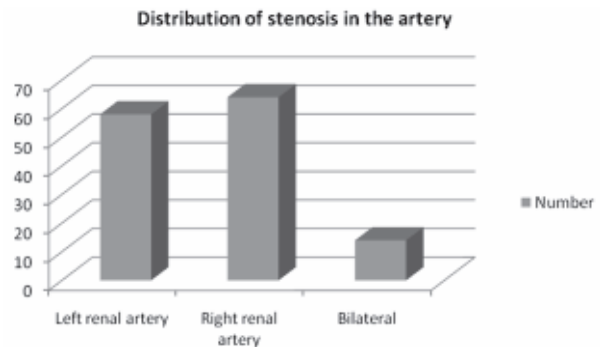


Fig.-2: *Distribution of stenosis in the artery*

Regarding stent size, mean length was 14.5 ± 1.9 mm for left and 14.67 ± 2.98 mm for right renal artery and mean diameter was 6.03 ± 0.700 for left and 6.07 ± 1.04 mm for right renal artery (Table –VII).

Table-VII
Length and diameter of unilateral and bilateral stent (in mm)

	Left renal artery	Right renal artery	Bilateral
	Mean \pm SD		
Length	14.50 ± 1.90	14.67 ± 2.98	1.57 ± 4.83
Diameter	6.03 ± 0.700	6.07 ± 1.04	0.662 ± 1.89

Out of 136 hypertensive patients, 60 patients were followed up for hypertension and blood pressure taken at 1 and between 3 and 6 months after the procedure. 40 (66.67%) patients showed

improvement in blood pressure ,20 (33.33%) patients remain unchanged and none of the patients showed deterioration in blood pressure(Table-VIII)

Table-VIII

Change in Blood pressure among patients with hypertension following the procedure (N=60)

Blood pressure response	Cured	Improved	Unchanged	Worse
Number of patients (%)	0(0)	40 (66.67)	20(33.37)	0

Among the 15 patients with hypertension and renal impairment, 5 (33.33%) patients showed improvement,7 patients (46.67%) remain unchanged and 3 patients(20 %) had worsening renal function(Table –XI).

Table-IX

Change in renal function among patients with renal impairment after the procedure (N=15)

Change in renal function	Improved	No change	Deteriorated
Number of patients (%)	5(33.33)	7(46.67)	3(20)

No major complications were noted during and after the procedures. Post-stenting angiogram did not observe any angiographic signs of distal embolization or intrarenal embolization. Only a very few patients had puncture site bleeding and small haematoma but did not require transfusion.

Discussion:

Atherosclerotic renal artery stenosis occurs much more frequently than previously considered in patients with mild to moderate hypertension, end stage renal disease and diffuse atherosclerosis and this obstructive process is progressive: stenosis become occlusions^{-4, 11} in -15 % of cases, and renal function deteriorates in 10 to 20 % of cases⁻¹¹and the more severe the initial stenosis, the more likely is the progression to occlusion⁻⁴ which correlated with a loss of renal mass⁻¹⁸.

Atherosclerotic renal artery stenosis predominantly affects the most proximal or ostial portion of the renal artery. This atherosclerotic plaque is often in continuity with aortic wall

plaque.⁻¹⁹ Ostial lesion is common in our series i.e. 78 % which is similar to other series.

Clinical suspicion is paramount in identifying renal artery stenosis because the initial presentation is often subtle and progress to a further degree of renal failure or hypertensive sequelae.⁻²⁰

Many series have shown a favorable reduction of antihypertensive medications after the successful resolution of renal artery stenosis^{-9, 21-26} which is very similar to our study. In Rees' study of 28 patients,3 were found to have been cured of hypertension,15 had improved and 10 failed to improve (total benefit, (64 %)·⁹. In Tsang study of 15 patient 9 had improved and 6 failed to improve (total benefit, 60 %)·¹⁷.

Remarkable improvement in creatinine level was not achieved after successful resolution of the renal artery stenosis. This is in accordance with Blum et al's study, in which the renal function in 20 patients who had mild or severe renal dysfunction before the intervention did not change during follow up⁻²⁵.Similarly in Tsang study,10(out of 13 patients) patients had renal impairment before the intervention did not change during follow up¹⁷.This finding is important ,because untreated stenosis may progress in severity, resulting in renal artery occlusion, loss of renal mass, and a subsequent decrease in kidney function⁻²⁶.

However, Boisclair et al reported improved creatinine levels in 7 of 17 patients (44 %) after successful stenting for atherosclerotic renal artery stenosis⁻²⁷.

The goal of surgical and stent revascularization has been restoration of renal artery blood flow to stabilize or improve renal function. However ,the high surgical peri-operative complication rate and the increased periprocedural mortalities ranging from 2.1 % to 6.1%⁻²⁸⁻³¹sharply contrast with those of stent revascularization.

Renal artery stent revascularization procedural results have been demonstrated to be superior to balloon angioplasty^{-32,33}as assessed by hemodynamic trans-stenotic pressure gradient measurement, complication rate, and restenosis rate.

Stent revascularization with its gratifying success rate acceptable procedural risk beneficial impact on

blood pressure control and renal function and excellent follow-up results in patients with normal baseline renal function, may become the procedure of choice for atherosclerotic renal artery stenosis³⁴.

In this study we have demonstrated prevention of further renal function impairment is possible with PTR. Twelve of fifteen patients (80%) who initially had renal function impairment showed either improvement in renal function or remain stable renal function.

Nevertheless, future study will demonstrate whether one can expect improved post-intervention

creatinine levels in patients with renal insufficiency

Conclusions:

Renal angioplasty and stenting is effective and safe for controlling hypertension due to atherosclerotic renal artery stenosis and this procedure may also be of value in improving renal function and preventing further impairment of renal function.

Study limitation:

This is a retrospective observational study and data has been collected from the hospital registry and could not able to follow up all the patients included this study even then it would be inspired to other investigators to see the favorable outcome of percutaneous renal intervention for atherosclerotic renal artery stenosis having renal function impairment.

Acknowledgement

We would like to express our sincere thanks to Dr Farzana Tabassum, Department of Epidemiology and cath lab staffs for their effort to prepare the manuscript.

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ORIGINAL ARTICLE

Comparison between Percutaneous Fine Needle Aspiration Cytology of Lung Tumor & Histopathological Analysis of Resected Specimen of Lung

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Abstract:

Aims: Needle aspiration of pulmonary mass may accurately delineate malignant from non malignant pulmonary lesion. A prospective study was carried out in NIDCH, Dhaka, Bangladesh to evaluate this.

Methods: 96 needle biopsies were done from May 2007 to May 2008 to correlate between needle aspiration cytology and histopathology of resected lung tumor.

Results: 60 patients out of 96 later under went resection. 36 patients were spared from resection, either due to distant metastases or compromised pulmonary function or as found to be benign tumors. There were 51 malignant tumors out of 60. Seven needle biopsies (13.7%, 7/51) were subsequently proved to be malignant. 44 needle biopsies were diagnosed as malignant neoplasm (86.2%, 44/51). 35 specimens showed the same cell type as the needle biopsy (79 percent 35/44). Nine resected specimens varied with the cell type from needle biopsy (20.4%, 9/44). Among nine resected specimens two were small cell and seven were non small cell carcinoma, among the patients only 4 patients (6.6%) developed small pneumothorax but did not require chest tube. Minimal hemoptysis occurred in 5 patients (8.3%).

Conclusions: Needle biopsy accurately indicated a malignant neoplasm in 86.2% cases and specimen from needle biopsy accurately predicted the cell type in 79% of the specimen.

[Chest & Heart Journal 2009; 33(2) : 110-117]

Introduction:

An early diagnosis of lung cancer is very important for proper management and long term survival. A specific diagnosis is difficult to make in case of small pulmonary lesion of few mm of diameter and asymptomatic pulmonary nodule with traditional diagnostic methods often requires such a long period of time that there is a risk of the lesion becoming incurable. 60% of lesion are inflammatory

or of a benign nature. So, the resection may not be necessary¹.

For the treatment of lung cancer like surgery, radiotherapy or chemotherapy histologic diagnosis is mandatory. Additional diagnostic procedure, bronchoscopy, sputum cytology and lymph node biopsy often unrewarding. FOB is important tool for diagnosis and cell type of lung cancer. But it is

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not available in all parts of the country and needs highly skill personal².

Thoracotomy also entail considerable morbidity and mortality which can be avoided if the benign nature of intra pulmonary lesion is diagnosed preoperatively. So, FNAC will be helpful for diagnosis of lung cancer in this situation. FNAC is safe, relatively easier procedure and results can be obtained within short time and it can be done even in remote area in the country with minimum facilities.

Objectives

General objectives:

To find an easier and reliable method for diagnosis of lung cancer.

Specific objectives:

To compare the accuracy of Fine needle aspiration cytology with histopathology of resected lung in lung malignancy.

Materials and Methods

Place of study:

The study was carried out in the department of Respiratory Medicine, National Institute of Diseases of the Chest & Hospital (NIDCH), Mohakhali, Dhaka.

Period of study:

The study was conducted from June 2007 to June 2008.

Type of study:

It was a cross-sectional study.

Study population:

Selected cases of lung cancer that fulfilling the inclusion and exclusion criteria were included in this study.

Sampling technique:

It was a consecutive method of sampling. The patient fulfilling the criteria of exclusion and inclusions.

Criteria for selection of patient:

Criteria of inclusion:

Persistent and gradually increasing radiological shadow measuring at least 3 cm or more in diameter, inspite of three weeks broad spectrum

antibiotic or one month anti TB drugs with or without following symptoms and signs:

1. Cough
2. Chest pain
3. Hemoptysis
4. Weight loss
5. Digital clubbing
6. Lymphadenopathy

Criteria of exclusion:

Significantly disable patient due to poor general condition. Associated systemic or pulmonary diseases, recent myocardial infarction.

Haemorrhagic diathesis, anti coagulant therapy. Sputum specimen positive for AFB.

Extensive metastasis beyond the stage-IIIB in case of non small cell cancer. Extensive disease in case of small cell carcinoma.

Study procedure:

Standard questionnaire has been designed with a view to collecting patients medical records.

Consent taking of the patient:

Written consent from all studied patients was obtained after discussion in details about the study procedure.

Recording of patients information:

In each case information about the patients was obtained and recorded in the questionnaire proforma.

Identification of patients clinically suitable for inclusion as cases:

The accumulated information were analyzed to find out the patients who meet clinical inclusion criteria.

Laboratory investigation:

Necessary investigation done for selection of cases included the following-

- X-ray chest P/A and lateral view
- Blood for TC, DC, ESR Hb%
- Sputum for malignant cell and AFB
- BT, CT and platelet count
- E.C.G
- RBS
- Spirometry
- CT/USG guided FNAC
- Histopathology of resected specimen.

Study proper:

FNAC was done by the researcher as per standard procedure in Radiology and Imaging department of NIDCH. The slider was immediately sent to pathology department. The patient remained in observation room for an hour to see any immediate complication. In necessary cases immediate X-ray was done and managed accordingly. In remainder patients CXR were done in next morning for detection of pneumothorax. Then patient was again examined and had gone for thoracotomy. After throacotomy patients were managed accordingly in postoperative care room. Then resected specimen of lung was sent to pathology department for histopathological examination.

Data collection and processing:

The results were collected from laboratory. Slides of FNAC were examined by Department of Pathology & Microbiology, NIDCH. Slides of resected specimen of lung were also examined in department of pathology and microbiology.

All data were recorded and processed in a proforma.

Result:

Age distribution:

Table 1 shows the age distribution of the patients. One-quarter (25%) of the patients were 50 years of age or below, 18.3% between 51 – 60 years, 38.3% between 61 – 70 years and the rest 18.3% above 70 years of age. The mean age of the patients was 61.5 ± 10.3 years and the lowest and highest ages were 41 and 80 years respectively.

Age (years)	Frequency	Percentage
d" 50	15	25.0
51 – 60	11	18.3
61 – 70	23	38.3
> 70	11	18.3

*** Mean age = (61.5 ± 10.3) years; range = (41 – 80) years.**

Sex distribution:

Figure 1 shows the sex distribution of the patients. Of the total 60 patients, 78% were male. The male to female ratio was roughly 4:1.

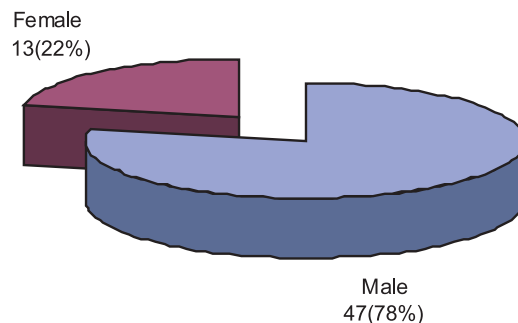


Fig.-1: Distribution of patients by sex (n = 60)

Occupation:

Table II shows that over 40% of the patients were farmer followed by 16.7% service-holders, another 16.7% businessmen, 15% housewives and 10% were involved in other jobs.

Occupation	Frequency	Percentage
Service	10	16.7
Business	10	16.7
Farming	25	41.7
Housewife	09	15.0
Others	06	10.0

Socioeconomic condition:

The socioeconomic condition of the patients is summarised in figure 2. Approximately 47% of patients were poor, 35% middle class and 18.3% rich (Fig 2).

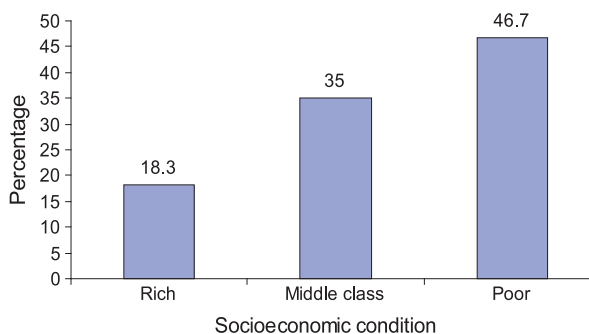


Fig.-2: Distribution of patients by socioeconomic condition (n = 60)

Affected lobe:

Distribution of the patients by affected lobe of the lung shows that over 58% of the patients had lesion

in the upper lobe, 13.3% in the middle lobe and the rest 28.3% in the lower lobe (Table III).

Table-III

Distribution of patients by affected lobe (n = 60)

Affected lobe	Frequency	Percentage
Upper	35	58.3
Middle	08	13.3
Lower	17	28.3

Clinical presentation:

Table IV shows that majority (81.7%) of the patients complained of gradual loss of weight. Two-third (66.7%) of the patients had anorexia, 65% cough, 53.3% dyspnoea, 36.7% chest pain and 35% haemoptysis.

Table-IV

Distribution of patients by clinical presentation (n = 60)

Clinical presentation	Frequency	Percentage
Cough	39	65.0
Haemoptysis	21	35.0
Dyspnoea	32	53.3
Chest pain	22	36.7
Weight loss	49	81.7
Anorexia	40	66.7

Smoking habits:

Figure 3 shows the distribution of patients by smoking habit. Of the 60 patients 43 (72%) were smokers, and the remaining 17(28%) were non-smokers.

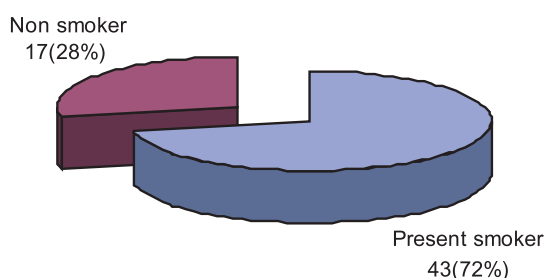


Fig.-3: *Distribution of patients by smoking habit (n = 60)*

History of smoking:

Smoking history reveals that the mean duration of smoking was 22.5 ± 6.5 years. The mean number of sticks consumed by the smokers was 18.7 ± 8.6

per day and mean time since giving up smoking was 10.9 ± 4.4 years (Table V).

Table-V

Distribution of patients by history of smoking profile (n = 98)

Smoking profile	Mean	S.D
Duration of smoking (yrs)	22.5	6.5
Number of sticks consumed (per day)	18.7	8.6
Time since quitting smoking (yrs)	10.9	4.4

Clinical examination:

Clinical examination findings demonstrate that 18.3% of the patients suffered from anaemia, another 18.3% clubbing, 20% hoarseness of voice and 23.3% palpable cervical lymph node (Table VI).

Table-VI

Distribution of patients by clinical examination (n = 60)

Clinical examination	Frequency	Percentage
Anaemia	11	18.3
Clubbing	11	18.3
Hoarseness of voice	12	20.0
Palpable cervical lymph node	14	23.3

Investigation findings:

Cytologic diagnosis shows that 85% of the patients primary lung cancer. Histologic diagnosis also shows that 85% of the patients had primary lung cancer and 15% benign tumour (Table VII).

Table-VII

Distribution of patients by investigation findings (n = 60)

Investigation findings	Frequency	Percentage
Cytologic diagnosis		
Primary lung cancer	51	85.0
Benign lesion	09	15.0
Histologic diagnosis		
Primary lung cancer	51	85.0
Benign tumour	09	15.0

Type of cell:

Figure 4 compares the cytologic cell type with histologic cell type among the patients. Cytologic cell type study reveals that 46.7% of the patients exhibited adenocarcinoma, 25% squamous cell carcinoma and 8.3% large cell carcinoma. Histologic

cell typing demonstrates that over half (53.3%) of patients had adenocarcinoma, 25% squamous cell carcinoma, 5% large cell carcinoma, 1.7% small cell carcinoma and 15% benign carcinoma.

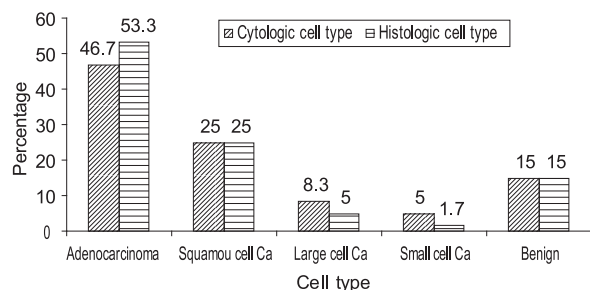


Fig-4: Distribution of patients by cell type (n = 60)

Benign lung lesions:

Of the 9 cases diagnosed as benign by FNAC, 5 were granuloma, 3 fibroma and 1 fibrous scar. Histopathology diagnosed 9 cases as benign lesion. Of them 5 were granuloma, 2 fibroma and 2 fibrous scar (Fig. 5).

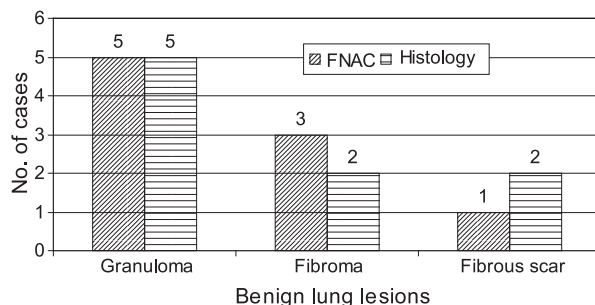


Fig-5: Type of benign cases diagnosed by FNAC and histopathology (n = 9)

Distribution of lung lesion according to location whether perihillar or peripheral lesions:

Out of 51 lung cancer, 7 lesion were perihillar region. Among them FNAC correlate with histopathology of resected lung lesion in 5 cases (71%).

Table-VIII

Comparison between FNAC and histopathology in case of perihillar lesion.

Lesion	Histopathology	FNAC
Squamous cell carcinoma	5	5
Fibrous scar	0	2
Small carcinoma	2	0

Accuracy of FNAC against Histologic diagnosis of lung cancer:

The present study was intended to find the accuracy of FNAC in diagnosing primary lung cancer. Before going to the test findings, it would be worthwhile to interpret the components of accuracy of a screening test against a diagnostic test which is considered as the ‘Gold Standard’. In Table VIII, the letter ‘a’ denotes those individuals found positive on test who have the disease being studied (i.e., true positives), while ‘b’ includes those individuals who exhibit a positive test result but who do not have the disease (i.e., false positives). The letter ‘c’ is the number of negative test results having the disease (i.e., false negatives) and the letter ‘d’ number of negative results who do not have the disease (i.e., true negatives).

Table-IX

Accuracy of a screening test against an established diagnosis

Screening Test	Established diagnosis		Total
	Diseased	Non-diseased	
Positive	a	b	(a + b)
Negative	c	d	(c + d)
Total	(a + c)	(b + d)	(a + b + c + d)

The following measures are used to evaluate a screening test:

1. Sensitivity = $a / (a + c) \times 100$
2. Specificity = $d / (b + d) \times 100$
3. Positive predictive value of the test (PPV) = $a / (a + b) \times 100$
4. Negative predictive value of the test (NPV) = $d / (c + d) \times 100$
5. Percentage of false +ve = $b / (a + b) \times 100$
6. Percentage of false –ve = $c / (c + d) \times 100$
7. Diagnostic accuracy = $(a + d) / (a + b + c + d) \times 100$

Table IX shows the accuracy of FNAC in differentiating primary lung cancer from benign lung tumours. From the table it appears that sensitivity of FNAC in correctly diagnosing primary lung cancer of those who have the disease is $(49/51) \times 100 = 96.1\%$, while the specificity of the test in correctly detecting those who do not have the malignancy is $(7/9) \times 100 = 77.8\%$. The positive predictive value (PPV) of the test is $(49/51) \times 100 =$

96.1% and the negative predictive value of the test is $(7/9) \times 100 = 77.7\%$. The overall diagnostic accuracy of FNAC in correctly detecting primary lung cancer is $(49 + 7)/60 \times 100 = 56/60 \times 100 = 93.3\%$.

Table-X
Diagnostic accuracy of FNAC in correctly diagnosing primary lung cancer

FNAC diagnosis	Histopathological diagnosis		Total
	Primary lung cancer	Benign lesion	
Primary lung cancer	49	2	51
Benign lesion	2	7	9
Total	51	9	60

Discussion

Percutaneous fine needle aspiration cytology of lung lesions have been performed for more than a century and have become an important method in evaluation of solitary and multiple pulmonary nodules. The use of FNAC has gained widespread acceptance in diagnosis of lung cancer. It is relatively simple and safe technique that can be performed on an outpatient basis.

This prospective study was carried out in the department of Respiratory Medicine of National Institute of Diseases of the Chest and Hospital (NIDCH) from June 2007 to May 2008. Initially ninety six (96) consecutive patients were included in the study but during the study period, thirty six (36) cases were excluded from the study and finally the total number of patients who completed the study was sixty (60).

Pulmonary mass can be safely and accurately diagnosed by fine needle aspiration cytology under the guidance of CT-scan or ultrasonography. This is true whether the lesion is large or small, central or peripheral and benign or malignant. It is usually performed on an outpatient basis in Radiology and Imaging Department with fine needle (23G) and local anesthesia was used so that little or no pain was experienced by the patient.

Socio-demographic data of study subjects were evaluated. Patients ≥ 40 years of age were enrolled in this study. This particular age range was considered from the fact that incidence of lung

cancer is unusual below this age group. The mean age of the study subjects was 61.5 ± 10.3 years (Table-I). This finding is similar to Ahmed (1998) where the mean age was 54.22 ± 16.24 .

Analysis of the patients with respect to sex indicates male predominance with a male: female ratio of 4:1. This finding correlates with the finding of Majumder⁴ where male: female ratio was 10:1. The male predominance may be explained by greater prevalence rate of lung cancer in male globally and males are more likely to be smokers than female.

Among the studied patients, 72% were smokers and 28% were non smoker. This finding is similar to finding of David⁶ where 80% were smokers. The mean duration of smoking among the studied patient was 22.5 ± 6.5 pack years ranging from 16 to 29 pack years. This pattern of smoking status is similar to Ahmed¹ where majority of the patients (58%) were smokers of more than 20 pack years.

Regarding predominant symptoms 39(65%) patients presented with cough. Strauss (1998) reported cough in 60% of their patients with bronchiogenic carcinoma (45-75%). This finding was similar to our study.

22(36.7%) patients presented with chest pain, 21(35%) patients presented with haemoptysis and 32(53.3%) presented with dyspnea. On examination 49(81.7%) had weight loss followed by clubbing 11(18.3%). This finding is similar to Strauss (1998) where chest pain, haemoptysis were 33-50% and 27 to 57% respectively.

X-ray chest was done in all patients. Right sided lesions was dominating 33(45%) and left sided lesion was 27(45%) but this was not statistically significant ($p > 0.05$).

20 patients (33.3%) had lesion 3-5cm in diameter and 40(66.6%) had lesion more than 5 cm in diameter.

In our series (n=60) FNAC procedure revealed 49(96%) malignant cases and 7(77.7%) non malignant cases, histopathology after thoracotomy revealed 51(100%) malignant and 9(100%) benign. So sensitivity of FNAC in diagnosis of lung cancer is 96.1%. Thus the accuracy of FNAC is correctly detecting primary lung cancer is 93.3%.

Douglas et al.⁹ conducted a study in USA, CT guided FNAC was done where diagnostic accuracy was 85%. Our present study findings correlate with their findings.

In another series Ang et al.¹⁰ conducted a study in National Taiwan University Hospital among 30 suspected lung cancer. USG-guided FNAC was done in all patients. Diagnostic Accuracy of 92% correlates with our finding.

In another series John et al.⁸ found in a series of 180 patients shows specificity of 100% and sensitivity of 82%. Our present study findings correlate with these findings.

In another series Huanqili et al.⁷ found in series of 95 patients. (FNAC CT guided) – sensitivity, specificity and accuracy 94%, 100% and 96% respectively. These findings are very much consistent with our findings.

In our series 53.3% were adenocarcinoma 25% squamous cell carcinoma, 5% large cell carcinoma and 1.7% small cell carcinoma. Of the non malignant cases, 5 cases revealed granuloma, 2 fibroma and 2 fibrosis scar. But in Samirs series malignancy was found in 41% cases, 48% cases revealed no malignancy and other remains undiagnosed. In his series also squamous cell carcinoma was predominating (50%); small cell carcinoma was 33%. Adenocarcinoma was 02% and no large cell carcinoma was found in his series. This finding is not similar to ours. This probably due to the number of cases in his series is only 29. If it were more than that the result would have been different.

Complication was minimum, only 02 cases revealed evidence of pneumothorax. But it was small, did not require chest tube.

Biopsy is the gold standard for diagnosis of lung cancer. In our study we compare fine needle aspiration cytology with histopathology of lung tumor. In our study we found, FNAC is also reliable for diagnosis of perihillar lesion also (71%). In abroad, there are some studies like this but our study is the first time in Bangladesh. From our study it is evident that efficiency of FNAC is almost equal to that done abroad. From our study we found that diagnostic accuracy of fine needle aspiration

cytology almost equal to histopathology of resected specimen of lung tumor. In our study, we found that we can rely on FNAC for diagnosis of lung cancer even in remote area where ultrasonogram imaging facilities are available.

From the limited study it may be concluded that FNAC is one of the effective diagnostic tool in detection of lung cancer. It is equal to histopathology regarding sensitivity, specificity and accuracy. Sometimes, it an avoid surgery by appropriate diagnosis. FNAC is an easier and reliable method in detecting lung cancer in case of peripheral lesion as well as perihillar lesion and complication is very minimum⁴.

Summary

Lung cancer is the commonest malignant tumour in male and it's frequency in female is rapidly on the raise. The main objectives of the study was to determine the accuracy of FNAC in diagnosis of lung cancer.

It was a cross sectional study carried out in the department of respiratory medicine, National Institute of Diseases of the Chest and Hospital (NIDCH), Mohakhali, Dhaka from June 2007 to May 2008. Total number of enrolled patients were ninety six (96) but finally sixty (60) were used for analysis. The patients were selected in consecutive method of sampling technique after meeting the selection criteria. Socio-demographic, clinical, bacteriological and radiological data of each patient was evaluated and enter in a preformed proforma. FNAC was done in all enrolled patients as per standard procedure in radiology and imaging department of NIDCH. Then the patients went surgery who fulfilled the selection criteria. The patients observed following both procedure for detection of any complication. Data's were analysed by the computer using the statistical package for social science (SPSS) program.

In our study sensitivity of FNAC 96.1%, specificity 77.8%, positive predictive value is 96.1%, negative predictive value 77.7% and overall diagnostic accuracy of FNAC in correctly detecting lung cancer is 93.3% complication rate was minimum, there was no death and no serious complication in this procedure. Diagnostic

accuracy of FNAC is almost equal to histopathology in diagnosis of lung cancer.

It may be concluded that FNAC may be relied upon for diagnosis of lung cancer in remote area where bronchoscopic facilities and expertise are not available.

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REVIEW ARTICLE

Sublingual Immunotherapy (SLIT): An Emerging Therapy ? – A Review

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[*Chest & Heart Journal 2009; 33(2) : 134-137*]

Asthma is a substantial health problem among children and adults worldwide, with increasing prevalence rates in many countries.¹ Allergic rhinitis is also a global health problem affecting at least 10-50 % of the population.² The prevalence of the disease is increasing in industrialized as well as industrializing countries. Epidemiological studies have shown that 80% of asthmatics have co-existent rhinitis.² Asthma in Bangladesh appears to be also a substantial public health problem: an estimated 7 million people including 4 million children suffer from asthma related symptoms.³

Among chronic illnesses, allergic rhinitis and asthma are the leading causes of absenteeism⁴. With two million annual lost school days attributed to allergic rhinitis⁵. While pharmacotherapy reduces symptoms of allergic rhinitis, immunotherapy (IT) is the only treatment offering potential long-term immune modification. Conventional subcutaneous immunotherapy (SCIT) requires frequent injections, and often results in patient noncompliance due to inconvenience or intolerance. In the 1980's, SCIT was deemed responsible for several deaths, causing the British Committee for the Safety of Medicine to raise concerns about its safety.⁶

Due to SCIT safety concerns, multiple non-injection IT routes have been investigated. Sublingual immunotherapy (SLIT) has been the most promising of the non-injection IT routes and has now been in use in Europe for over 20 years.⁷

Sublingual Immunotherapy is method of allergy treatment that uses an allergen solution given under the tongue, which reduces sensitivity to allergens. Sublingual immunotherapy, or SLIT, has a very good safety profile and is given at home in adults and children.⁸

The basis of sublingual immunotherapy is treatment of the underlying allergic sensitivity. Allergic symptoms improve as the allergic sensitivity improved. As a safe and effective method of treating the underlying disease, sublingual immunotherapy is capable of modifying the natural progression of allergic disease which can begin with allergic food sensitivities & eczema in young children and progress through allergic rhinitis and asthma in older children & adults.⁸

It has long been known that oral administration of an allergen favours the development of tolerance. Current understanding is that regulatory T cells secreting TGF- β are involved in this type of tolerance. Administration of high-dose allergen immunotherapy by means of subcutaneous injection also induces the development of regulatory T cells, with evidence that the secretion of both IL-10 and TGF- β is important in the mechanism of tolerance. Because many patients receiving SLIT show immunologic changes similar to those observed in patients receiving SCIT, such as suppression of the immediate and late-phase skin test responses, increased levels of allergen-specific IgG4, and in some studies suppression of allergen-induced lymphocyte

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proliferation, it is not unreasonable to suggest that stimulation of regulatory T cells underlies the response to immunotherapy by both routes.⁹

Low-dose sublingual immunotherapy (SLIT) for respiratory allergy was firstly described in a controlled trial in 1986¹⁰ and it appeared as a promising therapeutic option, especially for the favourable safety profile. The original rationale of SLIT was that of achieving a prompt and rapid absorption of the vaccine through the oral mucosa. It then became the most used noninjection route for immunotherapy in Europe. After a review of the literature existing in 1998, a panel of experts of the World Health Organization concluded that SLIT is a viable alternative to SCIT¹¹. This statement was confirmed in a position paper of the European Academy of Allergology and Clinical Immunology¹² and in the ARIA (allergic rhinitis and its impact on asthma) document¹³ that extended the indications of SLIT to children.

The history of SLIT is chronologically short and encompasses a period of only 20 years. The sublingual approach was initially proposed empirically, without knowledge of the bio-distribution of allergens and of the possible mechanism of action. As a consequence, the practical aspects of SLIT (i.e., allergen dose, frequency of administration, build-up modality) were selected by investigators on the basis of personal experience, often translating into SLIT, the protocols used for SCIT. The result is significant variability in administration schedules, dosages, and duration of SLIT courses. Nonetheless, the clinical trials in the latter 20th and early 21st century began to address this variability, and there is a trend toward more uniform SLIT protocols, similar to the previous development for SCIT. Because of regulatory issues SLIT is not used worldwide but is employed in clinical practice in Europe and other countries and regions including South Africa and Latin America.¹⁴

SLIT is currently marketed by several European and Indian manufacturers and the administration schedules and amount of allergen(s) largely vary, depending on the producer. Almost all the SLIT vaccines commercialized in Europe are standardized either biologically or immunologically¹⁴. The allergen extracts are labelled in units that differ from one manufacturer

to another. Some of the more common labelling units are allergen units (AU), index of reactivity (IR), biological units (BU) standard unit (STU). The content in microgram of the major allergens is available for many extracts, and thus has allowed a quantitative approach to determine the optimal SLIT dose. In general the maintenance dose of allergens is 5 to 300 times higher with SLIT compared to SCIT. The term "high-dose SLIT" is sometimes used to indicate this dose difference.

The vaccine of SLIT is available in two principle pharmaceutical forms.

- a) Buffered solution to be delivered by drop-counters, droppers, predosed actuators or disposable single dose vials.
- b) Tablets with appropriate composition facilitating slow (1-2 minutes) dissolution in the mouth upon contact with saliva.

For the build-up or the up dosing phase vials or blisters of tablet at increasing concentration are provided.

SLIT can be delivered by means of two methods. With sublingual spit, the vaccine is kept under the tongue, for a short period and then spat out. This method was used in some earlier studies but the majority of the studies used sublingual swallow method. In this method the vaccine is kept under the tongue for one to two minutes and swallowed. In a study that investigated the pharmacokinetics of the two techniques and the author concluded that the contact with the oral mucosa was a crucial step and the sublingual swallow method was the more appropriate and advantageous way to administer the allergen because the sublingual spit method led to a partial loss of allergen¹⁵. The vaccine or solution is usually administered in the morning with the patient in fasting state, but may be administered at any time of the day.

SLIT traditionally involves a build up phase (with gradually increasing doses) and maintenance phase with maximum dose. This approach is similar to SCIT but more accelerated. The build up phase is usually 4 to 6 weeks. The vaccine is prepared in separate vials at increasing concentrations. The treated subject starts the lowest concentration and gradually increases using the different doses preparations, until the maintenance dose is reached. The relative safety of SLIT doses not

strictly limit the maximum dose and this contributes to the variability of the maintenance doses used in clinical trials¹⁶. The suggested maintenance interval varies among manufacturer and investigators.

SLIT can be administered either pre seasonally (start prior to the season and stop at the beginning at the season), pre-co seasonally (start prior to the season and stop at the end of the season) or continuously. Pre-seasonal or pre-co seasonal schedules are commonly used for pollen allergy. In this case the treatment is commenced about two months before the expected pollen season. On the other hand for nearly perennial or perennial allergens, a continuous treatment (all year round is preferred).

The most used regimen is once daily or alternate day or once weekly or twice weekly administrations have been utilized. The studies reporting SLIT include doses that vary by 30,000 fold, frequency of dosing vary from daily to weekly and duration of treatment varying from two months to five years. There are very few comparative studies¹⁷.

SLIT appears efficacious for IgE-mediated respiratory allergy. SLIT is specific for the allergen and not the disease. The major issue to be determined before initiating SLIT, or any allergen immunotherapy, is the causal importance of a specific allergen or allergens. The allergy diagnosis is made by clinical history, physical examination, skin testing and or serum specific IgE assays. SLIT is self managed by the patient at home, thus detailed instructions, schedule of administration, and possible side-effect discussions are mandatory. The Manufacturers usually provide written instruction with SLIT but it is common practice for most allergists to see the patients before he/she starts the treatment, to provide additional information and verify understanding. A contact physician for telephone reporting of adverse events should be provided.¹⁸

As per guidelines, SLIT is indicated in patients with rhinitis or asthma or both, especially those who refuse injections or previously experienced severe adverse reactions to SCIT. Although there is no formal evidence of increased risk, SLIT is usually not recommended for patients with severe/uncontrolled asthma. The clinical efficacy of SLIT

in mild, intermittent rhinitis is less defined. Ideally, SLIT should be used in an integrated treatment plan, including avoidance measures and appropriate pharmaceutical therapy. SLIT is self-administered and usually managed at home, thus, concerns about compliance & monitoring. Adherence with SCIT is documented since it is given in the presence of physician. Some studies have attempted to quantify the adherence to SLIT therapy by means of unscheduled telephone interviews.¹⁹

SLIT may be associated with minor adverse reactions. By far the most common are local symptoms in the oral cavity; however, abdominal complaints, urticaria, and asthma have been reported, although all are uncommon. Anaphylactic reactions accompanied by hypotension and fatal reactions have not been reported. It should be recognized, however, that there has been little reported use of SLIT in patients with severe asthma, and multiple allergen SLIT has not been reported²⁰.

The cumulative dose of allergen given via sublingual route is greater than SCIT, and therefore, the cost of vaccine is greater. The cost of vaccine is offset by the reduced need for medical and nursing time, so the global cost of SLIT may be less than SCIT.²¹

Specific immunotherapy is a cornerstone in the management of respiratory allergy since it is allergen specific, immune modulating, and affects disease progression. SLIT, introduce about 20 years ago is potentially a significant advance offering an excellent safety and acceptance profile. But many questions remain unanswered regarding SLIT including effective dose and schedule, timing, mechanism and safety in high risk groups. Until the optimal effective dose and dosing schedule is established a cost benefit analysis of SLIT cannot be made. Currently there is no CPT (current procedural terminology of American Medical Association) code for SLIT. One barrier to endorsement of SLIT is the absence of FDA approved product for SLIT. Physicians prescribing SLIT should provide specific instruction for managing the different variables that might be anticipated with this home based therapy, such as gaps in the treatment and clinical situations for which the treatment should be withheld.

Mechanism to monitor patients' adherence and adverse treatment should be carefully considered before this treatment is prescribed.²²

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ORIGINAL ARTICLE

Effects of Beclomethasone and Montelukast on Asthma Control

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Abstract

The study was carried at NIDCH, Mohakhali, Dhaka to compare the effects of a leukotriene receptor antagonist & an inhaled corticosteroid to determine whether they provided equivalent effects, as judged by days of asthma control. In a randomized, double-blind, placebo-controlled, parallel-group study, asthmatic patients (n = 100) with FEV₁ percent predicted values of between 50% and 85% and a weekly average 3-agonist use of more than 2 puffs per day were randomized to receive montelukast (10 mg daily), beclomethasone (200 µg twice daily) for 6 weeks in a double-dummy fashion. We examined the distribution of the primary end point: percentage of days of asthma control. Secondary end points included FEV₁, salbutamol use, occurrence of an asthma attack, asthma flare-up, sustained asthma control, and adverse experiences. The percentage of days of asthma control was almost identical between the montelukast and beclomethasone groups (98% overlap in the distribution). Beclomethasone was at least equal to Montelukast on the basis of frequency of asthma attacks and asthma flare-ups. Beclomethasone had a greater effect than montelukast at improving FEV₁. Beclomethasone was as effective as Montelukast, as judged by indices of clinical control other than FEV₁. When evaluating the outcome of Beclomethasone therapy, FEV₁ might underestimate clinical effectiveness.

[Chest & Heart Journal 2009; 33(2) : 102-106]

Introduction

Asthma is an inflammatory disease leading to episodic worsening of airway function, mucus production, cough, and other symptoms.¹ According to the National Asthma Education and Prevention Program asthma treatment

guidelines,² drugs capable of providing long-term control of asthma are indicated when symptoms become persistent. Inhaled corticosteroids (ICSs) are often recommended as initial controller therapy for the management of persistent asthma because of their anti-inflammatory effects

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and proven benefits. However, the inhaled form of drug delivery is associated with lower adherence to therapy compared with that seen with drug delivered by means of the oral route,^{2,3} and many patients experience difficulty in using inhaled therapy.⁴

Several large clinical trials in adults with chronic asthma have documented the beneficial effects of oral montelukast, a leukotriene receptor antagonist, in improving asthma outcomes (eg, decreased asthma exacerbations), asthma symptoms, and lung function.⁵⁻⁷ Additionally, studies in asthmatic adults and children have demonstrated that adherence to therapy is substantially greater with oral montelukast than with inhaled asthma therapy.⁸

Although the objective of chronic therapy for asthma is to minimize symptoms and to avoid asthma exacerbations, typical assessment based on conventional measures of airway function. Measurement of asthma control should include the need for rescue medications or unscheduled asthma-related health care.⁹ When defined in this way, a measure of days of asthma control conflates with patient symptoms.² Consecutive days with asthma flare-ups should be avoided.

The primary objective of the present study was to compare the effects of the 2 therapies (beclomethasone and montelukast), as judged by days of asthma control. Secondary variables included FEV₁ b agonist use, asthma attacks and flare-ups, days of sustained asthma control, and rescue corticosteroid use.

Methods

Study design

This was a randomized, parallel-group study consisting of a 1-week prestudy screening period, and a 6-week double-blind treatment period. A 6-week treatment period was chosen because it has been shown to be a sufficient period of time to achieve most of the effects of these 2 therapies.⁷ Clinic visits were scheduled at the end of the 1-week prestudy screening period, at the end of the 2-week single-blind period, and every 3 weeks during double-blind therapy.

The study was conducted at NIDCH, Mohakhali, Dhaka between August 2008 and March 2009. The 100 eligible patients were randomly assigned, according to a blinded allocation schedule produced by the study sponsor, to receive either beclomethasone dipropionate (200 µg [4 puffs] twice daily administered by means of inhalation), montelukast sodium (10-mg tablet once daily in the evening) respectively. Each patient received one tablet daily (active or matching placebo) and one inhaler dose twice daily (active or matching placebo) for both the single-blind and double-blind treatment periods. The use of a spacer device was permitted and was not provided; data regarding spacer use were not collected.

Inclusion and exclusion criteria

Male and female patients at least 15 years of age with at least a 1-year history of clinical symptoms of asthma were enrolled in the study. Patients' asthma treatment could include only short-acting (3-agonist (salbutamol) at the time of randomization. Patients were eligible for randomization if they had an FEV₁ of between 50% and 85% of the predicted value at rest and at least a 15% increase in FEV₁ after salbutamol administration. In addition, all patients were required to have average salbutamol use of greater than 2 puffs per day (which might include those for exercise prophylaxis) during the baseline run-in period. Eligible patients were nonsmokers for at least 1 year before enrollment, with a smoking history of no more than 7 pack-years.

Patients with upper respiratory tract infections within the past 3 weeks, emergency care for asthma within 1 month, or hospitalization for asthma within 3 months were excluded. Systemic corticosteroids were not allowed for 1 month before the first study visit; ICSs were not allowed for 2 weeks before the first study visit. Patients were required to stop other antiasthma therapy 1 week before the first study visit. Inhaled albuterol for symptomatic relief of asthma and short-acting antihistamines were permitted. According to a standard action plan, up to 2 uses of rescue oral corticosteroid for the treatment of worsening

asthma were allowed during the double-blind period. Patients who needed additional oral corticosteroid treatment discontinued study therapy.

Statistical methods

The prespecified primary end point was the percentage of days of asthma control during the 6 weeks of double-blind treatment. Secondary end points were average daily salbutamol use, percentage of patients with or without an asthma attack, asthma flare-up, occurrence of sustained asthma control, rescue corticosteroid use, and change from baseline in FEV₁. The frequency of adverse experiences was also evaluated.

Analysis, The prespecified analysis for the primary end point was the overlap between treatment groups in the distributions of patient response. The comparison of the full range of efficacy responses in the 2 active treatment groups provides valuable information that extends beyond the comparison of group means data; the overlap method was developed to provide a statistical treatment of this comparison. The overlap was analyzed for percentage of days of asthma control (primary end point) and change in FEV₁ (secondary end point) by using a modification of the nonparametric Mann-Whitney U test.^{3,4} The “U” statistic estimates the probability that a randomly chosen patient in the inhaled beclomethasone group will experience a greater treatment effect than a randomly chosen patient in the montelukast group and was expressed as a percentage overlap of response distributions, as previously described.⁸ The Mann-Whitney U test is equivalent to the frequently used non-parametric Wilcoxon rank sum test.⁷

Between-group comparisons of mean values were performed for days of asthma control, change from baseline in FEV₁, and average daily (3-agonist use by using ANOVA. A logistic-regression model was used to analyze patients with or without asthma attacks, asthma flare-ups, episodes of sustained asthma control, and rescue corticosteroid use. The percentage of days of asthma control (Sum of total days that were part of a sustained asthma control episode/Days in study] x 100) was analyzed in a similar manner as the primary end point. The Fisher exact test was used to compare overall

between-group incidence of clinical and laboratory adverse experiences.

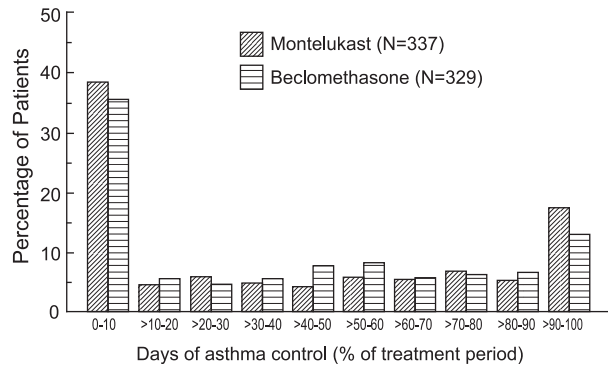


Fig.-1: Frequency distributions of days of asthma control (expressed as percentage of days during the 6-week treatment period) for montelukast and beclomethasone. The overlap between montelukast and beclomethasone in the patient response distributions for days of asthma control was 97.7% (95% CI, 89.0-100.0).

Result

The percentage overlap of days of asthma control for montelukast and beclomethasone was 97.7% (95% CI, 89.0%-100%; Fig 1). The group mean values for the percentage of days of asthma control during the treatment period were 41.4% (95% CI, 37.4%-45.4%) for montelukast, 41.1% (95% CI, 37.0%-45.3%) for beclomethasone, and 26.8% (95% CI, 20.0%-33.5%) for placebo. The difference between montelukast and beclomethasone with respect to the mean percentage of days of asthma control was not significant (0.24%, $P = .929$). For both montelukast and beclomethasone, the difference from placebo in the percentage of days of asthma control was significant (14.6% [$P < .001$] and 14.4% [$P < .001$], respectively; Table II). The effect of both therapies on asthma control days increased gradually with time

Analyses of the individual components of an asthma control day were performed and were consistent with the primary end point of asthma control days (data not shown). β -Agonist use was responsible for the greatest percentage of noncontrol days (45.2% and 44.4% in the montelukast and beclomethasone groups, respectively).

End point	Montelukast (n = 50)	Beclomethasone In = 50)
FEV ₁ , (change from baseline)	0.24 ± 0.03*†	0.38 ± 0.03*
Daily β-agonist use, puffs/d (% change from baseline)	−30.3 ± 2.4*	−31.9 ± 2.5*
Patients without an asthma attack, %	97.0 ± 0.9*	96.1 ± 1.1
Patients without asthma flare-up, %	22.0 ± 2.3*	17.6 ± 2.1*
Patients with at least 1 sustained asthma control episode, %	55.5 ± 2.7*	59.3 ± 2.7*
Patients without rescue corticosteroid, %	97.3 ± 0.8*	96.4 ± 1.0

Discussion

Although maintenance of airway function is an important feature of asthma control, optimizing airway function (eg, FEV₁) is not the sole objective of asthma therapy according to current National Asthma Education and Prevention Program and Global Initiative for Asthma treatment guidelines.^{†9} In fact, current consensus guidelines suggest that even asthmatic patients with normal measures of airway function (FEV₁ >80% of the predicted value) who experience frequent symptoms of asthma should be treated with daily controller therapy. The present study was undertaken to determine the relative effect of an established first-line therapy for the treatment of persistent asthma, inhaled beclomethasone, compared with the leukotriene receptor antagonist montelukast. Both of these drugs have been shown to control asthma symptoms and improve airway function. The current study confirms the efficacy of both drugs and suggests that both are capable of improving asthma control for patients with persistent disease. Furthermore, it suggests that the clinical efficacy of the leukotriene receptor antagonist montelukast is underestimated by an index of airway caliber, such as FEV₁.

In the present study multiple clinical control indices were combined into a single end point, referred to as days of asthma control, to describe a desired and clinically recognized element of asthma control. The end point of days of asthma control incorporates elements that have been routinely measured in previous studies: daily albuterol use, nighttime awakenings, oral rescue corticosteroid use, and unscheduled medical care for the treatment of an asthma exacerbation.^{5,7} A day of asthma control represents a day in which a patient's asthma was well controlled, similar to the episode-free day described by Scupher and

Bux-ton.^{5,6} The latter was a measure proposed as a means of assessing effectiveness in a cost-effectiveness analysis. Such outcome measures are relevant to patients and prescribing physicians because they are quantifiable measures of the objectives of asthma treatment (controlling asthma and preventing asthma exacerbations).^{1,6}

As measured on the basis of this composite index and the individually incorporated elements, Montelukast and Beclomethasone did not differ in the extent of clinical control achieved. Similarly, they did not differ in commonly measured indices of clinical effectiveness, such as reduction in β-agonist use or reduction in need for oral corticosteroids. Furthermore, they did not differ in the extent of sustained relief achieved.

In the present study neither treatment group achieved a high level of asthma control; however, the study's aim was to compare efficacy, not to explore therapeutic interventions required to achieve full control. The doses of both beclomethasone and montelukast were fixed during the 6-week treatment period at a well-established and accepted initial starting dose (400 ig daily).^{7,8} Although this fixed-dose approach is commonly used to evaluate relative effects of therapies in a clinical research setting, it differs from clinical practice, in which prescribing physicians will adjust therapies and doses to achieve a desired level of control. Although it is possible to use higher doses of ICSs, there appears to be a relatively flat dose-response relationship for the efficacy of ICSs at greater than the dose used in this study.^{9,10} Furthermore, increased ICS absorption occurs with increased dose, which might lead to unwanted dose-related effects. In this context the combination of a leukotriene receptor antagonist and an inhaled corticosteroid have been shown to provide additional control⁶ and might be

appropriate in patients whose symptoms are uncontrolled with either drug alone.

Conclusion

The current study demonstrates similar of patient response to montelukast and beclomethasone when assessed by using broad and clinically relevant measurements of asthma control. It supports the use of montelukast as an effective initial alternative to inhaled controller therapies like inhaled beclomethasone for the treatment of chronic asthma. Furthermore, it suggests that ICSs, compared with leukotriene modifiers, might produce an effect on FEV₁ that is disproportionate to the clinical effect achieved. Therefore when identifying response to treatment, clinicians might need to put greater weight on clinical indices, as opposed to measurements of airway caliber.

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ORIGINAL ARTICLE

Positive Direct Anti globulin test in Normal Healthy Blood Donors

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Abstract

Direct antoglobulin tests (DATs) was performed on 1525 normal healthy donors. A positive DAY was observed in only three donors and rest 1522 were DAT negative. However it is Unknown wheather DAT positive healthy donors are prone to haemolysis with out any clinical evidence and the clinical estimation of self life of red cell transfused. So DAT positive donors are required long term 1'6110W up 1'6r haematological diseases and other complications.

[Chest & Heart Journal 2009; 33(2) : 107-109]

Introduction

Antiglobulin test, Coombs test or AGT refers to two clinical blood tests used in immunohaematology and immunology. The two antiglobulin tests are antiglobulin test or DAT or Direct Coombs test and Indirect antiglobulin test or IAT or also known as Indirect coombs test.

Direct antiglobulin test or DAT is used to detect antibodies or complement system factors have bound to RBC stn-(ace antigens in vivo. DAT is performed I'm pre transfusion testing by some laboratories. Direct antiglobulin test is used clinically when

immune-mediated destruction of RBCs is suspected. A positive direct antiglobulin test is observed due to coating of red cells RBCs in vivo by antibodies of different immunoglobulin isotypes or complement.¹²¹ A DAT may be used to help III diagnosis of haemolytic disease of the newborn (HDN) due to an incompatibility between the blood types of a mother and baby. A DAT may also be used to investigate a suspected transfusion reaction. 11' you are being transfused and have a fever or other significant symptoms suggesting a

potential for a hemolytic transfusion reaction, a DAT is also done to determine an antibody to the transfused RBCs. The proportion of positive DATs among the blood donors ranges 1:1000 to 1:36000⁴⁻⁶ and is higher in older donors than in younger donors.⁷ Several risk factors have been associated with a positive DAT result, including cardiolipin antibodies. Normal donors has a positive DAT is often first discovered when the donors red cells are used in crossmatching. It is not known whether the positive DAT in normal donors is the risk of malignancy or autoimmune haemolytic anaemia (AIHA) is often related to Rh (but may be outside the Rh system).¹⁰ This study is performed to evaluate whether a positive DAT result among healthy blood donors without any clinical evidence of haemolysis and to estimate clinically the self life of red cell transfused.

Materials and Methods

This prospective study was carried out and data were collected from the blood bank of Lab aid Cardiac Hospital, Dhaka Bangladesh from December 2007 to June 2009. Donor were selected by using a set of questionnaire, short medical

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examination eg, height. Weight pulse, blood pressure etc and also hb estimation routinely. Selected donors came from different corners of this country. After selection they were undergo testing using blood grouping equipment as a part of the routine blood type determination of donated unit using tube method. All were subsequently selected as DAT. All DAT were performed by using the tube method (AABB Technical Manual 15th ed. PP760 - 61) and with the reagent Antihuman globulin anti IgG/ C₃ DAT was defined as a reaction strength of +2 or +3 or greater in any single donation. For analysis of the study populations characteristics, continuous variables, computer software was used.

Result

A total of 1525 blood donors 1224(80.26%) were male, 301 (19.74%) were female. Donors were of higher or upper socio economic class 669 (43.87%), middle class 800 (52.46%) and lower socio economic class 56 (3.67%). Out of 1525 donor only 3 (.20%) donors had DAT positive and DAT negative 1522 (99.80%). The age limit of the donor 18- 59 years. Blood grouping of those donor were recorded:

Table-I
Distribution of blood group

Name of Blood Group	Distribution of blood Group	Percentage
Gr.A	479	31.41
Gr.B	444	29.11
Gr.O	497	32.59
Gr. AB	105	6.89
Total	1525	100%

Rh D positive 93.44% and Rh D negative 6.55%
Charts are given below:

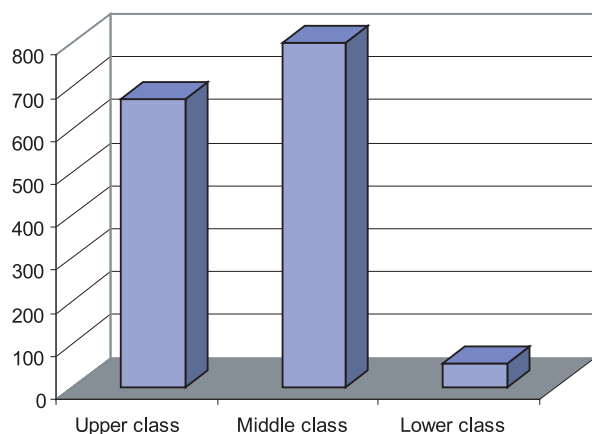


Fig-1: *Distribution of socio economic condition*

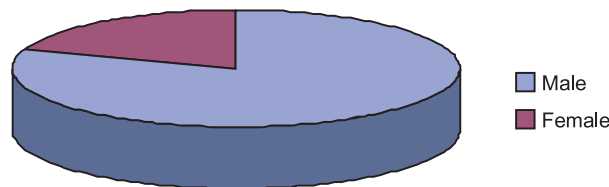


Fig.-2: *Distribution of Sex*

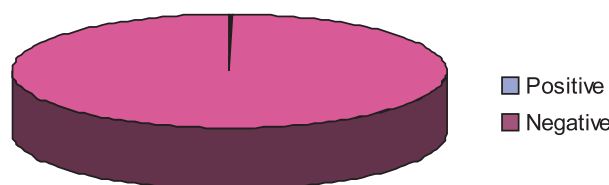


Fig.-3: *Distribution DAT*

Discussion

Among the 1525 healthy normal donors only 3 had positive DAT. Out of three positive DAT donors only one had a history of blood transfusion 10 years back. The other two positive DAT donors are of young age (22 and 35) with no history of transfusion, operation. The DAT negative donors were 99.8%. The fact that an apparently normal donor has a positive DAT is often first discovered when the donor's red cells are used in cross matching. Sixty five cases were found in this way during a period in which one million donations were collected¹⁰. DAT were discovered either by antiglobulin testing or by noting autoagglutination of a blood sample in an automated or manual test and then doing an antiglobulin test. In this study auto control negative donors were selected. Among the three positive DAT donors only one was aged 55 years gave a history of transfusion 10 years back but no clinical problem mentioned. In normal donors with a positive DAT the specificity of the autoantibody, as in patients with AIHA is often related to Rh¹ but may be outside the Rh system for example anti -Jk^a. But we have same limitations in this study because of non availability of reagents; even we can not differentiate AHG IgG or Cad and Cod. In case of other two positive DAT they were young male adult having age 22 and 35 with no history of transfusion drug or any haematological abnormality. They donated blood several times. No complication was noticed. Follow up of the DAT positive donors were necessary for further evaluation.

Awareness of the donor is required for long term follow up reporting in the Transfusion medicine department for diagnosis as well as treatment or any other complications

Conclusion

Normal healthy donor with a positive DAT often first discovered when the donors red cell are used in cross matching . To avoid incompatibility as well as red cell survival after transfusion donor should be checked carefully and positive DAT donors to be advised long term follow up.

Key Words

DAT- Direct Antiglobulin Test. AHG- Anti Human Globulin.

Acknowledgement

The authors thank all patients blood donors and the technical staff of the Blood Bank , Labaid Cardiac Hospital, Dhaka for their assistance.

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ORIGINAL ARTICLE

Extra Salt Intake as Determinant of High Blood Pressure

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Abstract

Background: To find out causal relationship between high blood pressure and extra table salt intake, this quasi-experimental study was done at the community level through door-to-door health education intervention counseling for not taking extra table salt.

Material and Method: This intervention study was conducted among 4,930 respondents, 196 (69.5%) male and 86 (30.5%) female, out of 7,474 population (response rate was 65.96%) all aged 18 years or above in Mohammadpur area of Dhaka city, during the period August 2005 to February 2009 including intervention for 18 months. Cluster randomized sampling was done to collect 282 unaware, untreated stage-I hypertensives without any co-morbidity. The intervention was given person-to-person after the respondents signed the informed consent form for avoidance of extra table salt. Global standard tools were used to collect data. Follow-up of for selected parameters were done after 6, 12, and 18 month of intervention. Data analysis and interpretation were done through SPSS.

Result: Mean Blood Pressure of the respondents is found to be 121/78 mmHg. Overall prevalence of hypertension is 20.1% (JNC-7 criteria). After 18m intervention percent reduction of SBP is -7.0% and DBP is -9.9%. Blood pressure of 14.9% (n=42) goes up in spite of behavioural risk reduction while 7.8% hypertensives became normotensives, 48.9% becomes pre-hypertensives while 17.7% remains at stage-I but their baseline blood pressure is reduced. Multinomial regression analysis shows chi-square value of 25.8 df 13 p=0.018 between use of extra table salt and systolic blood pressure while the value is 28.684 df 11 p= 0.003 for diastolic blood pressure in a -2 Log Likelihood reduced model. This reduced model is equivalent to the final model because omitting the effect does not increase the degrees of freedom. Salt intake behaviour is significantly reduced although the intervention period. At baseline level 124 respondents (44%) used extra salt while eating. After 6m, 12m and 18m of intervention salt intake is found among 58(20.6%), 14(5.0%) and 05(1.8%) respondents respectively. 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). Quality of life was evaluated for both subjective and objective indices. Subjective index for anxiety/ depression scale of the respondents reduced from 8.2 to 2.4 over 18months on a scale from 0 to ten.

Conclusion: Reversal of hypertensives was 56.7% by lifestyle modification and behavioural changes including salt intake reduction. This study confirms relation of salt with hypertension and also confirms reduction of blood pressure after reducing salt intake. This study recommends no extra salt intake for patients with high blood pressure.

Key words: Salt Intake, Hypertension, Prevalence in Bangladesh.

[Chest & Heart Journal 2009; 33(2) : 127-133]

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Introduction

Salt containing sodium chloride retains water in human body. Increased volume of water causes increased plasma volume resulting increased cardiac output and ultimately increase blood pressure. Increased salt intake causes increased secretion of ouabain by adrenal gland. Ouabain regulates the sodium and calcium present in the smooth muscle cells of the arteries by regulating the proteins. Excess amount of ouabain secretion disrupts cellular sodium and calcium balance.¹ Sodium accumulates in arteries, causing protein regulators to bring in more calcium causing hypertension by constricting artery. Excessive salt consumption can make narrowing the renal artery resulting restriction of blood flow throughout. This results in secretion of the kidney hormones renin and angiotensin. Renin and angiotensin increase pressure on peripheral arteries and cause hypertension.² Sodium excretion increases when there is an acute increase in blood pressure. In patients with hypertension a rightward shift in the *pressure-natriuresis* curve occurs meaning that they need to excrete higher sodium load.³ An study conducted by researchers at the University of Erlangen, the Max Delbrück Center for Molecular Medicine (MDC) Berlin-Buch and Regensburg, in collaboration with scientists from Finland and Austria found a new storage area for salt within skin in the body and defected process behind this storage cause hypertensive. Salt is also stored in cells and in the interstitium. Jens Titze and colleagues have now shown that a high-salt diet in rats leads to the accumulation of salt in the interstitium in the skin. This process is carefully regulated by the macrophages. The researchers found a gene regulator (transcription factor) called TonEBP (tonicity-responsible enhancer binding protein) in those macrophages. TonEBP is activated in these cells in response to high salt and turns on a gene (VEGF-C - vascular endothelial growth factor C) that controls the production of lymphatic blood vessels. With high-salt diet the lymphatic vessels increase. The researchers found that when these macrophages are depleted or if the receptor for VEGF-C is absent, the animals are not able to *store their salt* and become hypertensive.⁴ Effect of salt on hypertension has been documented in several articles.^{5,6}

This study was designed to find out prevalence of extra salt intake habit among patients with hypertension and also to analyze any causal relationship between high blood pressure and extra table salt intake as a baseline study. At the end of this quasi-experimental study tests were done to prove whether reduction of extra salt intake can have any influence on reduction of blood pressure among stage-I hypertensive.

Materials and Method

This intervention, quasi-experimental, time-series type of community trial was conducted from August 2005 to February 2009 with an intervention period of 18 months at Mohammadpur area of Dhaka City in Bangladesh. Adults with 18 years age or above as recorded in voter list were the population comprising 7,474 persons. Data collection was done among 4,930 respondents comprising a response rate of 65.96%. Cluster randomized sampling⁷ was done to collect 282 unaware, untreated adults, 196 (69.5%) male and 86 (30.5%) female, with stage-I hypertension without any co-morbidity. Informed consent was taken for intervention adopting WHO-MONICA protocol. Counseling was done for avoidance of extra table salt. Global standard tools were used to collect data through a semi-closed questionnaire. Follow-up for selected parameters was done every 6, 12, and 18 month for collecting data and providing counselling. One-to-one counselling 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. Quality of life was measured using the GHQ-28, PHQ-9 and SF-36 questionnaire.^{8,9,10} Equipments for anthropometric measurement or clinical examination were 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.

Any non-compliant or complicated case was immediately referred to cardiologist or nearby specialized nephrology 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, and qualitative changes of life. Measurement of Blood Pressure was done as per standard protocol using proper machine with appropriate cuff size.¹¹⁻¹⁵ Machine was calibrated at the beginning of the day. Blood pressure was measured at the home-setting with comfortable room temperature without background noise, without tension of muscles or bladder. Blood pressure was not taken if respondents consumed nicotine or alcohol within half an hour before recording. The person sat legs uncrossed without talking. Respondent was then asked to remove clothing covering the cuff area of the arm. A second reading on right arm was taken after 5 minutes. If the difference between the two readings was more than 5 mm of mercury, a third reading was taken again at right arm after another 5 minutes of relaxation. The mean value of the right arm readings was taken as the blood pressure of the individual. In case of any confusion, a second day visit was scheduled to measure BP again. Blood pressure was also measured in standing posture if required. If BP fall was more than 20/10 mmHg on standing from sitting, that case was excluded from study and was referred to consultants. Data

analysis and interpretation were done using SPSS programme version 17.0 for windows.

Result

This study started to follow 282 respondents. As a whole, 72 respondents (25.5%) dropped from study at the end of 18 month follow-up. Attrition of male members was found to be more than female members. Drop-out of male from study was 65.2% while female 34.8%. Drop-out rate is found to be higher during the follow-up period between 06 month and 12 months periods (Table-I).

Causes of drop-out was explained in Table-II showing of 11.3% cases referred to the consultant cardiologists to start pharmacological treatment. While 5.7% respondents withdrew their consent to continue study, another 5.7% respondents changed their residents elsewhere at different times of the study period and 2.8% respondents are dropped because of their non-CVD co-morbidity like pregnancy, identification of DM etc.

Mean Blood Pressure of the respondents was found to be 121/78 mmHg all measured in sitting condition. Overall prevalence of hypertension was 20.1% (JNC-7 criteria). After 18m intervention reduction of SBP was -9.1 and DBP was -8.4 mmHg.

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-III). Mean diastolic blood pressure was 91.2 ± 4.8 mmHg at baseline but became 82.3 ± 4.6 after 18m intervention.

Table-I
Distribution of non-respondents by duration (n=282)

Duration	Respondents started with	Respondents ended with	Number dropped	Percent	Cumulative (%)
6 months	282	258	24	8.5	24 (8.5)
12 month	258	224	34	12.1	58 (20.6)
18 month	224	210	14	4.9	72 (25.5)

Table-II
Causes of Drop-out (n=72)

Period	BP not Controlled	Refused to Continue	Address Change	Co-morbidity	Total (%)
After 06 month	8	4	10	2	24 (8.5)
After 12 month	16	12	4	2	34 (12.1)
After 18 month	8	0	2	4	14 (4.9)
Total	32 (11.3%)	16 (5.7%)	16 (5.7%)	8 (2.8%)	72 (25.5%)

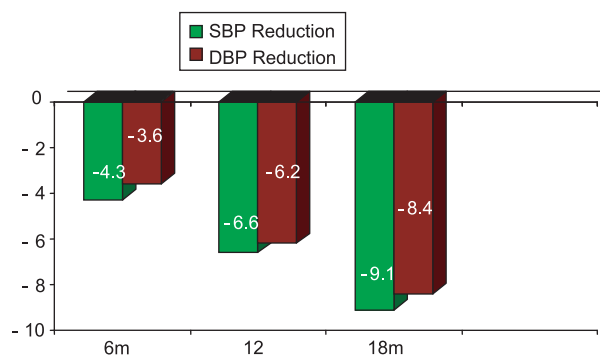


Fig-1: Change of BP after Intervention

Table-III
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	

Blood pressure of 14.9% (n=42) went up in spite of behavioural risk reduction while 7.8% hypertensives became normotensives, 48.9% becomes pre-hypertensives while 17.7% remains at stage-I but their baseline blood pressure is reduced (Table-IV).

Extra table salt was taken in 44% respondents with stage-I hypertension at the beginning of the study. Amount of salt intake was very high amounting to 7 tea spoonful per week on average (Table-V).

Multinomial regression analysis showed chi-square value of 25.8 df 13 p=0.018 between use of extra table salt and systolic blood pressure while the value is 28.684 df 11 p= 0.003 for diastolic blood

pressure (Table-VI) in a -2 Log Likelihood reduced model. The chi-square statistic was the difference in -2 log-likelihoods between the final model and a reduced model. The reduced model was formed by omitting an effect from the final model. The null hypothesis is that all parameters of that effect are zero.

(a) This reduced model was equivalent to the final model because omitting the effect does not increase the degrees of freedom.

Salt intake behaviour was significantly reduced after the intervention. After 6m, 12m and 18m of intervention salt intake was found among 58 (20.6%), 14 (5.0%) and 05(1.8%) respondents

Table-IV
Outcome of Intervention: Stage-I Hypertension respondents (n=282)

Outcome	Reversed to Normal BP	Reversed to Pre-HTN	Remained Stage-I HTN	Drop-out		Total
				Went up Stage-II HTN	Other causes	
Baseline			282			
After 06 months	14(5%)	128(45.4%)	116(41.1%)	8(2.8%)	16(5.7%)	282(100%)
After 12 months	20(7.7%)	132(51.2%)	72(27.9%)	26(10.1%)	8(3.1%)	258(100%)
After 18 months	22(9.8%)	138(61.6%)	50(22.3%)	8(3.6%)	6(2.7%)	224(100%)
End Result	22(7.8%)	138(48.9%)	50(17.7%)	42(14.9%)	30(10.7%)	282(100%)

Table-V
Distribution of stage-I hypertension by extra salt intake (n=282)

Description	Number	Percentage
No use of extra table salt	158	56.0
Use of extra table salt	124	44.0

Table-VI
Likelihood ratio tests between BP and Salt intake at baseline

Effect for <i>Systolic</i> BP	-2 Log Likelihood of Reduced Model	Chi-Square	df	p
Intercept	81.551(a)	.000	0	.
SLTUS	107.346	25.795	13	.018
Effect for <i>Diastolic</i> BP	-2 Log Likelihood of 1 Reduced Mode	Chi-Square	df	p
Intercept	51.432(a)	.000	0	.
SLTUS	80.116	28.684	11	.003

respectively (Fig-2). Quantity of salt intake also reduced from 07 teaspoonfuls per week at beginning to 0.3 teaspoonfuls after 18m intervention.

Change of salt intake significantly related 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) (Table-VII).

Multiple regression analysis was done for testing individual role of change of salt intake, after removing the effect of other individual intervention or socio-economic variables. For systolic BP reduction of salt intake was found to be the best predictor (Beta =0.273, t= 4.148, p=0.000) (Table-VIII). Role of reduction of weight in 18 months

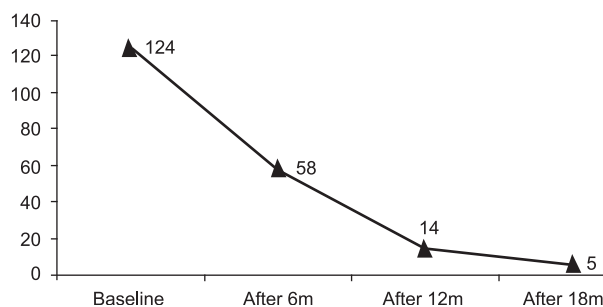


Fig-2: Change of number of respondents with HTN taking extra salt (n=282)

Table-VII
GLM Test between change of salt intake and BP
Dependent Variable: Change of BP at 18m

Statistic	Type III Sum of Squares	df	Mean Square	F value	p
Corrected Model	591.175(a)	2	295.588	9.688	.000
Intercept	178.324	1	178.324	5.844	.016
SLTUS18 for sBP	591.175	2	295.588	9.688	.000
Corrected Model	263.861(a)	2	131.930	6.544	.002
Intercept	1779.401	1	1779.401	88.261	.000
SLTUS18 for dBP	263.861	2	131.930	6.544	.002

a r² = 0.086 (Adjusted r² = 0.077) for sBP and a r² = 0.059 (Adjusted r² = 0.050) for dBP

Table-VIII
Predictor co-efficient and significance for BP at 18m

Systolic Blood Pressure <i>Predictors</i>				
Sl. 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 <i>Predictors</i>				
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

was critical to decide (Beta =0.126, t= 1.860, p=0.064) with no significant role of reduction of smoking tobacco (Beta =0.009, t= 0.124, p=0.902) for systolic BP. For dBP weight reduction was also found to have significant role (Beta =0.144, t= 2.038, p=0.043) and smoking contributed no significant reduction (Beta =0.025, t= 0.340, p=0.735) with salt reduction best predictor (Beta =0.173, t= 2.462, p=0.015) (Table-VIII).

Quality of life was evaluated for both subjective and objective indices. Subjective index for anxiety/ depression scale of the respondents reduced from 8.2 to 2.4 over 18months on a scale from 0 to ten.

Discussion

This was a multi-variable intervention study focusing life style modification and behavioural changes. Impact of other variables was also important confounder for study. Percentage contribution of salt use was very difficult to isolate. Correlation of salt with hypertension was tested during baseline study. Relationship between use of extra table salt and blood pressure was tested with multinomial regression analysis showing statistically significant association. The chi-square statistic obtained was the difference in -2 log-likelihoods between the final model and a reduced model. This reduced model was equivalent to the final model because omitting the effect did not increase the degrees of freedom. The reduced model was formed by omitting an effect from the final model. The null hypothesis was that all

parameters of that effect were zero. Counselling was done to reduce intake of extra table salt. At the end of 18 month salt intake was found to be reduced both in quantity and also frequency. This reduction in salt intake was again tested for correlation with the change of blood pressure. Positive correlation was observed again. This observation strongly indicated role of salt intake as causation of hypertension and confirms the role for reducing blood pressure when discontinued. Similar observation was reported also in other study reports.^{16,17} This study also statistically proved that reduction of salt intake could significantly reduce both systolic and diastolic blood pressure. Salt was also found to be the best predictor for occurrence and reduction of both systolic and diastolic blood pressure.

Extra salt intake was reduced from 44% at beginning of intervention to 1.8% at the end of 18 month intervention. This change of reduced salt intake significantly influenced 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 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 contributes more for systolic blood pressure reduction than comparable diastolic blood pressure reduction. In brief, salt intake is found significantly associated with causation of blood pressure and also reduction of salt intake significantly contributes to reversal of blood pressure.

Conclusion:

Reversal of hypertensives was 56.7% by combined impact of lifestyle and behavioural changes including salt intake reduction. But individually salt intake reduction was found to be more contributory than any other individual risk factors under study. This study confirms relation of salt with hypertension and also confirms reduction of blood pressure after reducing salt intake. This study recommends no extra salt intake for patients with high blood pressure.

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