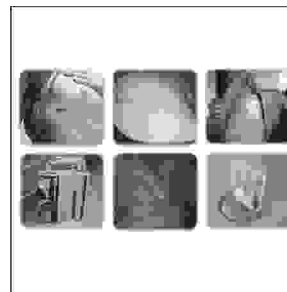


ORIGINAL

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SPONTANEOUS PNEUMOTHORAX SECONDARY TO COPD; EFFECTS OF CHEMICAL PLEURODESIS IN THE RECURRENCE



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ABSTRACT... Introduction: The high recurrence rate of spontaneous pneumothorax secondary to COPD highlights the need for the prevention of recurrence with cheap and cost effective method. Chemical pleurodesis with tetracycline hydrochlorides may be a good option for the prevention of recurrence of pneumothorax and thereby enables satisfactory patient outcome. **Objectives:** (i) To compare the recurrence rate of spontaneous pneumothorax treated with chemical pleurodesis with tetracycline hydrochloride and tube thoracostomy alone. (ii) To make a standard protocol for management. **Study design:** A prospective randomized case control study. **Setting:** The dept. of thoracic surgery of the National Institute of Diseases of the Chest and Hospital (NIDCH), Dhaka, Bangladesh. **Period:** From January 2003 to December 2003. **Material & Methods:** Sixty patients with spontaneous pneumothorax, secondary to COPD. After randomization, 30 patients were treated with tube thoracostomy followed by pleurodesis with tetracycline hydrochloride and another 30 patients of control group were treated with tube thoracostomy alone. **Results:** Patients were followed up upto 6 months and were looked for recurrence. Patients with spontaneous pneumothorax were of 4th to 6th decades of life and most of them were male. Most patients presented with moderate size of pneumothorax and required 91-110 hours for lung expansion after tube thoracostomy. Recurrence rate of spontaneous pneumothorax secondary to COPD in the tetracycline group was 3.3%, whereas in control group it was 30%. Intrapleural instillation of tetracycline hydrochloride significantly reduces the recurrence of spontaneous pneumothorax secondary to COPD. (P=0.015). Morbidity related to tetracycline was negligible. Moreover, tetracycline is cheap, easily available, non-toxic,

well tolerated. **Conclusion:** It is concluded that recurrence rate of spontaneous pneumothorax secondary to COPD can be reduced effectively by chemical pleurodesis with tetracycline hydrochloride without any significant morbidity related to tetracycline hydrochloride and it is also very cost effective.

Key words : Chemical pleurodesis, spontaneous pneumothorax

INTRODUCTION

Pneumothorax is defined as an accumulation of air in the pleural space with secondary lung collapse. This accumulation may come from different sources, but rupture of the visceral pleura with secondary air leak from the lung is the single most common cause¹.

Pneumothoraces can be classified according to their cause and clinical presentation. They can either be spontaneous, traumatic, or iatrogenic, the first category includes both primary and secondary varieties. Spontaneous pneumothorax develops annually in 17,000 individuals in the United States². A primary spontaneous pneumothorax happens in individuals with no known pulmonary disease¹. Secondary Spontaneous pneumothorax may arise from a variety of pulmonary and non-pulmonary disorders. Pneumothorax complicating chronic obstructive pulmonary disease is the most common variety of secondary pneumothorax. It occurs in patients older than 50 years of age and is the result of rupture of a bulla into the pleural space¹.

In most cases diagnosis is made by chest radiographs. Tube thoracostomy is a good option of treatment of spontaneous pneumothorax. Recurrence rate in the secondary spontaneous pneumothorax are high³. The ipsilateral recurrence rate for patients with primary spontaneous pneumothorax treated with tube thoracostomy has varied from 23% to 52%. Although less data are available with secondary spontaneous pneumothorax, the recurrence rates seem to be comparable².

Pleurodesis, either chemical or surgical, is an effective procedure for prevention of recurrent spontaneous pneumothorax. Pleurodesis should be performed for every COPD patient with pneumothorax in order to

prevent recurrence⁴. Many agents have been injected into the pleural cavity through a chest tube to induce pleural adhesion between the parietal and visceral pleurae. Historically silver nitrate, guaiacol, hypertonic glucose, iodoform, iodized oil, autologous blood, cyanoacrylate tissue adhesive and talcum have been used. Now a days tetracycline hydrochloride has been advocated.⁵ It is believed that the local irritating effect of the drug is related to its low pH which causes sterile inflammation with subsequent adhesion of visceral pleura to parietal pleura and obliteration of pleural space¹. Tetracycline hydrochloride is chosen as the sclerosing agent because it seems to be the most effective sclerosing agent because it is widely available and because it is devoid of significant systemic toxic effects when used intrapleurally².

Despite significant social impact of spontaneous pneumothorax few epidemiologic data are available for the study of spontaneous pneumothorax using intrapleural tetracycline hydrochloride in developing countries including Bangladesh. The present study was carried out : (i) To study the outcome of chemical pleurodesis with tetracycline hydrochloride in the recurrence of spontaneous pneumothorax secondary to COPD. (ii) To compare the recurrence rate of spontaneous pneumothorax treated with chemical pleurodesis with tetracycline hydrochloride and tube thoracostomy alone. (iii) To make a standard protocol for management.

MATERIALS AND METHODS

A prospective randomized case control study was carried out in the dept. of thoracic surgery of the National Institute of Diseases of the Chest and Hospital (NIDCH), Dhaka, Bangladesh during the period January 2003 to December 2003. A total number of 60 patients had been

taken in this study. These patients were divided into 2 groups randomly. In group A, 30 patients were treated with tube thoracostomy followed by chemical pleurodesis after lung expansion and in group B, 30 patients were treated with tube thoracostomy only.

Patient selection criteria

Inclusion criteria

Patients having spontaneous pneumothorax secondary to COPD admitted in NIDCH, Mohakhali, Dhaka, during the study period. The diagnosis of spontaneous pneumothorax secondary to COPD was based upon history, clinical findings, chest x-ray and lung function test. Lung function test was done after tube thoracostomy and when the patients condition was improved and became stable.

Exclusion criteria

- * Spontaneous pneumothorax secondary to COPD with broncho-pleural fistula.
- * Secondary spontaneous pneumothorax due to COPD requiring thoracotomy.
- * Primary spontaneous pneumothorax.
- * Secondary spontaneous pneumothorax due to COPD with failure of lung expansion after tube thoracostomy.
- * Hypersensitivity to tetracycline.

Patients with spontaneous pneumothorax, who were hospitalized and required tube thoracostomy and met no exclusion criteria were eligible for the study. After evaluation, tube thoracostomy was done under aseptic condition. A 32 French size tube was inserted through the 4-6th intercostal space along the anterior axillary line under local anaesthesia, into the pleural space depending upon the side of the pneumothorax and the tube was connected with underwater seal drainage system. After tube thoracostomy, evaluation of the patients was done both clinically and radiologically. First

x-ray was done after 24 hours to see the re-expansion of the lung. Further evaluation of the patients was done clinically and by chest x-ray. When the lung was expanded, the patients were randomized to the tetracycline or the control group.

The following treatment protocol was followed for individuals assigned to the tetracycline group;

20 ml of 1% Inj. lignocaine hydrochloride was introduced through the chest tube into pleural space, tube was clamped for 15 minutes. 2 gm of Tetracycline hydrochloride introduced through chest tube, 20ml of normal saline was introduced to flush the tube, the tube was then clamped for 6 hours. Patient was told to change posture hourly. After 6 hours tube was declamped and allowed drainage. Patients in both tetracycline and control groups were observed carefully for 24 hours period and any complication related to tetracycline were recorded. Tube was removed usually after 24 hours both in the tetracycline and control groups and when the drainage was less than 50ml in 24 hours.

The following outcomes were measured: Age and sex distribution of the patient, height and weight of the patient, duration of pneumothorax, side of pneumothorax, size of pneumothorax, time of lung expansion after tube thoracostomy, lung function test, duration of hospitalization, recurrence of pneumothorax, side effects after tetracycline instillation, mortality, patients were followed up upto 6 months after hospital discharge and were looked for- recurrence of pneumothorax

All the relevant collected data were compiled on a master chart. Data analysis were done by using computer software devised with statistical package for social sciences (SPSS). Baseline characteristics between group A and group B were compared by chi-square test. Treatment comparisons for recurrence were made using chi-square test. Lung function tests were compared using unpaired t-test. The P-value of less than 0.05 was considered significant.

RESULTS

Data were prospectively collected on 30 patients assigned to the tetracycline group and 30 patients assigned to the control group. The patient group comprised of 29 male (96.7%) and 1 female (3.3%) in each group with male female ratio was 29:1. Patients age ranged from 40 years to 70 years in each group with mean 54.8 ± 7.8 years in group A and 56.2 ± 9.2 years in group B, which were similar and did not differ significantly. Distribution and comparison of age of the patients are shown in table-I. All the patients in each groups were in fourth to sixth decades of life, no patients were below fourth decade.

Age in years	Group A (No of pts)	Group B (No of pts)
40-50	11(36.7)	12(40.0)
51-60	12(40.0)	10(33.3)
61-70	7(23.3)	8(26.7)
Total	30(100%)	30(100%)
Mean \pm SD	54.8 ± 7.8	56.2 ± 9.2

Figures in parenthesis indicate percentage, Chi-square = 0.292, df = 2, P > 0.05 (Not significant)

Patients heights ranges from 5 feet to 6 feet 5 inches in each group with mean 5.6 ± 0.14 feet in group A and 5.6 ± 0.17 feet in group B respectively. Most patients i.e. 70% in group A and 80% in group B however, were in the range of 5 feet 6 inches to 6 feet 5 inches. These two groups were similar and did not differ significantly. Distribution of heights and their comparison between two groups were shown in table-II.

Patients weight ranges from 40 to 60 kg in each group with mean 50.8 ± 5.6 kg in group A and 51.1 ± 4.4 kg in group B. But most patients weights were in the range of 46 to 50 Kg, i.e. 46.7% in group A and 40% in group B. Distribution of weights and comparison between two groups are shown in table -III.

Height in feet/inches	Group A (No of pts)	Group B (No of pts)
5'-5'.5"	9(30.0)	6(20.0)
5'.6"-6'.5"	21(70.0)	24(80.0)
Total	30(100)	30(100)
Mean \pm SD	5.6 ± 0.14	5.6 ± 0.17

Figures in parenthesis indicate percentage, Chi-square = 0.800, df=1, P > 0.05 (Not significant)

Weight in Kg	Group A (No of pts)	Group B (No of pts)
40-45	4(13.3)	3(10.0)
46-50	14(46.7)	12(40.0)
51-55	6(20.0)	7(23.3)
56-60	6(20.0)	8(26.7)
Total	30(100)	30(100)
Mean \pm SD	50.8 ± 5.6	51.1 ± 4.4

Figures in parenthesis indicate percentage, Chi-square = 0.659, df = 3, P > 0.05 (Not significant)

Duration of pneumothorax

Duration of pneumothorax ranged from 45 to 170 hours in each group with mean 95.8 ± 44.2 hours in group A and 97.3 ± 33.4 hours in group B respectively. Duration of pneumothorax of most patients in each group were from 66 to 107 hours (Shown in table IV).

Side of pneumothorax

60% of patients in group A had right sided pneumothorax and 40% had left sided pneumothorax, on the other hand half of the patients in group B had right sided and half had left sided pneumothorax shown in table -V.

Percentage of lung collapse

Percentage of lung collapse ranged from 15 to 45% in

each group with mean (29.5 ±5.3) in group A and (29.0±4.8) in group B respectively. But most patients i.e. 93.3% in group A and 96.7% in group B ranged from 21 to 40%. Shown in table –VI and in photograph-1.

Hours	Group A (No of pts)	Group B (No of pts)
45-65	6(20.0)	4(13.3)
66-86	10(33.3)	10(33.3)
87-107	7(23.3)	9(30.0)
108-128	1(3.3)	2(6.7)
129-149	2(6.7)	2(6.7)
150-170	4(13.3)	3(10.0)
Total	30(100)	30(100)
Mean ±SD	95.8±44.2	97.3±33.4

Figures in parenthesis indicate percentage, Chi-square = 1.126, df = 5, P>0.05 (Not significant)

Side	Group A (No of pts)	Group B (No of pts)
Right	18(60.0)	15(50.0)
Left	12(40.0)	15(50.0)
Total	30(100)	30(100)

Figures in parenthesis indicate percentage, Chi-square = 0.606, df = 1, P>0.05 (Not significant)

%age	Group A (No of pts)	Group B (No of pts)
<20	1(3.3)	1(3.3)
21-40	28(93.3)	29(96.7)
40+	1(3.3)	-
Total	30(100)	30(100)
Mean ±SD	29.5±5.3	29.0±4.8

Figures in parenthesis indicate percentage, Chi-square = 1.018, df = 2, P>0.05 (Not significant)

Time for lung expansion after tube thoracostomy

Time for lung expansion after tube thoracostomy ranges from 50 to 144 hours in group A and from 50 to 120 hours in group B with mean time for expansion 90.6±17.3 hours for group A and 93.3±15.3 hours for group B. This time ranged from 91 to 110 hours for 50% patients of group A and 53.3% of patients of group B. Shown in table -VII.

Hours	Group A (No of pts)	Group B (No of pts)
50-70	1(3.3)	1(3.3)
71-90	12(40.0)	10(33.3)
91-110	15(50.0)	16(53.3)
111-144	2(6.7)	3(10.0)
Total	30(100)	30(100)
Mean±SD	90.6±17.3	93.3±15.3

Figures in parenthesis indicate percentage, Chi-square = 0.414, df = 3, P>0.05 (Not significant)

Recurrence rates of spontaneous pneumothorax

The recurrence rate was 3.3% in the tetracycline group and 30% in the control group (P=0.015). The intrapleural administration of tetracycline resulted in a significant decrease in the ipsilateral recurrence rate of spontaneous pneumothorax. Shown in table –VIII and fig 1.

Recurrence rates of spontaneous pneumothorax at different intervals after randomization

All recurrences (3.3%) in the tetracycline group were in the first month after randomization, and in the control group 16.6% recurrence were in the first month. In the control group 10% recurrence was between 2-3 months, and 3.3% recurrence between 4-6 months respectively. Shown in table-IX and fig 2.

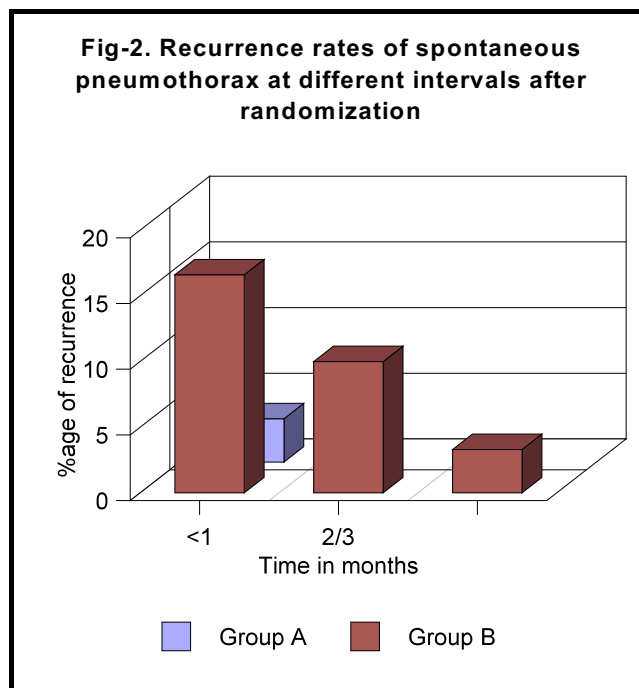
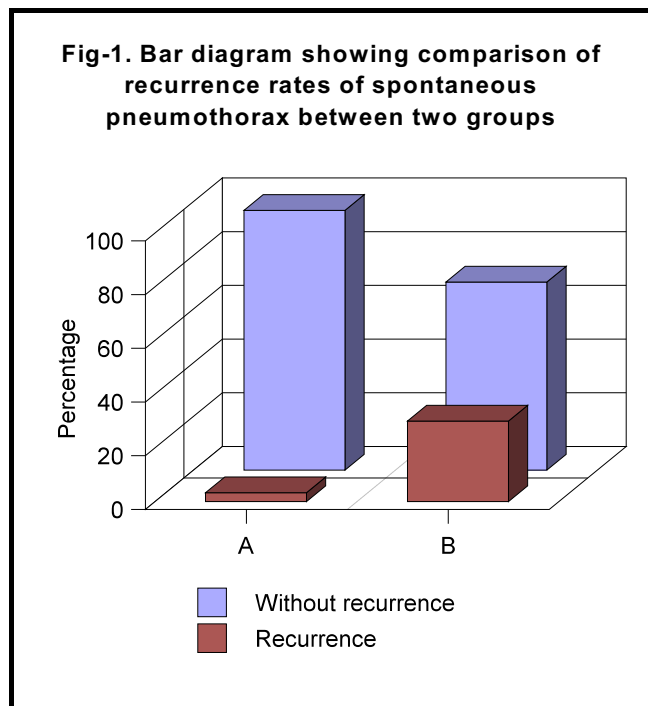
Group of pts	No of pts having recurrence	%age	No. of pts without recurrence	%age
Tetracycline group	1	3.3	29	96.7**
Control group	9	30	21	70

Chi-square=5.88, df=1, **P<0.01 (Significant)

Time in months	Group A (No of pts)	Group B (No of pts)
<1	1(3.3)	5(16.6)
2-3	-	3(10)
4-6	-	1(3.3)

Figures in parenthesis indicate percentage

using tetracycline hydrochloride plays a substantial role in the prevention of recurrence of spontaneous pneumothorax secondary to COPD. This study is particularly designed to study the outcome of chemical pleurodesis with tetracycline hydrochloride in the recurrence of spontaneous pneumothorax, to compare the recurrence rate of spontaneous pneumothorax treated with chemical pleurodesis by tetracycline hydrochloride and tube thoracostomy alone.



DISCUSSION

This study, which was conducted in the National Institute of the disease of the Chest and Hospital, the only referral hospital in Bangladesh, shows that chemical pleurodesis

In this study patients with spontaneous pneumothorax secondary to COPD are of 4th to 6th decades of life with mean age 54.8 ± 7.8 years for group A and 56.2 ± 9.2 years for group B (p=0.892). Age incidence of secondary spontaneous pneumothorax due to COPD is consistent with the study of Light and his colleagues². Most of the

patients in this series were male (96.7%) and all were smoker showing strong likelihood of association of smoking with COPD and pneumothorax. Sex distribution and smoking history is also consistent with previous study of DeVries et al. (1980) and Limthongkul et al. (1992) and smoking history is almost similar with the study of Light et al. 1990.^{2,4,5}

Patients with spontaneous pneumothorax having COPD are usually tall (mean height 5.6 ± 0.14 feet for group A and 5.6 ± 0.17 feet for group B ($P=0.371$) and underweight (mean weight 50.8 ± 5.6 kg for group A and 51.1 ± 4.4 for group B $p=0.883$) causing increasing height to weight ratio predisposing pneumothorax.

In this study mean duration of pneumothorax was 95.8 ± 44.2 hours in group A and 97.3 ± 33.4 hours in group B ($p=0.952$). This duration of pneumothorax in this study seems to be prolonged and may be due to the fact that, NIDCH is the only referral chest disease hospital in Bangladesh. So patients from remote areas loose their time from being referred from one hospital to another before reaching to NIDCH.

Right sided pneumothorax in the study group was 60% and left sided 40% and in control group 50% in each side ($p=0.936$). In the previous study by Light et al. (1990) left sided pneumothorax was 52.2% in study group and 53.5% in control group². But no significant differences were noted between two groups. In previous study of Getz et al. (1983) a slight predilection for right side was noted (54%) compared with left side. It is consistent with present study⁶.

Most patients had moderate size of the pneumothorax with mean (29.5 ± 5.3)% for group A and (29.0 ± 4.8)% for group B ($p=0.601$). This is consistent with the previous study of Limthongkul and associates which was 29.3 ± 23.3 percent of hemithorax⁵, but differs from previous study by Light and his colleagues. Their result were 54.0 ± 28.1 percent for group A and 57.6 ± 27.6 percent for group B respectively i.e. most of their patients had large size pneumothorax². This is because they included patients with primary spontaneous

pneumothorax and secondary spontaneous pneumothorax due to pneumonia and asthma along with COPD.

Time required for lung expansion between two groups are identical (Group A- $m \pm SD=90.6 \pm 17.3$, group B- $m \pm SD=93.3 \pm 15.3$ hours, $p=0.937$). Most of the patients required 91-110 hours for lung expansion after tube thoracostomy. Which is almost similar to previous study (median time 120 hours) of Limthongkul and associates⁴

The main adverse effect associated with tetracycline instillation was chest pain only in 2 patients in spite of intrapleural administration of lignocaine ; and slight rise of temperature in 4 patients that subsided in the next day. This is much less compared with previous study of Light et al., (1990). The pain and rise of temperature did not alter the general wellbeing of the patients.

In this study intrapleural instillation of tetracycline hydrochloride resulted in a significant ($P=0.015$) decrease in the rate of recurrence of spontaneous pneumothorax secondary to COPD which is 3.3% for group A but 30% for group B. Most of the recurrences happened within 6 months of initial episode.

Present study shows that the recurrence rate following instillation of tetracycline is 3.3%, whereas it was 25% in previous study of Light et al. (1990). On the otherhand recurrence rate in tube only group in this study is 30%, whereas it was 41% in previous study of Light and his associates². Both in this study and in the previous study tetracycline hydrochloride significantly reduced the recurrence rate of spontaneous pneumothorax, but the recurrence rates of the previous study are higher than the present study possibly because of their long follow up period and use of tetracycline at lower dose².

In a previous study it was shown that recurrence rate was 13% after tetracycline instillation compared with 36% in patients with chest tube drainage alone¹. Differences in these recurrence rates were not statistically significant because they used tetracycline at

lower dose (500mg). Present study showed much lower recurrence rate (3.3%) of spontaneous pneumothorax after tetracycline instillation. Tetracycline hydrochloride at a dose of 35mg/kg was more effective than at a dose of 7 or 20 mg/kg.

As intrapleural tetracycline decreased the recurrence rate in the present study, it should be considered the agent of choice in attempts to create a chemical pleurodesis. We believe that it should be considered the agent of choice for the following reasons- aerosolized talc is more difficult to administer, intrapleural instillation of dissolved talc has been associated with the development of acute respiratory distress syndrome, quinacrine is no longer available, administration of silver nitrate is even more painful than tetracycline, and lastly, tetracycline is cost effective, easily available in our country and relatively nontoxic^{1,2}.

CONCLUSION

Chemical pleurodesis with tetracycline hydrochloride is a good option for the prevention of recurrence of pneumothorax. This prospective study was conducted in the NIDCH from January 2003 to December 2003 on 60 patients with spontaneous pneumothorax secondary to COPD. Recurrence rate of spontaneous pneumothorax secondary to COPD in the tetracycline group was 3.3%, whereas in control group it was 30%. Chemical pleurodesis with tetracycline hydrochloride significantly reduces the recurrence of spontaneous pneumothorax due to COPD ($P=0.015$). Morbidity related to tetracycline was negligible, moreover tetracycline is cheap, easily available, non-toxic, well tolerated. From this study we

conclude and recommend that in Bangladesh including other developing countries, where treatment facilities are minimum, recurrence rate of spontaneous pneumothorax secondary to COPD can be reduced effectively by chemical pleurodesis with tetracycline hydrochloride without any significant morbidity and it is also very cost effective.

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