

## Original Research Article

# Complications and residual pleural thickening after intrapleural instillation of streptokinase with pigtail catheter drainage of tuberculous pleural effusion

Sandeepa H. S.<sup>1</sup>, Narendra U.<sup>2\*</sup>, Gajanan S. Gaude<sup>3</sup>, Supriya Sandeepa<sup>4</sup>

<sup>1</sup>Department of TB and Chest Disease, Akash Institute of Medical Sciences, Bengaluru, Karnataka, India

<sup>2</sup>Department of TB and Chest Disease, Shridevi Institute of Medical Sciences and Research Hospital, Tumkur, Karnataka, India

<sup>3</sup>Department of TB and Chest Disease, Jawaharlal Nehru Medical College, Belgaum, Karnataka, India

<sup>4</sup>Department of Pathology, Akash Institute of Medical Sciences, Bengaluru, Karnataka, India

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### \*Correspondence:

Dr. Narendra U.,

E-mail: [drsandeeps@gmail.com](mailto:drsandeeps@gmail.com)

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## ABSTRACT

**Background:** Tuberculosis is the most common cause of exudative lymphocytic pleural effusion in India. Residual pleural thickening (RPT) is observed in about 50 percent of patients even after proper treatment with ATT. Pleural fluid drainage either with simple aspiration or with intercostal drainage and addition of corticosteroids along with antitubercular drugs have not shown to influence the incidence of RPT. The present study was undertaken to study the complications and residual effects of tubercular pleural effusion on the patients during the follow up period following intrapleural streptokinase instillation.

**Methods:** Clinical profile, hospital course and outcome of tuberculous pleural effusion patients at the end of six months of anti-tubercular treatment of 50 patients from January 2009 to June 2010 were analyzed. These patients were randomly divided into two groups. One group (n=25) received intrapleural streptokinase via pigtail catheter and the other group (n=25) received intercostal drainage without intrapleural streptokinase instillation. All the patients received standard daily anti TB regimen of 2HERZ/4HR for a total duration of six months. All the patients were followed up for a total duration of 1 year for evidence of any residual pleural thickening.

**Results:** Majority of the patients were above 40 years of age (60%). The male to female ratio was 2.3:1. The major symptoms of the patients were, fever in 44 patients (88%), cough in 42 patients (84%), breathlessness in 33 patients (66%), loss of appetite in 25 patients (50%) and chest pain in 25 patients (50%). Most of the patients had ADA levels between 40-70IU/L (48%) and only 6% had ADA levels below 40IU/L. The incidence of residual pleural thickening in the study group was less as compared to the control group (2.36±0.49mm vs 9.28±1.50mm) (p <0.0001).

**Conclusion:** Intrapleural streptokinase instillation with pigtail catheter drainage less number of complications associated with study group and is successful with the decreased incidence of residual pleural thickening during the follow up period.

**Keywords:** Pigtail catheter, Residual pleural thickening, Streptokinase, Tuberculosis

## INTRODUCTION

Presence of excessive quantity of fluid in the pleural space is called pleural effusion. The diagnosis of tuberculous pleural effusion is important because

tuberculosis is normally a treatable cause of exudative lymphocytic pleural effusion. Other differential diagnoses of exudative lymphocytic Pleural effusions are malignancy, fungal infection, melioidosis, sarcoidosis, and connective tissue diseases. The primary difficulty in

getting a diagnostic confirmation of tuberculous pleural effusion is the identification of mycobacterium in the pleural fluid. Pleural biopsy is usually the main diagnostic support, but its invasive nature and the difficult technique that limits its practice.<sup>1</sup> Tuberculous (TB) pleurisy can cause clinical symptoms and pleural fibrosis with resultant residual pleural thickening (RPT). Therapeutic thoracentesis or initial complete drainage in addition to anti-TB drugs has been tried in order to rapidly relieve dyspnea caused by effusions and decrease the occurrence of RPT. Delayed diagnosis and or treatment of TB pleurisy may cause disordered fibrin turnover in the pleural cavity with subsequent fibrin deposition and loculation of pleural fluid, and may impair uneventful resolution of pleural effusion.<sup>2</sup>

## METHODS

The study was done at KLES Dr Prabhakar Kore Hospital, which is a tertiary care hospital.

### *Inclusion criteria*

- Patients above 18 years diagnosed as a case of tubercular pleural effusion at KLES Prabhakar Kore Hospital, Belgaum.

### *Exclusion criteria*

- A history of invasive procedures directed into the pleural cavity.
- Recent severe trauma.
- Hemorrhage or stroke.
- Bleeding disorder or anticoagulant therapy.
- Patients below the age of 18 yrs.
- Use of streptokinase in the previous 2 yrs.

Detailed history was taken; respiratory system was examined. All the basic investigations were done in all patients as per the protocol. Chest radiograph of posterior-anterior view were done in all the cases. CT scan of thorax was done wherever required.

The diagnosis of tubercular pleural effusion was done by the combination of various diagnostic modalities like sputum for AFB and Pleural fluid analysis for: Proteins, Sugars, Total count, Differential count, ADA level estimation, PCR for MTB DNA, Pleural fluid for AFB staining.

### *Procedure of pigtail catheter insertion*

Prior to commencing pigtail catheter insertion, the procedure is explained fully to the patient and consent recorded. The best site to insert the catheter is the "safe triangle". This is the triangle bordered by the anterior border of the latissimus dorsi, the lateral border of the pectoralis major muscle, a line superior to the horizontal level of the nipple, and an ape below the axilla.

After identifying the site of maximum dullness, the part is infiltrated with a local anesthetic like 2% lignocaine under aseptic precautions. In contrast to large bore catheters, the pigtail catheter is inserted with the aid of a guide wire by a Seldinger technique. Blunt dissection is unnecessary as dilators are used in the insertion process. After infiltration with local anesthesia, a needle and syringe are used to localize the position for insertion of pigtail catheter (point of maximum dullness). A guide wire is then passed down the hub of the needle, the needle is removed, and the tract enlarged using a dilator. A small-bore pigtail catheter is then passed into the thoracic cavity along the wire. It is held securely to the chest wall with the help of purse string sutures. A three way stop cork is then connected to the free end of the pigtail catheter and the three way is further attached to an ICD bottle or a Romodrain bag with fluid level to create a closed system which prevents the development of iatrogenic pneumothorax.

The patients were then divided into two groups randomly using odd and even method. Group 1 (control) received Intercostal Tube Drainage alone using large bore (28F) polymed thoracic chest tube. Group 2 (study) received Intercostal Tube Drainage using small bore (7F) Pigtail catheter along with intrapleural instillation of streptokinase (2.5 lakh units) daily for 3 days. All patients in both groups received anti tubercular treatment (2HRZE, 4HR).

### *Procedure of streptokinase instillation*

Intrapleural injection therapy was started on the following day, with intrapleural injection of solution containing 250,000 IU of dissolved streptokinase in 100ml of normal saline. After injection, the pigtail tube was clamped for 2 h and subsequently opened for free drainage. Intrapleural instillation of streptokinase was repeated for three consecutive days. Chest X-ray is performed after the third day of treatment. Complete drainage was defined as no or minimal pleural effusion on CXR. The pigtail tube was removed when the net drainage was <50 ml in the previous 24 h. Repeat chest radiography was obtained after 3 days, at the time of discharge and at the end of completion of anti-tubercular therapy. The following outcome variables were studied, and the results were analyzed statistically by using unpaired t-test.

- Complications if any.
- Residual pleural thickening as assessed by chest radiography.

## RESULTS

A total of 53 patients in tertiary care hospital over a period of 1 and half years from 1st January 2009 to 30th June 2010 were included in the study. In the final analysis 3 patients were excluded due to the following

reasons: two patients lost follow up and one patient was later proved to have malignant pleural effusion.

Thus 50 cases were analyzed in detail. There were 25 cases in the study group and 25 cases in control group as shown in Table 2.

**Table 1: Age wise distribution of patients.**

Age group	Total No. (%)	Study group No. (%)	Control group No. (%)
<20 years	05(10%)	03(12%)	02(08%)
21-30 years	08(16%)	03(12%)	05(20%)
31-40 years	07(14%)	03(12%)	04(16%)
41-50 years	11(22%)	08(32%)	03(12%)
>51 years	19(38%)	08(32%)	11(44%)

Majority of the patients (38%) were in the age group of >51 years and 11 (22%) patients belong to the age group between 41-50 years and 8 patients belong to age group 21-30 years. Five patients were less than 20 years.

**Table 2: Gender wise distribution of the patients.**

Sex	Total No. (%)	Study No. (%)	Control No. (%)
Male	35(70%)	16(64%)	19(76%)
Female	15(30%)	9(36%)	6(24%)

Total number of male patients were 35 (70%) and total female patients were 15 (30%). Thus, male to female ratio was 2.3:1.

**Table 5: Complications in both groups.**

Group	PTX No. (%)	Infection of wound No. (%)	Chest pain No. (%)	HYD no. (%)	PYO no. (%)	Tube block no. (%)
Study group	02(8%)	04(16%)	07(24%)	00(00%)	00(00%)	05 (20%)
Control group	00(00%)	09(36%)	05(20%)	02(8%)	02(8%)	00 (00%)
Total	02(4%)	13(26%)	12 (24%)	02(4%)	02(4%)	05(10%)

It is observed that the most common complication in both groups was infection at the site of insertion (n=13) 26%, the infection was more in control group as compared with the study group may be because of the wound size. Pneumothorax was observed only in 2 cases in the study group, this was probably due to faulty procedure initially and no such cases were observed once the expertise with the technique was achieved. The most important complication with pigtail catheter was catheter blockage, it was easily overcome by flushing the catheter with 20-50ml of normal saline. Seven cases in the study group and 5 cases in control complained of chest pain. Two cases each of pyothorax and hydropneumothorax were noted in the control group.

**Table 3: Major symptoms of the patients.**

Symptoms	Total patients No. (n=50)	Percentage (%)
Cough	42	84
Fever	44	88
Breathlessness	33	66
Loss of appetite	25	50
Weakness	10	20
Chest pain	25	50

The major symptoms of the patients were, fever in 44 (88%) patients, cough in 42 (84%) patients, breathlessness in 33 (66%) patients, loss of appetite in 25 (50%) patients and chest pain in 25 (50%) patients.

**Table 4: Pleural fluid ADA levels in all the patients.**

Groups	<40 IU/ml No. (%)	40-70 IU/ml No. (%)	>70 IU/ml No. (%)
Study	03(12%)	13(52%)	09(36%)
Control	03(12%)	11(44%)	11(44%)
Total	06(12%)	24(48%)	20(40%)

From Table 4 it is observed that 24 patients (48%) patients had ADA levels between 40-70 IU/ml, 20 (40%) patients had an ADA level above 70 IU/ml, whereas in only in 6 (12%) cases the ADA levels were below 40 IU/ml.

During the follow up period it is observed that 30 patients (60%) of all cases developed residual pleural thickening (RPT) at the end of 6 months of ATT.

**Table 6: Comparison of residual pleural thickening in both the groups during follow up period.**

Group	Cases (N) No. (%)	RPT (CMS)
Study	14 (56%)	2.36±0.49 CMS
Control	16 (64%)	9.28±1.50 CMS
p value	p<0.0001	

RPT= residual pleural thickening

Among the study group 14 patients (54%) and in the control group 16 patients (64%) developed RPT

respectively. The mean thickening in study group was significantly less ( $2.36\pm 0.49$ cms) as compared to the control group ( $9.28\pm 1.50$ cms) ( $p < 0.0001$ ).

## DISCUSSION

The present study was done in a tertiary care KLES Dr Prabhakar Kore hospital and medical research center, Belgaum. A total of 53 patients were included in the study, among them three patients were excluded from the final analysis because two patients lost follow up and one patient was diagnosed as a case of malignant pleural effusion. Hence the remaining 50 patients were divided into two groups containing 25 patients each (study and control).

Majority of the patients in the study were in the age group above 51 years (38%) and overall 60% of patients were above the age of 40 years. This in contrast to study done by Ibrahim et al, who observed that the mean age of 100 patients with tuberculous pleural effusion was 31.5 years.<sup>3</sup> This findings are in part consistent with the reports from the study of Baumann et al who studied 14,000 patients with tuberculous pleuritis reporting to the Communicable Disease Center in the United States between 1993 and 2003.<sup>4</sup> In their study the mean age of the patients was 49.9 years. In another study done by Sharma et al the mean age of patients with tuberculous pleural effusion was 33years.<sup>5</sup> The difference in the age distribution of the present study with other studies might be due to a relatively small sample size. In the present study, males to female ratio was 2.3:1 which was consistent with the study done by Singla in which there were 35 males and 11 females among the 46 patients with tuberculous pleural effusion.<sup>6</sup> Seibert et al studied seventy patients of tuberculous effusion and among them 47 patients were males and 23 were females.<sup>7</sup> The major symptoms of the patients were fever (88%), cough (84%), dyspnea (66%), loss of appetite (50%), chest pain (50%) and generalized weakness (20%). These findings were consistent with the study done by Berger et al.<sup>8</sup> They observed cough (70%), fever (68%) and chest pain to be the most common symptoms. In another study done by Kwak et al the predominant symptoms were chest pain (80%), cough (76%), fever (70%) and dyspnea (55%).<sup>9</sup>

In our study, majority of the patients had an ADA level exceeding 40IU/L which is in consistency with the studies done by Ocana et al.<sup>10</sup> In their study of 221 patients with pleural or peritoneal effusions, all patients with a pleural fluid ADA of 70IU/L had TB, whereas no patient with a pleural fluid ADA below 40 IU/L had tuberculous pleuritis. Verma et al studied 50 patients above the age of 12 years with pleural effusion and among them 34 patients were diagnosed as having tuberculous pleural effusion and observed that the pleural fluid ADA level was more than 36 IU/L in all cases of tuberculous pleural effusion.<sup>11</sup> They also concluded that when 36IU/L is taken as cut off point, sensitivity and specificity of ADA for TB is 100% and 77%. Sulochana

et al. studied 3 groups of pleural effusion.<sup>12</sup> Group 1 had 15 patients with tuberculous effusion, group 2 had 15 patients with malignant pleural effusion and the third group had 15 patients with non-tuberculous and non-malignant pleural effusions. They found that the mean ADA levels in group 1 was  $53.8\pm 8.9$  IU/L and this was significantly higher than the other two groups which had mean ADA levels of  $34.8\pm 4.82$  IU/L and  $9.9\pm 1.39$  IU/L respectively. In another study done by Gupta et al, all 36 patients with tuberculous pleural effusion had ADA levels above 50.75 IU/L.<sup>13</sup>

In the present study, intercostal drainage alone was not associated with decreased incidence of residual pleural thickening. This was consistent with the findings of Lai et al who studied the role of pigtail drainage in the treatment of tuberculous pleural effusion.<sup>14</sup> In their study sixty-one patients with tuberculous effusion were divided into two groups. Thirty patients received pigtail drainage along with anti-tubercular treatment and thirty-one patients received only anti tubercular treatment. At the end of their study they concluded that addition of pigtail drainage to an effective anti-TB treatment does not reduce the level of residual pleural thickening. But in the present study small bore (7F) pigtail catheter was as effective as large bore (32 F) Polymed Intercostal Tube in draining the pleural fluid and was associated with less number of procedure related complications like infection at the wound site. This was consistent with the study done by Gammie et al, who concluded that the pigtail catheter offers reliable treatment of pneumothoraces and simple effusions and is safe and less invasive alternative to tube thoracostomy.<sup>15</sup> The use of intrapleural streptokinase therapy at the dose used in the present study (2,50,000IU/ day for 3 days) was not associated with any obvious systemic side effects which was similar other studies done by Chin et al who studied complicated pleural effusion cases with 1to 10 intrapleural instillations of streptokinase and observed no complications.<sup>16,17</sup> At the end of 6 months of anti-tubercular treatment, we noted that the occurrence of residual pleural thickening in the streptokinase group was significantly less than the study group ( $2.36\pm 0.4929$ mm vs  $9.280\pm 1.508$ mm). This finding was consistent with the studies done by Chung et al who observed that only two of their patients in the streptokinase group had a residual pleural thickening of more than 10mm as compared to control group in which 10 patients had a residual pleural thickening of  $>10$ mm.<sup>17</sup> Our findings also correlate with the findings of Kwak et al who observed the mean RPT in their study group to be  $4.59\pm 5.93$ mm after intrapleural streptokinase instillation.<sup>9</sup>

## CONCLUSION

Tuberculosis being the most common cause of exudative lymphocytic pleural effusion in India, no effort should be left in arriving at specific diagnosis to give the most rational treatment. Residual pleural thickening (RPT) is observed in about 50 percent of patients even after proper

treatment with ATT. In conclusion, this study has shown that the intrapleural streptokinase instillation along with Small bore Pigtail catheter (7F) is associated with less number of complications and less incidence of residual pleural thickening.

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