

## Original Research Article

# Efficacy of intrapleural instillation of streptokinase with pigtail catheter drainage in the treatment of tuberculous pleural effusion

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## ABSTRACT

**Background:** Tuberculosis is the most common cause of exudative lymphocytic pleural effusion in India. The present study was undertaken to evaluate the efficacy of intrapleural instillation of streptokinase with pigtail catheter drainage in the treatment of tuberculous pleural effusion.

**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.

**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 40-70 IU/L (48%) and only 6% had ADA levels below 40 IU/L. The mean pleural drainage was 2615±126.1 ml in the study group (intrapleural streptokinase) and 1858 ± 93.3 ml in the control group (p <0.0001). Mean duration of intercostal drainage in the study group was 3.76 ± 0.144 days and it was 5.08±0.199 days in the control group (p <0.0001). The mean duration of hospitalization in the study group was 6.60±0.91 days and it was 8.60 ± 0.57 days in the control group (p=0.06).

**Conclusion:** Intrapleural streptokinase instillation is successful in increasing the total drainage of pleural fluid and results in effective drainage of tuberculous pleural effusion. It is also associated with increased amount of pleural fluid drainage, decreased duration of intercostal drainage, decreased length of hospital stay.

**Keywords:** Efficacy, Pleural effusion, Streptokinase, Tuberculosis

## INTRODUCTION

Pleural effusion is the presence of excessive quantity of fluid in the pleural space.<sup>1</sup> Though it produces minimal clinical manifestations; it should be considered as an ominous sign of a serious disorder. So, no effort should be left in arriving at specific diagnosis to give the most

rational treatment. Effusion may be transudative due to abnormalities of hydrostatic, or osmotic pressures and exudative resulting from increased permeability or trauma. Etiological diagnosis is often difficult in cases of pleural effusion. In developing countries tuberculosis is the most common cause of effusion even then other causes should be excluded before concluding as

tuberculosis. Investigation of a pleural effusion demands a pleural aspiration and biopsy. The pleural fluid is sent for measurement of proteins and glucose content, cytological and microbiological examination. Cytology and microbiology benefit from testing as large as quantity of fluid as possible. A "diagnostic tap" of 10-20 ml of pleural fluid without a pleural biopsy is inadequate. In as many as 20% of all pleural effusions basic testing does not establish the diagnosis and even thoracotomy or thoracoscopy may not reveal the cause of the effusion.<sup>2</sup> The present study is being undertaken to investigate the usefulness of early effective drainage of pleural effusion in the treatment of TB pleurisy using a pigtail catheter which is relatively atraumatic and is associated with less number of complications as compared to the routine drainage using large bore tube thoracostomy.

## 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, 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 apex 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 Intercoastal Tube Drainage alone using large bore (28F) polymed thoracic chest tube. Group 2 (study) received Intercoastal 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 results were analyzed statistically by using unpaired t-test.

- Total amount of pleural fluid drained.
- Total duration of pleural fluid drainage.
- Total duration of hospitalization.
- Radiological resolution.

## RESULTS

A total of 53 patients in tertiary care hospital over a period of 1 and half years from 1st January 2009 to 30<sup>th</sup> 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.

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

Age group	Total No. (%)	Study group No. (%)	Control group No. (%)
<20 years	5(10%)	3(12 %)	2(08%)
21-30 years	8(16%)	3(12%)	5(20%)
31-40 years	7(14%)	3(12 %)	4(16%)
41-50 years	11(22%)	8(32%)	3(12%)
>51 years	19(38%)	8(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 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. (%)	>70iu/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 40-70IU/ml, 20(40%) patients had an ADA level above 70IU/ml, whereas in

only in 6(12%) cases the ADA levels were below 40IU/ml.

**Table 5: Total amount of drainage in the study and control group.**

Groups	Drainage (ml) Mean±sd
Study group	2615±126.11
Control group	1858±93.39
p value	p<0.0001

From Table 5 it was observed that the mean intercostal drainage in the study group was 2615±126.1 ml while the mean intercostal drainage in the control group was 1858±93.39 ml. This was highly statistically significant (p <0.0001).

**Table 6: Duration of intercostal drain in study and control groups.**

Group	Duration of drain (days)Mean ± sd
Study group	3.76±0.144
Control group	5.08±0.1993
p value	p<0.0001

From Table 6 it was observed that the mean duration of drainage in the study group was 3.76±0.144 days while the mean duration of drainage in the control group was 5.08±0.199 days. This was highly statistically significant (p <0.0001).

**Table 7: Duration of hospitalization in both groups.**

Group	Number of days Mean±sd
Study group	6.60±0.91 days
Control group	8.60±0.57 days
p value	p=0.06

From Table 7 it is observed that the mean duration of hospitalization in the study group was 6.60 ± 0.91days and in the control group it was 8.60 ± 0.57 days respectively.

Although the mean duration of stay in the hospital was less in the study group as compared with the control group, the difference was not statistically significant (p=0.06). This might be due to associated symptoms of the patients like generalized weakness, intolerance of ATT in the form of gastritis, hepatitis and hypersensitivity which delayed the discharge of the patient.

**Table 8: Level of radiological resolution at discharge in study and control groups.**

Group	Cases (n)	Clear	Minimal effusion
Study	25	20(80 %)	5(20 %)
Control	25	16(64%)	9(36 %)
Total	50	36(72 %)	14(28%)

From Table 8, it was observed that the chest radiographs were clear in 20(80%) patients in the study group and in 16(64%) patients in the control group respectively. In 5(20%) cases in the study group and in 9(36%) cases in the control group there was evidence of minimal residual pleural effusion at discharge.

## DISCUSSION

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> Our 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 33 years.<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 et al 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 40 IU/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 40IU/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 36IU/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±8.9IU/L and this was

significantly higher than the other two groups which had mean ADA levels of 34.8±4.82 IU/L and 9.9±1.39IU/L respectively. In another study done by Gupta et al, all 36 patients with tuberculous pleural effusion had ADA levels above 50.75IU/L.<sup>13</sup> The main aim of the present study was to study the role of intrapleural instillation of streptokinase in the treatment of tuberculous pleural effusion. Our study demonstrated that the intrapleural streptokinase instillation was consistently associated with a significant increase in the drainage of pleural fluid than the control group (2615±126.1ml vs 1858±93.39 ml) ( $p < 0.0001$ ), which was also observed in the study done by Chung et al.<sup>14</sup> They observed the mean pleural drainage in the streptokinase group was significantly higher than the saline group (2.59±1.77 L vs 1.28±1.21 L). In the present study we also observed that the mean duration of intercostal drain in the study group was 3.760±0.1447 days which was significantly less than the study group who had a mean duration of 5.080±0.1993 days ( $p < 0.0001$ ). It is also observed that the mean duration of hospitalization in the study group was less than the control group although the difference was not statistically significant ( $p=0.0695$ ). The level of radiological resolution at the time of discharge was higher in the streptokinase group than in the control group. Similar findings were also noted by Chung et al in their study.<sup>14</sup> They observed that the mean pleural drainage in streptokinase group was 2.59±1.77 L and the total duration of intercostal drainage in the same group was 5±2 days as compared to their control groups. Kwak et al compared intrapleural urokinase with anti-tuberculous medication only.<sup>9</sup> They observed that the mean drainage without intrapleural urokinase was 470 ± 466 ml and this increased to 936±724 ml following intrapleural urokinase instillation

## CONCLUSION

Intercostal drainage along with intrapleural instillation of streptokinase is associated with increase in the total drainage of pleural fluid as compared to the control group. The duration of pigtail catheter in the pleural cavity is considerably for a shorter period as compared to ICD alone. Intercostal drainage along with intrapleural streptokinase is successful in reducing the duration of hospitalization with better radiological improvement.

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