ISSN: 0975-3583,0976-2833 VOL15, ISSUE 9, 2024

AN ANALYTISCAL STUDY OF ROLE OF INTRAPLEURAL STREPTOKINASE FOR PLEURAL ADHESIOLYSIS IN LOCULATED PLEURAL EFFUSIONS

Dr PANTHAM SUNITHA,[1] Dr MERUGU NEERAJA,[2] Dr L DIVYASREE,[3] Dr POLAM RADHIKA,[4] Dr PASULA RAVI,[5]Dr BARAJU RAMANA PRAKASH.[6]

[1]Associate professor. Department of Pulmonary Medicine, Kakatiya Medical College, Warangal.

[2]Postgraduate, Department of Pulmonary Medicine, Kakatiya Medical College, Warangal.

[3]Assistant professor, Department of Pulmonary Medicine, Kakatiya Medical College, Warangal.

[4]Associate professor, Department of Pulmonary Medicine, Government Medical College Mulugu.

[5]Associate Professor, Department of Pulmonary Medicine, Government Medical College Bhupalpally.

[6]Associate Professor, Department of General Surgery, Government Medical College, Mahabubabad.

Corresponding Author: Dr. MERUGU NEERAJA

Postgraduate, Department of pulmonary medicine, Kakatiya Medical College, Warangal, Telangana, Mobile No:8328398509,gmail:neerajamerugu161@gmail.com.

ABSTRACT:

BACKGROUND: Loculated pleural effusions present as a challenging clinical scenario due to the formation of loculations, often leading to increased morbidity and prolonged hospital stays. Intrapleural Streptokinase(STK) has been proposed as a potential therapeutic option to facilitate pleural adhesiolysis and improve pleural fluid drainage in these cases.

METHODOLOGY: Designed as an analytical study in a prospective manner. Conducted from July 2022 to June 2024 at Government Chest Diseases and TB Hospital, Hanamkonda, Warangal. 30 patients having loculated pleural effusions were included in the study. All the cases were evaluated with detailed history, examination, blood workup, pleural fluid analysis and after informed written consent, all the cases were given Intrapleural streptokinase at a dose of 2,50,000 IU per day for 2 – 7 days. Patients were assessed based on amount of pleural fluid drained before and after instillation of streptokinase, improvement of chest x ray and ultrasound clearance of loculations. All the patients were carefully monitored for the possible complications.

RESULTS: In 73.3% of the patients there is complete lysis of adhesions and drainage of pleural fluid with the use of intrapleural streptokinase.

.

KEYWORDS: Loculated effusions, intrapleural fibrinolytics, intrapleural streptokinase, ultrasound.

I. INTRODUCTION

Loculated pleural effusions are those with ultrasound evidence of fibrin strands or septa floating inside the pleural space(1). Loculated pleural effusions remain a common and burdensome clinical entity, with the commonest cause being empyema, malignancy and hemothorax. Empyema and parapneumonic effusions develop in 36-66% of patients

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 9, 2024

hospitalized with bacterial pneumonia. In empyema and complicated parapneumonic effusions, white blood cells migrate to the infected pleural space and release permeable factors causing fibrinogen to spill into the pleural space. The fibrinogen is then converted into fibrin. Fibrin causes tissue surfaces to adhere and this will trap the causative micro organism. This entrapment will prevent host defense mechanisms and antibiotics from reaching the site of infection. Infected effusions have been shown to have low fibrinolytic activity and elevated concentrations of plasminogen activator inhibitors. Presence of loculations carries a poor prognostic factor,(2) and if untreated leads to pleural thickening and fibrosis. Intrapleural fibrinolytics will destroy the fibrin membranes and facilitate drainage of pleural fluid.(3)

So, intrapleural fibrinolytics may be a safe, easy, cost effective management option and also an alternative for conventional thoracotomy and VATS in remote areas. Tillet(4) and Sherry first introduced fibrinolytic therapy in 1949 as a treatment for empyema and complicated para pneumonic effusion. Fibrinolytic therapy was re introduced by Bergh(5) et al in 1977 using a more purified form of streptokinase. Since then there have been many studies which support the use of intrapleural fibrinolytics in empyema and complicated para pneumonic effusions. The purpose of our study was to assess the efficacy of streptokinase for intrapleural fibrinolytics in patients with loculated pleural effusions.

II. AIMS AND OBJECTIVES:

AIM :

To evaluate the role of intrapleural streptokinase as a fibrinolytic agent in the management of pleural effusion with loculations.

OBJECTIVES :

1. To assess the rate of successful pleural adhesiolysis following the administration of intrapleural streptokinase in patients with loculated pleural effusions.
2. To assess the amount of pleural fluid drained before and after streptokinase administration.
3. To evaluate the reduction in pleural fluid volume post treatment using sonographic measurements.
4. To identify and document any adverse effects associated with intrapleural administration of streptokinase.

III. PATIENT AND METHODS

This study was designed as an analytical study in a prospective manner.
Sample size is 30.
Study was conducted from July 2022 to June 2024 at Government Chest Diseases And TB Hospital, Hanamkonda.

INCLUSION CRITERIA :

- Patients who have given consent.
- Presence of sonographically documented pleural effusion intrapleural adhesions.
- Patients in whom Pleural fluid drainage was indicated.
- Difficult thoracentesis.

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 9, 2024

- Failure of satisfactory pleural fluid drainage 24hours after intercostal tube placement provided that tube was not obstructed and properly positioned.

EXCLUSION CRITERIA:

- Patients with recent trauma, haemorrhage or stroke.
- Patients having bleeding disorders.
- Patients on anticoagulation therapy.
- Patients with bronchopleural fistula.

PRE WORK UP:

- Detailed history and examination.
- Routine blood investigations like CBP, LFT, RFT, RBS.
- Coagulation profile (clotting time, bleeding time, prothrombin time, activated partial thromboplastin time, INR).
- Chest radiograph.
- Ultrasound chest.
- Pleural fluid analysis.
- CT chest.

METHODOLOGY:

- All the patients underwent closed tube thoracostomy.
- Test dose of streptokinase was given to all patients prior to intrapleural administration.
- First dose of streptokinase was given 24 hours after Intercostal tube placement.
- Streptokinase was given as a dose of 2,50,000 IU dissolved in 50ml NS once a day through the chest tube.
- Patient was positioned in lateral decubitus position with unaffected lung dependent during instillation to make sure that all of the agent is drained into the pleural cavity.
- The tube is then clamped for 2 to 4 hours and patient was asked to repeatedly change the position, so that streptokinase could spread thoroughly in the pleural cavity to break all the loculations.
- We continued daily instillation as long as the fluid drained is > 100 ml in 24hours in 3 consecutive days.
- On an average 2 to 7 doses were given to the patients to let out the entire fluid.
- Data about amount of pleural fluid drained before and after giving Streptokinase were recorded.
- Chest radiograph and ultrasound were performed daily to assess improvement.
- All the patients were closely observed for possible complications.
- Effectiveness of the study was assessed by
  -monitoring the volume of fluid drained from the chest tube daily.
  -chest ultrasound to check for dissolution of adhesions

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 9, 2024

- chest radiography to see radiological clearance.

- Based on the outcome of the study, patients are classified into three groups.
    1. Successful group, when there is complete lysis of adhesions on ultrasound and complete drainage of pleural fluid.
    2. Partially successful group, when there is partial lysis of adhesions on ultrasound and incomplete drainage of pleural fluid.
    3. Failure group when there is no lysis of adhesions on ultrasound and incomplete drainage of fluid.
- Patients addressed as failure and partially successful were transferred to cardio thoracic surgeon to decide further line of treatment.
- In successful group, intercostal tube is removed and patients are advised to continue the treatment according to the underlying etiology.

IV.OBSERVATIONS ANDRESULTS:

Total number of patients included in the study was 30. Following observations are seen.

- Mean age of the patients included in the study is 45.6years.
- There was male predominance with 60% of the patients being males and 40% of the patients are females.
- Chest pain was the most common presenting symptom, followed by cough, breathlessness and fever.
- Tubercular effusion is the most common etiology which is seen in 18 (60%) patients, followed by parapneumonic effusion in (16.7%) of patients, followed by empyema in (16.7%) of patients and malignant effusion in (6.7%) of patients.
- Majority of the pleural effusions were moderate effusions (46.6%), followed by mild effusions (33.3%) and massive effusions (20%).
- Minimum number of streptokinase doses are 2 and maximum number of doses are 7.
- Mean volume of fluid drained before instillation of streptokinase is 500ml and after instillation of streptokinase is 1253ml.
- There is complete lysis of adhesions in 73.3% of patients, partial lysis of adhesions in 20% of patients and no lysis in 6.7% of patients.
- No major complications were seen in the study group, except for transient chest pain after streptokinase instillation which is seen in 7 patients (23.3%) and fever in 4 patients (13.3%).
- Chest pain was mild (Visual Analog scale score 3) in 4 patients and moderate (Visual Analog scale score 5) in 3 patients and managed with analgesics.
- Fever was moderate grade (100.6 to 102.4F) in all the patients and managed with antipyretics.

Table 1: Demographic and clinical data of the patients in the study.

DEMOGRAPHIC AND CLINICAL DATA	
AGE (Mean)	45.6 Years

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 9, 2024

GENDER (M/F)	18/12
CLINICAL SYMPTOMS	
Chest Pain	30(100%)
Cough	26(86.6%)
Breathlessness	20(66.6%)
Fever	18(60%)
Loss of Appetite	26(86.6%)
Loss of Weight	20(66.6%)
ETIOLOGY	
Tuberculous effusion	18(60%)
Bacterial parapneumonic effusion	5(16.7%)
Empyema	5(16.7%)
Malignant Effusion	2(6.6%)
NUMBER OF DOSES OF STK(Average)	2-7
VOLUME OF FLUID DRAINED	
Before STK Instillation (Mean)	500ml
After STK Instillation (Mean)	1253ml
RADIOLOGICAL CLEARANCE	
Complete Clearance	22(73.3%)
Partial Clearance	6(20%)
No Clearance	2(6.7%)
ADVERSE REACTIONS	
Chest Pain	7(23.3%)
Fever	4(13.3%)
None	19(63.4%)

V. DISCUSSION :

The present study included 30 patients in which high incidence of loculated pleural effusions seen in age group 21-40 with a mean age of 45.6 years which is comparable with the study done by Kushboo Saxena (6) et al. Our study has male predominance, with 60% of the patients being males, which is comparable with the study done by Okur (7) et al. These age groups and male gender represent the most productive years of life and the socio-economic impact is thus, tremendous.

Most common etiology of loculated pleural effusions in our study is tuberculosis which explains the male predominance. Males in general are more prone to mechanical stresses due to their tall stature and strenuous work. Smoking is a more frequent habit, and tuberculosis and COPD are more frequent in males.

Our study reported marked difference between fluid drained before and after streptokinase, with mean fluid of 1253ml which is similar to the study done by Bouros (8) et al. The number of doses required for intrapleural adhesiolysis is 2 (minimum) and 7(maximum)

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 9, 2024

In our study, 73.3% of the patients had good clinical improvement, and shown a success rate of 73.3% where there is complete resolution of septations on ultrasonography, lung expansion on chest radiograph which is similar to studies done by Henke (9) et al and Taylor (10) et al.

In the present study, complete clearance was seen in 72.2% of tubercular effusions, 100% of parapneumonic effusions and 80% of the empyemas. Partial clearance was seen in 100% of the patients of malignant effusion, 20% of empyema and 16.7% of tubercular effusions. There was no clearance in 11.1% of tubercular effusions and 6.7% of malignant effusions. The lower radiologic response rates in our study could be partially explained by the reason that we included malignant effusions and tubercular effusions unlike earlier studies which included only parapneumonic effusions. In such patients, the presence of pleural thickening would lead to residual radiologic opacities despite optimal fluid drainage, which would lead to a lower radiologic response rate.

There were no life threatening adverse events seen. Transient Chest pain was seen in 7 patients and fever in 4 patients which is similar to studies done by Jerjes- Sanchez (11) et al.

VI. LIMITATIONS OF THE STUDY:

1.The sample size in our study is only 30, studies with a greater sample size would be helpful to derive further conclusions.

2. The variability in the severity of pleural effusions among patients and the lack of a standardized grading system for loculations could cause bias.

3. Without a control group, it is challenging to attribute the observed effects solely to the intrapleural streptokinase as concurrent treatments could confound the results.

VII. FUTURE ASPECTS:

- Future research should focus on larger multicentre trials to validate our findings and explore the long term outcomes of streptokinase therapy.
- This treatment modality can be particularly valuable in resource limited settings were access to advanced surgical interventions like VATS and Thoracoscopy are not available.
- Emerging research is focused on optimizing fibrinolytic therapy, including development of new agents (Tissue plasminogen activators, Deoxyribonucleases) with improved safety profiles and exploration of combination therapies like Streptokinase and urokinase, tissue plasminogen activators and deoxyribonucleases.

VIII. CONCLUSION :

- Present study has reported marked difference between the fluid drained, clinical and radiological improvement before and after streptokinase instillation due to lysis of adhesions by streptokinase. There were no major or life threatening adverse events.
- So intrapleural streptokinase can be considered as a safe, simple, affordable, effective treatment option which reduces the rate of surgical referrals in loculated pleural effusions. In resource limited settings it can be used as an alternative to VATS and Medical Thoracoscopy. Intrapleural Streptokinase is a promising therapeutic agent for the management of loculated pleural effusions due to its ability to lyse adhesions,

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 9, 2024

improve clinical outcomes making it a valuable addition to the current treatment protocol.

IX. REFERENCES

1) P.C. Yang, K.T. Luh, D.B. Chang, et al, Value of sonography in determining the nature of pleural effusion: analysis of 320 cases, AJR 159 (1992) 29.
2) S. Bielsa, J.M. Juan, J.M. Porcel, et al, Diagnostic and prognostic implications of pleural adhesions in malignant effusions, J. Thorac. Oncol. 3 (2008) 1251–1256.
3) Barthwal, M. S. (2008). Intrapleural fibrinolytic therapy in complicated parapneumonic effusion and empyema: present status. *The Indian Journal of Chest Diseases & Allied Sciences*, *50*(3), 277-282.
4) Tillett WS, Sherry S, Read CT. The use of streptokinase streptodornase in the treatment of postpneumonic empyema.]Thorac Surg. 1951;21:275-297.
5) Bergh NP, Ekroth R, Larsson S, et al. Intrapleural streptokinase in the treatment of haemothorax and empyema. Scand J Thorac Cardiovasc Surg. 1977;11 :265-268.
6) Saxena K, Maturu VN. A Comparative Study of the Safety and Efficacy of Intrapleural Fibrinolysis With Streptokinase and Urokinase in the Management of Loculated Pleural Effusions. Cureus. 2022 Jun 24;14(6):e26271. doi: 10.7759/cureus.26271. PMID: 35898352; PMCID: PMC9308892.
7) Okur E, Baysungur V, Tezel C, Ergene G, Okur HK, Halezeroglu S: Streptokinase for malignant pleural effusions: a randomized controlled study. Asian Cardiovasc Thorac Ann. 2011, 19:238-43. 10.1177/0218492311410874.
8) Bouros D, Schiza S, Tzanakis N, Chalkiadakis G, Drositis J, Siafakas N: Intrapleural urokinase versus normal saline in the treatment of complicated parapneumonic effusions and empyema. A randomized, double-blind study. Am J Respir Crit Care Med. 1999, 159:37-42. 10.1164/ajrccm.159.1.9803094.
9) Henke CA, Leatherman JW: Intrapleurally administered streptokinase in the treatment of acute loculated nonpurulent parapneumonic effusions. Am Rev Respir Dis. 1992, 145:680-4. 10.1164/ajrccm/145.3.680.
10) . Taylor RFH, Reubens MB, Pearson MC, et al. Intrapleural streptokinase in the management of empyema. Thorax 1994;49:856–9.
11) Jerjes-Sanchez C, Ramirez-Rivera A, Elizalde JJ, et al. Intrapleural fibrinolysis with streptokinase as an adjunctive treatment in hemo-thorax and empyema. Chest 1996;109:1514–9.