EFFICACY, SAFETY AND TOLERABILITY OF STREPTOKINASE IN MULTILOCULATED EMPYEMA

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Background: Empyema thoracis is a common illness with significant morbidity and mortality. Standard treatment of Empyema includes tube drainage and antibiotics. But the tube drainage often fails if the fluid is loculated. Intrapleural Streptokinase has been used in multiloculated empyemas with good success rate. We evaluated the efficacy and safety of intra-pleural Streptokinase in loculated empyemas. **Methods:** A total of 15 patients admitted in Pulmonology unit with multiloculated empyemas whose drainage via drainage tube was less than 100 ml during the last 24 hours were included in the study. Aliquots of 250,000 units of Streptokinase in 100 ml of normal saline were instilled into the pleural cavity and the tube clamped for 3 hours. Response was assessed by clinical outcome, measurement of drain output after unclamping and subsequent chest radiography and serial chest ultrasounds. **Results:** Streptokinase enhanced drainage in all patients with complete resolution of Empyema in 13 patients. Two patients with thickened visceral pleura following empyema drainage were referred to thoracic surgeon for decortication. The number of instillations of Streptokinase per patient ranged from 1 to 3 and the volume of drained empyema fluid ranged from 60 ml to 600 ml per patient. Streptokinase was well tolerated in all patients. **Conclusion:** Intrapleural Streptokinase is a safe and effective means of increasing the tube drainage in multiloculated Empyema without causing systemic fibrinolysis.

Key Words: Streptokinase, Multiloculated Empyemas, Fibrinolysis.

INTRODUCTION

Pleural Empyema is a well-known complication of Pneumonia, recognized since the time of Hippocrates.[1] Antibiotics and tube drainage are the first line of treatment for empyema. Sometimes tube drainage fails due to loculations in the empyema, which carries a significant mortality.[2] Tillet and Sherry[3] have used intrapleural fibrinolytic agents as early as 1949 in this setting to achieve fibrinolysis and increase tube drainage. But the enthusiasm for intrapleural Streptokinase soon waned due to systemic adverse effects. It was so, until Bergh and colleagues,[4] who used a purified Streptokinase with good success and insignificant adverse effects. This study evaluates the efficacy and safety of intrapleural Streptokinase in multi-loculated empyemas.

MATERIAL AND METHODS

Between October 11, 1998 and March 20, 2000, 15 patients were admitted to Postgraduate Medical Institute, Lady Reading Hospital Peshawar with multiloculated pleural empyemas due to Pneumonia. All failed to respond satisfactorily to antibiotics and intercostals chest intubation. Chest ultrasounds confirmed the presence of multiloculations in the empyemas. Intrapleural Streptokinase was used in these patients in order to achieve pleural fibrinolysis and increase the drainage. Inclusion criteria for the study were multiloculated pleural empyema and failure of drainage via intercostal chest tube (less than 100 ml during the last 24 hours). Exclusion criteria were a

history of allergy to Streptokinase, bleeding disorders, recent surgery/haemorrhage, abortion or just after delivery, severe hypertension (systolic value more than 200 mm Hg or diastolic value more than 100 mm Hg) and severe kidney or liver disease.

Streptokinase Instillation

2,50,000 units of Streptokinase in 100 ml normal saline were instilled into the pleural cavity via intercostal drainage tube and the drainage tube was clamped. Patients were then rotated in various positions to improve the dispersal of Streptokinase. The drainage tube was released after 3 hours.

Response to Streptokinase was assessed by 1) Clinical outcome (reduction in pain, dyspnoea, cough, fever and improvement in general well being 2) Quantity of output per day after unclamping of drainage tube 3) Daily Chest X-rays to see radiological clearance and 4) Serial chest ultrasound to check dissolution of adhesions.

Any adverse effects such as chest pain, febrile reaction, haemorrhage, allergic reactions, etc. were noted.

Reinstillation of Streptokinase was done if the pleural fluid drainage was below 100 ml during the previous 24 hours and residual fluid presence confirmed by ultrasound.

RESULTS

Streptokinase enhanced drainage in all patients. Out of a total of 15 patients, 11(73%) were males and 04(27%) were females (Figure 1) giving a male:female ratio of 2.75:1.

Their ages ranged from 6 to 50 years with a mean age of 21.1 $\pm$ 16.1 years. The major pathogen isolated was Staphylococcus aureus (Table 1).

Table 1: Results of culture and sensitivity testing in patients (n = 15)

Pathogen isolated	Number of cases	Percentage of total
Staphylococcus aureus	06	40
E. coli	01	0.067
None	08	53.33

The number of Streptokinase instillations per patient ranged from one to three. Drainage after Streptokinase instillation ranged from 60-600 ml per day. Complete evacuation of empyema fluid and re-expansion of underlying lung was seen in 13(86%). Patients remained well during follow up (Table 2).

Table 2: Outcome in patients after Streptokinase instillation (n = 15)

Outcome	No. of patients	Percentage of total
Clinically improved	15	100
Drainage (60-600 ml)	15	100
Complete Resolution	13	86.7
Thickened pleura with decortication	02	13.34
No loculations on Ultrasonography	15	100

Two patients with thickened visceral pleura and trapped lung underwent successful decortication following empyema drainage. Clinical improvement in terms of fever, dyspnoea, chest pain and general well being was seen in all patients (Table 2).

Thirteen(86%) patients had transient rise of temperature and 12(80%) had mild chest pain, which responded well to analgesics. Mild intrapleural haemorrhage with blood staining of the empyema fluid was seen in 09(60%) of patients. No other adverse reactions were noted (Table 3).

Table 3: Complications in patients after Streptokinase instillation (n = 15)

Complications	Number of patients	Percentage of total
Fever	13	86.7
Chest Pain	12	80
Haemorrhage Mild Severe	9 0	60 0
Allergic Reactions	0	0
Anaphylaxis	0	0

Chest ultrasound confirmed the successful fibrinolysis and resorption of loculations in all the cases. The overall improvement in chest radiographic score of II (improved between one-third and two-thirds) was seen in 03(20%) patients, of I (less than one-third improvement) in one(6.7%) patient and of III (more than two-thirds improvement) in 12(80%) patients.

DISCUSSION

In our study intrapleural Streptokinase was used in a dose of 2,50,000 units diluted in 100 ml of normal saline in 15 patients with multiloculated pleural empyemas that failed to resolve with chest intubation and antibiotics. The drainage tube was clamped for 3 hours[5] and not 4 hours as suggested by Bergh et al.[4] This duration of 3 hours and fewer instillations[6] (1-3 per patient) were sufficient to achieve complete resorption of loculations and re-expansion of the underlying lungs in 13 of 15(86.7%) patients, obviating the need for thoracic surgery and thus avoiding the mortality and morbidity associated with decortication.[7] Failure of the lung to re-expand in two cases was due to formation of thickened visceral pleura as a result of organized fibrin peel.

We have found intrapleural Streptokinase more useful in multiloculated empyemas if it is used as early as 3-4 weeks[8] after the onset of illness, before the empyema fluid is fully organized.

The success rate of over 86% is comparable to that obtained in the randomized clinical trials by Aye[9] and Roupie.[10] Apart from transient chest pain, mild fever and intrapleural haemorrhage, no major adverse reactions were seen in our series, perhaps due to the purified nature of Streptokinase[8,11,12] and shorter exposure resulting in poor absorption of Streptokinase from the pleural surfaces.

CONCLUSION

Intrapleural Streptokinase is a safe and effective adjunct in the management of multiloculated empyemas, obviating the need for surgical intervention.

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