Role of Intra Pleural Streptokinase in Treating Complicated Parapneumonic Effusions

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ABSTRACT

BACKGROUND

Pneumonia remains one of the most common community and hospital acquired infections despite the advent of potent anti-microbial agents. Pneumonia may be associated with pleural effusion. It may be simple or complicated. Intra pleural administration of fibrinolytic agents have been in use for the treatment of Complicated Parapneumonic Effusions (CPE). The non-surgical medical approach with use of fibrinolytic agents is an alternative modality in the treatment of complicated para-pneumonic effusions. With the introduction of purer forms of Streptokinase (STK), there has been renewed interest in the use of intra pleural fibrinolytics with successful drainage of difficult to drain complicated para-pneumonic effusions. It is a safe and effective method and obviates the need for surgery in most cases. Our study was done to evaluate the role of intra pleural Streptokinase as an adjunctive therapy in the treatment of complicated para-pneumonic effusions.

METHODS

75 patients of complicated para-pneumonic effusions with intercostal tube properly positioned and patent were given intra pleural fibrinolytic therapy with streptokinase when drainage through inter-costal tube was minimal, i.e., less than 50 ml/24 hrs. Streptokinase was administrated in 3 dosage variants; 25 patients with 2,50,000 IU in 50 ml NS once a day for 1 week, 25 patients with 5,00,000 IU in 50 ml NS once a day for 1 week, & 25 patients with 7,50,000 IU in 50 ml NS once a day for 3 to 5 days. Clinical, radiological resolution, and volume of fluid drained, were assessed for final outcome.

RESULTS

There was significant drainage of 1,500 ml in patients treated with 7,50,000 IU and around 1,000 ml in patients treated with 5,00,000 IU and 300 to 500 ml in patients treated with 2,50,000 IU. Clinical, radiological resolution, and volume of pleural fluid drained were assessed for final outcome. Chest pain was reported in 7 patients (9.3%), fever in 5 patients (6.6%), and haemoptysis in 3 patients (4%). There was no allergic reaction in any patient.

CONCLUSIONS

Intra pleural fibrinolytic therapy with streptokinase is a safe and effective adjunctive therapy in the treatment of complicated para-pneumonic effusions.

KEYWORDS

Fibrinolytic Agents, Streptokinase (STK), Complicated Parapneumonic Effusions (CPE), Haemoptysis
BACKGROUND

Pneumonia is one of the most common community and hospital acquired infection despite the advent of potent anti-microbial agents. A significant number of patients with pneumonia develop para-pneumonic effusions. Para-pneumonic effusions may be “Simple” consisting of free-flowing, clear exudative fluid, which almost resolves completely with antibiotics alone. In case of delayed or inappropriate treatment, some of these simple effusions progress to “Complicated” para-pneumonic effusions. The management of these types of effusions with intercostal tube drainage and antibiotics fails most of the time due to thick viscous fluid and multiple pleural space loculations. Intra pleural instillation of fibrinolytic agents has been found to be useful adjunctive therapy in treating these complicated para-pneumonic effusions. The use of intra pleural fibrinolytic is a safe, easier and cost-effective option.

METHODS

The present study was conducted on 75 patients of complicated para-pneumonic effusions admitted in the department of Respiratory Medicine, NRI Medical College & General Hospital, Chinakakani, Mangalagiri Mandal, Guntur District.

Inclusion Criteria

1) All patients of pneumonia with intrapleural confirmation of septations by Ultrasoundography (USG).
2) All patients with inadequate drainage of pleural space by intercostal tube even after confirmation of fluid by ultra-sonography.
3) Patients of age group above 18 years were included.

Exclusion Criteria

1) Patients with bleeding disorders, stroke, haemorrhage in the preceding 6 months, and the use of STK in the past 2 years.
2) Patients with confirmation of pus in the pleural cavity.
3) Patients with poor general condition.

All the patients gave written and informed consent for treating with intra pleural Streptokinase (STK). Investigations done included haemogram, microbiological examination, chest X-ray, ultra-sonography, Contrast Enhanced Computed Tomography (CECT) / High Resolution Computed Tomography (HRCT) Chest in needed cases and ELISA for HIV in all patients. Diagnostic pleural fluid aspiration was done, patency of the inter-costal tube was maintained by flushing with normal saline daily.

Intra pleural streptokinase was given as adjunctive therapy when drainage through inter-costal tube was minimal (i.e., less than 50 ml/24 hrs), and USG showed significant amount of pleural fluid. STK was given in the dosage of 3 variants, 2,50,000 IU/day in 25 patients, 5,00,000 IU/day in 25 patients, and 7,50,000/day in 25 patients. The tube was clamped for 2 to 4 hours after a dose of STK. Chest X-ray was done initially, then 48 hours after STK therapy, and later on depending on the response to therapy. The total net pleural fluid drainage after intrapleural STK till the removal of the chest tube was noted.

The criteria used for radiological clearance are: Normal or near-Normal chest radiograph / Moderate Clearance of fluid (50-80%) / Minimal Clearance of fluid (less than 50%) / None (No change).

The fibrinolytic therapy in 7,50,000 IU group patients was needed for only 3 days, but was continued till 7 doses in 5,00,000 IU & 2,50,000 IU patients until the drainage was minimal. Repeat USG was done to check the quantity of fluid left in the pleural cavity. The criteria for successful outcome were the Clinical, Radiological resolution, and Volume of pleural fluid drained.

RESULTS

The study was conducted on 75 patients (50 males and 25 females) with mean age of 40 years. Bedside inter-costal tube drainage was done by conventional chest tube (24-32F) in all patients. The minimum number of doses of STK was 7 in 25 patients with 2,50,000 IU and it was 5 in 25 patients with 5,00,000 IU and it was only about 3 in 25 patients with 7,50,000 IU. There was significant drainage of 1,500 ml and better radiological clearance in 20(80%) of 25 patients with a dose of 7,50,000 IU of STK. In patients who were treated with 5,00,000 IU & 2,50,000 IU there was moderate clearance of fluid (50-80%).

In our study we came across only 3 adverse reactions
1) Chest Pain in 7(9.3%) cases - 3 in 7,50,000 IU treated cases, 2 in 5,00,000 IU treated cases, and 2 in 2,50,000 IU treated cases.
2) Fever in 5(6.6%) cases - 2 each in 7,50,000 IU and 5,00,000 IU treated cases, 1 in 2,50,000 IU cases.
3) Haemoptysis in 2(4%) cases - 1 in 7,50,000 IU treated cases, 1 in 2,50,000 IU treated cases.

However, the other adverse effects like hypotension, massive expectoration, haemorrhage and anaphylaxis, though reported by other workers, were not seen in our study. The average duration of hospital stay is 15 days. There was significant evidence of reduction in the need for surgery and mortality.
Despite the advent of potent antibiotics, bacterial pneumonia still results in significant morbidity and mortality. 40% of hospitalized patients with bacterial pneumonia have an accompanying pleural effusion. Para-Pneumonic Effusions (PPE) account for a large percentage of pleural effusions. The morbidity and mortality rates in patients with pneumonia and pleural effusions are higher than those in patients with pneumonia alone. In assessing risks of patients with Community Acquired Pneumonia (CAP), the presence of a pleural effusion is given the same weightage as PO2 less than 60 mmHg. Patient with pneumonia and a loculated effusion or an effusion greater than 2 cm in thickness on the decubitus film should be hospitalized.

Pleural infection (complicated para-pneumonic effusion and empyema) is rising in incidence across all age groups worldwide. Though most pleural effusions associated with pneumonia resolve without any specific therapy directed toward the pleural fluid, approx. 10% require operative intervention.

Recommendations which formed the basis for treatment today-

1) Pleural fluid should be drained, but one must avoid an open pneumothorax in the acute exudative phase.
2) Care should be taken to avoid a chronic empyema by rapid sterilization and obliteration of the infected cavity.
3) Careful attention should be paid to the nutrition of the patient.

UK trial on intra pleural streptokinase by Maskell et al, showed that intra pleural administration of streptokinase does not improve mortality, the rate of surgery, or the length of the hospital stay among patients with pleural infection, which is contrary to what we found. In our study there was better outcome regarding morbidity, need for surgery, and length of hospital stay.1

Apart from antibiotic therapy, treatment in patients with pleural effusion consists mainly of drainage of the infected pleural fluid by inter-costal tube, and intra-pleural administration of fibrinolytic agents in loculated effusions. Such therapy is intended to lyse the fibrinous septations within infected pleural fluid collections and is supported by management guidelines.

RJ Davies et al, concluded that intra pleural streptokinase probably aids the treatment of pleural infections by improving pleural drainage without causing systemic fibrinolysis or local haemorrhage. In our study also streptokinase aided in treating the complicated pleural effusions by improving the drainage without causing life threatening adverse effects.2

AH Diacon et al, concluded that intra pleural streptokinase adjunctive to chest tube drainage reduces the need for surgery and improves the clinical treatment success in patients with empyema. This is in agreement with our study as streptokinase showed the same effect of helping the pleural fluid drainage and simultaneously reducing the
need for surgery and improving clinical condition of the patient.³

RJ Cameron et al, summarized that intra pleural fibrinolytic therapy confers significant benefit in reducing the requirement for surgical intervention for patients. Intra pleural fibrinolytics have not been shown to significantly increase adverse events. In our study also we have seen only 3 adverse effects of fever, chest pain, and haemoptysis but no allergic reactions.⁴ Antibiotics play an important role in the management of para-pneumonic effusions. Antibiotics namely Clarithromycin, Moxifloxacin and Levofloxacin diffuse rapidly into the pleural fluid after they are administered intravenously. Metronidazole penetrates most easily, followed by Penicillin, Clindamycin, Vancomycin, Ceftriaxone, and Gentamicin. In our study we treated our patients according to culture & sensitivity reports, clarithromycin and metronidazole were the most commonly used antibiotics (75%).

T Laisaar et al, concluded that usage of intra pleural streptokinase in the treatment of multi-loculated pleural effusions reduces the need for major surgical interventions like Video Assisted Thoracoscopic Surgery (VATS) or Decortication in large group of patients.⁵ CT Yao et al, concluded that intra pleural fibrinolytic treatment with streptokinase is safe and effective, and it can obviate the need for surgery in most cases. The combination treatment should be attempted early on, when complicated para-pneumonic effusion is first diagnosed. In our hospital we started treating the complicated para-pneumonic effusions with a combination treatment approach which led to more successful drainage of pleural fluid and better outcome of the patient.⁶

CWH Davies et al, suggested that intra pleural streptokinase may be useful in the drainage of malignant multi-loculated pleural effusions in patients who fail to drain adequately with a standard chest tube. Malignant pleural effusions should not be considered a contra-indication to intra pleural streptokinase. We also have seen 2 cases of malignant loculated pleural effusions with a more successful outcome.⁷ D Bouros et al, concluded that intra pleural instillation of streptokinase is an effective and safe mode of treatment for complicated para-pneumonic effusions and pleural empyemas and alleviates the need for thoracotomy.⁸

CA Henke et al, concluded that intra pleural administration of streptokinase is an effective adjunct to the management of non-purulent, loculated para-pneumonic effusions that may reduce the need for multiple chest tubes or surgical drainage.⁹ ME Mitchell et al, concluded that intra pleural instillation of streptokinase may be a useful adjunct in the treatment of a complicated para-pneumonic effusion.¹⁰

CONCLUSIONS

Intra pleural instillation of streptokinase plays a huge and important role in treating complicated para-pneumonic effusions, it is safe, effective, decreases the morbidity and mortality to some extent, obviates the need for surgery (VATS or Decortication), decreases the length of hospital stay. The dosage is dependent on the size of pleural effusion and on characteristics of septations/loculations. In our study treating with 7,50,000 IU showed a better outcome than treating with a lower dose of streptokinase.

REFERENCES