

Case Reports

Intrapleural Streptokinase in Parapneumonic / Complicated Pleural Effusion/Empyema: Experience in Dhaka Shishu (Children) Hospital

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Abstract

Background: Parapneumonic effusion/complicated pleural effusion/empyema thoracis in children causes significant morbidity. Standard treatment of pleural effusion includes tube drainage and antibiotics. But the tube drainage often fails. Intrapleural Streptokinase has been used in empyema thoracis as well as complicated pleural effusion with good success rate. Though its efficacy is documented in Western literatures and textbooks, there are no clinical trials in children has been reported from Bangladesh.

Objectives: We evaluated the efficacy of intra-pleural Streptokinase in the management of Parapneumonic effusion / complicated pleural effusion/ empyema thoracis even in advanced stages.

Patients and Methods: A total of 3 patients with parapneumonic effusion requiring intercostal tube drainage, aged 4 year 6 month to twelve years were included in the study who were admitted in Pediatric respiratory medicine unit in Dhaka Shishu (Children) Hospital. Intercostal chest tube drain was given in all patients and inj: Streptokinase (10,000 units/kg/dose) was instilled into the pleural cavity and kept the Streptokinase for 4 hour in pleural cavity. Response was assessed by clinical outcome, after unclamping and serial chest ultrasounds and subsequent chest radiography.

Results: Streptokinase enhanced drainage of pleural fluid and complete resolution of effusion in all the 3 patients.

Conclusions: Intrapleural Streptokinase is the preferred treatment for treating pediatric empyema/parapneumonic effusion/complicated pleural effusion even in advanced stages and can avoid surgery.

Key words: parapneumonic effusion/complicated pleural effusion/empyema

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Introduction

Pleural effusion develops in about 36% to 57% of patients with pneumonia. Of these patients, about 10% develop empyema or complicated parapneumonic effusion, which has a 14% to 20% mortality rate.¹ The mortality is higher in patients with pneumonia who have a pleural effusion. In one study, the mortality risk was 6.5 times higher if the effusions were bilateral, whereas the mortality risk was 3.7 times higher if the effusion was unilateral.² Parapneumonic effusion is any pleural effusion secondary to pneumonia (bacterial or viral) or lung

abscess. Empyema is, by definition, pus in the pleural space. Pus is a thick, viscid fluid that appears to be purulent.^{1,2} A complicated parapneumonic effusion is a parapneumonic pleural effusion for which an invasive procedure, such as tube thoracostomy, is necessary for its resolution, or a parapneumonic effusion on which the bacterial cultures are positive.¹ The reason for the latter part of this definition is that if it were known that the cultures were going to be positive, then an invasive procedure would be indicated. Although some classifications have been used for the management and treatment of empyema, we have preferred to use the classification of the American Thoracic Society which has expanded the definition of empyema into three stages.³ In this classification, initial reaction to the infectious agent is fibrin deposition on both pleural surfaces known as the early exudative phase (stage I). This is followed by an intermediate fibrino-purulent phase characterized by fibrinous septations forming loculations within the pleural space (stage II). Prolonged enhanced fibroblastic activity prevents lung re-expansion by covering the pleural space as a spider web and this is called the late organizing phase (stage III)³ There are only few case reports from Bangladesh describing the use of intrapleural streptokinase in adults. To the best of the author's knowledge the use of intrapleural streptokinase in pediatric patients in Bangladesh is yet to be reported.

How intrapleural Streptokinase act?

Fibrinolytics are infused via the chest catheter into the pleural space to allow lysis of pleural septations and fibrinous strands and to clear lymphatic stomata so as to reestablish physiologic drainage from the pleural space.⁴

Adverse effect of intrapleural streptokinase?

Laissar T, Puttsepp E have showed in their study, eleven patients experienced some adverse effects of streptokinase therapy, most frequently chest pain and elevation of body temperature. In one case pleural fluid became hemorrhagic, and one patient had nasal bleeding.⁵

Contraindications for giving Streptokinase:

Patients with known streptokinase sensitivity, bleeding diatheses; coagulation defects; oesophageal varices; recent haemorrhage; recent

surgery, recent symptoms of possible peptic ulceration; coma; history of cerebrovascular disease, pericarditis; recent trauma; aneurysm; aortic dissection; bacterial endocarditis; severe hypertension.⁶

Case series

Case-1

A girl of four and half year age admitted with the complaints of high grade intermittent fever for 10 days, non productive cough for same duration. Before admitting in this hospital she visited different hospital without any significant improvement. No history of contact with TB patient. On examination she was toxic, febrile, mildly anemic, tachypnea and tachycardia were present, BCG mark present. On respiratory system examination chest wall was bulge on left side, chest expansibility reduced on left side, mediastinum not shifted, vocal fremitus reduced on left side, breath sound diminished on left side from left 4th intercostal space. We provisionally diagnosed as left sided parapneumonic effusion. Then diagnostic thoracocentesis was done at bed side, and it was pus. On investigation, CXR shows left sided pleural effusion, CBC shows neutrophilic leukocytosis, moderate anemia (Hb 8.4 gm/dl), CRP 95.5 mg/L, MT 05mm/72 hour. Gastric lavage for ZN staining AFB not found and gene Xpert negative, pleural fluid for gram staining negative, Z-N stain negative, culture shows no growth, Cytology shows numerous neutrophil and lymphocyte no malignant cell, pleural fluid protein 5.9 gm/dl, sugar 41.4 mg/dl. Blood LDH 320 U/L (120- 300). Pleural fluid LDH 24759 U/L, Pleural fluid ADA 392.58 U/L (0.00-24.0). Coagulation profile and platelet count normal. LFT normal. USG of chest shows left sided pleural effusion (263 ml), CT chest shows left sided massive pleural effusion with pleural thickening.

Treatment start with injectable antibiotics (ceftriaxone & flucloxacillin) and intercostal chest tube drainage. When we have seen less amount of fluid coming out one day after thoracentesis we gave intrapleural inj; streptokinase 10,000 iu/kg, for 3 consecutive days and pleural fluid drainage improved. Intrapleural STK was given as an adjunctive therapy when drainage through intercostal tube was minimal (i.e., less than 50 ml/day), We have added anti-TB drugs as pleural fluid ADA was raised.



Oishi before thoracocentesis

Chest tube in situ



After removal of chest tube

Oishi during follow-up

Case-2

A 14 year old immunized child presented with high grade continued fever associated with non productive cough for 14 days and breathing difficulty for 3 days. He had no history of weight loss, contact with TB patient and such type of illness previously. He was ill-looking, febrile, dyspneic, having BCG mark. His chest movement was restricted on left side. There was evidence of mediastinal shifting to right side. Chest expansibility was reduced on left side & percussion note was stony dull from 2th - 6th ICS to downwards along midclavicular, midaxillary & scapular line respectively on left side. Vocal fremitus, vocal resonance and breath sound was absent on left side in above mentioned areas. Right side of chest was normal. We provisionally diagnosed the patient as left sided pleural effusion due to pneumonia



CXR: Nazmul before thoracocentesis



Nazmul: Chest tube in situ with CXR

CXR shows homogenous opacity occupying left middle and lower zones. Pleural fluid study: Cytology: Total leucocyte- 40,000/mm³, Differential count -Polymorphs 95%, Lymphocyte 5%. Biochemistry :Protein 4.95 gm/dl, Glucose : 30 mg/dl. Microbiology : Gram staining not detected, AFB staining- not detected, Culture sensitivity No growth, Gene Xpert- MTB not detected. Mantoux test : 00mm/72 hours. We manage the patient with proper counseling the parents, Propped up position, Oxygen inhalation with face mask (3L/min), Maintenance of nutrition, antipyretics, Inj. Ceftriaxone, Inj. Flucloxacillin, Tube thoracostomy under water seal drainage. After one day when we saw pleural fluid flow through chest tube is not significant then we check for position of drain and do USG of chest for staging of pleural effusion. After confirming adequate amount of fluid in pleural space and loculated septum in pleural space, we gave injection streptokinase and kept it for 4 hours after that we saw significant amount of fluid comes out. We gave inj. streptokinase for 3 consecutive days.

Case-3

A ten years old male child, only issue of his consanguineous parents admitted in DSH with the complaints of non productive cough and high grade intermittent fever for 7 days. No h/o weight loss but contact with TB patient present. Arfat is febrile, toxic, irritable, mildly anemic, anecteric, no lymphadenopathy. Respiratory rate 38 br/m, chest indrawing absent, trachea shifted to left side, percussion dull on right side, breath sound diminished on right side.

CXR shows right sides massive pleural effusion, CBC: HB-11 gm/dl, total count 8300/cumm, DC: N-73%, L-19%. Pleural fluid analysis : Total leucocyte

900/cumm, Differential count: smears shows lymphocytic predominance. Protein in pl.fluid 5.75 gm/dl, sugar 86 mg/dl, pl. fluid for C/S shows no growth of any organism, Gene Xpert negative, ADA 44.3 U/L, LDH 608 U/L. Sputum for Gene Xpert and AFB staining negative. USG of chest reveals free fluid (365 ml) noted at right costophrenic angle with septation.

We started IV antibiotics and water seal chest tube given but only 30 ml fluid comes out on the day of chest tube insertion. Then we decided to give inj.streptokinase 10,000 u/kg once daily for 3 days, after giving intrapleural streptokinase pleural fluid drainage improved dramatically. We kept chest tube in situ for 5 days after confirming no minimum fluid in pleural space by USG of chest.



CXR: Chest tube in situ



Arafat: Before thoracocentesis



Inj: Streptokinae in situ



After removal of chest tube

Discussion

Parapneumonic/complicated pleural effusion / empyema often associated with pneumonia due to Streptococcus pneumoniae, although Staphylococcus aureus is most common in developing nations and Asia. Haemophilus influenzae, group A Streptococcus, gram negative organisms, tuberculosis, fungi, malignancy and trauma are other causes.⁷ Though empyema thoracis in children carries very little (20%) mortality as compared to adults, it causes lots of morbidity.²

The optional management remains controversial regarding a variety of treatment options, such as antibiotics alone or in combination with thoracocentesis, tube thoracostomy, fibrinolytic agents, thoracoscopy, minithoracotomy, debridement and decortication.⁷ Bose K, Saha S et al,² (2015) Ekingen G³ (2004), and Andreas H. Diacon, Johan Theron⁸(2004), all conclude that intrapleural streptokinase adjunctive to chest tube drainage reduces the need for surgery and improves the clinical treatment success in patients with pleural empyema Parapneumonic /complicated pleural effusion.^{2,3,8}

In all the three patient in our study we gave injectable antibiotics as well as chest tube drainage after confirming a lot of fluid in intrapleural space radiologically. When the chest tube drainage became insignificant (less than 50 ml/day),^{3,8} the chest tube was patent, properly positioned and ultrasonography revealed still significant amount of pleural fluid, it was decided to initiate intrapleural streptokinase (STK). The contraindications in the form of bleeding diathesis or haemorrhage in the preceding six months and the use of streptokinase by any route in the previous two years were ruled out before starting the therapy.⁹ Baseline and 24 hours post streptokinase prothrombin time (PT) and partial thromboplastin time (PTT) were initially done. The dosage schedule followed was 10,000 IU per kg of streptokinase dissolved in 50 ml of normal saline single dose through chest tube. The tube was clamped for four hours after each dose of STK.¹⁰⁻¹²The total net pleural fluid drainage after intrapleural STK till the removal of chest tube was noted. Chest radiology was initially done 48 hours after STK therapy and subsequently depending upon the response to therapy. Fibrinolytic therapy was discontinued if after two doses of STK there was no significant drainage and repeat ultrasonography or computed tomography of chest showed multiple loculations and significant pleural thickening.¹³ The patients were closely monitored for side effects. The criteria for successful outcome were the volume of pleural fluid drained and the radiological resolution. In our cases intrapleural streptokinase improves pleural fluid drainage significantly and radiologically improve the condition. When pleural fluid drainage is <1ml/kg/day⁴, clinical and radiological evidence of no or minimum fluid in situ then we withdraw the water seal drainage.

Conclusion

In dealing with parapneumonic /complicated pleural effusion / empyema intra pleural fibrinolytics may be a useful alternative for others such as use of video assisted thoracic surgery or the conventional thoracotomy. The use of intrapleural fibrinolytics may be safer, easier and cost effective management option that can promote pleural fluid drainage.

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