

Role of Intrapleural Streptokinase in Children with Empyema - Randomised Controlled Trial

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ABSTRACT

Introduction: Collection of pus like material in the pleural space is known as empyema and it generally occurs as a serious complication of pneumonia. Empyema generally occurs in children after pneumonia of acute bacterial origin and it is generally associated with significant morbidity and mortality. The main aim of the present study was to determine the perks and advantages of adding intrapleural streptokinase to the conventional therapy for managing cases of childhood empyema.

Material and methods: The present retrospective study was conducted in the Department, Institute, State during a period of 2 years. The study consisted of 20 subjects that were admitted to the hospital with the complaint of pneumonia complicated by empyema. Chest radiograph, ultrasound or CT scan was performed as required based on the patients conditions. Pleural fluid culture and analysis was done in empyema cases. Initial diagnostic thoracentesis was performed amongst all the patients with 14 gauge venula on admission to hospital. Further biochemical analysis of the sample was done. Levels of LDH, glucose and protein were determined. The criteria's of comparison were duration of chest tube drainage, stay in hospital, fever and decrease in incidence of hospital stay were considered as successful treatment. All the data was arranged in a tabulated form and analysed using SPSS software. Chi square test and mann Whitney test was used for comparison. Probability value of less than 0.05 was considered significant.

Results: The study enrolled total of 20 subjects, out of these 10 belonged to conventional group and 10 were administered intrapleural streptokinase. The mean age of the subjects in conventional group was 4.3 +/- 2.4 years and in the streptokinase group was 3.6 +/- 2.2 years. The male to female ration in conventional group was 3:2 and in the streptokinase group was 4:1. The mean hospital stay in conventional group was 19.3 +/-5.7 days and in streptokinase group was 18.9 +/- 4.8. The mean duration of hospital stay after surgery was 9.6 +/-2.1 and 8.5 +/- 3.5 in the conventional and streptokinase group respectively. Duration of afebrile state after surgery was 6.4 +/- 2.3 and 5.2 +/- 4.1 in the conventional and streptokinase groups respectively.

Conclusion: From the above study that Effect of streptokinase is better that emperical therapy. it is clear that addition of intrpleural streptokinase along with the conventional therapy provides no additional advantage. Effect of streptokinase is better that emperical therapy.

Keywords: Empyema, Intrapleural, Streptokinase

empyema and it generally occurs as a serious complication of pneumonia. Empyema generally occurs in children after pneumonia of acute bacterial origin and it is generally associated with significant morbidity and mortality. The major problems of concern are recurring episodes of fever and collection of fluid in pleural space. There is a controversy regarding the appropriate management of these cases. The management option include use of antibiotics either alone or in combination with thoracentesis or thoracostomy, use of fibrinolytic agents, debridement followed by decortications, thoracoscopy etc.² Injection of various fibrinolytic agents like streptokinase, urokinase in the intrpleural space are increasingly being used for the management of such conditions.³⁻⁶ Previous studies that were conducted were generally uncontrolled.⁷⁻⁹ The use of these fibrinolytic agents for managing cases of childhood empyema resulted in reduced hospital stay, increased chest tube drainage and decrease in intensity of fever.^{10,11} Three randomised studies have recently described the use of streptokinase and urokinase amongst adults for managing empyema cases.¹²⁻¹⁴ They have shown that benefits occur both clinically and radiographically in all the cases. As per a recent review by Cameron et al, there is lack of sufficient data and evidences to support the use of fibrinolytic therapy for managing cases of empyema and parapneumonic effusion.¹⁵ The main aim of the present study was to determine the perks and advantages of adding intrapleural streptokinase to the conventional therapy for managing cases of childhood empyema.

MATERIAL AND METHODS

The present retrospective study was conducted in the Department, Institute, State during a period of 2 years. The study consisted of 20 subjects that were admitted to the hospital with the complaint of pneumonia complicated by empyema. The study was approved by the Institutional ethical board. Patients with lung cancer, tuberculosis, post traumatic or post operative pneumonia were excluded from the study. Diagnosis of effusion was established on the basis of clinical and radiological examination. Chest radiograph, ultrasound or CT scan was performed as required based on

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INTRODUCTION

Approximately 40% of the subjects of community acquired pneumonia develop parapneumonic effusion.¹ Collection of pus like material in the pleural space is known as

the patients conditions. Pleural fluid culture and analysis was done in empyema cases. Initial diagnostic thoracentesis was performed amongst all the patients with 14 gauge venula on admission to hospital. Further biochemical analysis of the sample was done. Levels of LDH, glucose and protein were determined. Differential leukocyte count was also performed. Both anaerobic and aerobic cultures were performed and Gram staining was also done. Using a 24F chest tube, closed tube thoracentesis was performed bedside amongst patients with large pleural collections. Chest tube placement was done by specialist surgeons under ultrasonic guidance. Initially patients were given empirical treatment with ampicillin-sulbactam and cefotaxime. If there was no response during the initial 72 hours, i.e. failure to improvement or deterioration of the condition then this ampicillin and sulbactam was changed to vancomycin. Based on the type of response and medical and surgical condition, the duration of antibiotic therapy was decided.

Half of the patients received intrpleural streptokinase. The dose of streptokinase was 250,000 U in 100 ml of saline. Streptokinase was started within initial 24 hours of admission. It was allowed to rest in the pleural cavity for 4 hours and later manual aspiration was done and passive drainage of fluid was done in a water seales container. The procedure was done daily. Any adverse events associated with streptokinase administration were noted like allergy, pain or fever. Regular follow up of all the patients were performed by the same medical and surgical personnel. Medical records of all the patients were evaluated for demographic details, presentations, surgical method used, use of fibrinolytic agent, radiographic evaluation. Both the groups of patients were compared with each other, the one who received conservative treatment and the other receiving streptokinase therapy. The criteria's of comparison were duration of chest tube drainage, stay in hospital, fever and decrease in incidence of hospital stay were considered as successful treatment.

STATISTICAL ANALYSIS

All the data was arranged in a tabulated form and analysed using SPSS software. Chi square test and mann Whitney test was used for comparison. Probability value of less than 0.05 was considered significant.

RESULTS

The study enrolled total of 20 subjects, out of these 10 belonged to conventional group and 10 were administered intrapleural streptokinase. The mean age of the subjects in conventional group was 4.3 +/- 2.4 years and in the streptokinase group was 3.6 +/- 2.2 years. The male to female ration in conventional group was 3:2 and in the streptokinase group was 4:1. Cough was presented by 80% subjects in conventional group and 90% subjects in streptokinase group. Fever was seen in 90% subjects in conventional group and 90% subjects in streptokinase group. Dyspnea was seen amongst 70% subjects in conventional group and 80% subjects in streptokinase group. Chest pain was associated

with 20% subjects in conventional group and 10% subjects in streptokinase group. GI symptoms were seen in 10% subjects in conventional and streptokinase group. There was no significant difference between the two groups. Oxygen saturation in conventional group was 91.4 +/- 5.2 and 89.9 +/-4.8 in streptokinase group. Positive blood cultures were seen in 10% subjects of conventional group and 20% subjects of streptokinase group. Pleural effusion culture was positive in 40% Subjects and 20% subjects of conventional group and streptokinase group respectively. The mean haemoglobin levels in convention group and streptokinase group was 10.2 +/-2.7 and 9.5 +/-1.5 respectively. The mean platelets count in conventional group and streptokinase group was 395,423 +/- 34,654 and 452,332 +/- 30,543 respectively. The mean LDH level in pleural fluid was 3216 +/-3220 and in streptokinase group was 4321 +/- 2987. The mean glucose levels were 30.9 +/- 21.4 and 27.8 +/- 19.7 in conventional and streptokinase group respectively. There was no significant difference between the groups (table-1).

The mean hospital stay in conventional group was 19.3 +/- 5.7 days and in streptokinase group was 18.9 +/-4.8. The mean duration of hospital stay after surgery was 9.6 +/-2.1 and 8.5 +/- 3.5 in the conventional and streptokinase group respectively. Duration of afebrile state after surgery was 6.4 +/- 2.3 and 5.2 +/- 4.1 in the conventional and streptokinase groups respectively. The mean duration of chest tube drainage in conventional group was 5.8 +/- 4.5 days and in streptokinase group was 9.2 +/- 8.8 days. There were 10% in drainage group and 20% in streptokinase group that resorted to surgery. Pneumothorax as a complication was seen in 20% subjects in conventional group and 10% subjects in streptokinase group. There was no significant difference in the variables between the two groups as the p value was more than 0.05 (Table-2).

DISCUSSION

Pleural effusions are generally uncomplicated, simple to manage and do not require any specific therapy or management protocol. But they have the tendency to progress to certain life threatening conditions that can contribute to the morbidity and mortality. They can either lead to sepsis, respiratory failure, lung fibrosis or metastatic conditions.¹⁶ Various management protocols have been put forward for the management of cases of effusion and empyema.¹⁷ but there is still no standard guidelines that should be followed in all the cases. Since more than 50 years the intrpleural thrombolytic agents are in use for the management of empyema cases but the stage and time of action of these agents is still controversial.¹⁸ There have been few randomised trials in literature that report the use of these agents amongst adults. In a study conducted by Buoros et al in the year 1991 found that both urokinase and streptokinase are equally effective in managing empyema cases but urokinase was found to be much safe.¹⁹ In another study conducted by Davies et al amongst 24 patients in whom streptokinase and placebo was administered through chest tube, found that there was no significant difference between the case and control group.

Characteristics	Drainage Group (n=10)	Streptokinase Group (n=20)	P Value
Age	4.3 +/- 2.4 years	3.6 +/- 2.2 years	>0.05
Male : female	16:9	18:7	>0.05
Presenting signs and symptoms			
Cough	80%	90%	>0.05
Fever	90%	90%	>0.05
Dyspnea	70%	80%	>0.05
Chest pain	20%	10%	>0.05
GI symptoms	10%	20%	>0.05
Oxygen saturation	91.4 +/- 5.2	89.9 +/-4.8	>0.05
Lung affected (R/L)	6/4	8/2	>0.05
Blood culture (positive)	10%	20%	>0.05
Pleural effusion culture (positive)	40%	20%	>0.05
Blood tests			
WBC (/uL)	15,487 +/- 6123	16,104 +/- 6221	>0.05
Hb (g/dl)	10.2 +/-2.7	9.5+/-1.5	>0.05
Platelets(/cumm)	395,423 +/-34,654	452,332 +/- 30,543	>0.05
Pleural results			
LDH (U/l)	3216 +/-3220	4321+/- 2987	>0.05
Protein (g/dl)	4.2 +/-3.1	3.9+/- 2.8	>0.05
Glucose (mg/dl)	30.9 +/- 21.4	27.8 +/- 19.7	>0.05

Table-1: Showing the details of the study population

Characteristics	Drainage group (n=10)	Streptokinase group (n=10)	P value
Length of hospital stay (days)	19.3 +/-5.7	18.9 +/-4.8	>0.05
Duration of hospital stay after surgery (days)	9.6 +/-2.1	8.5 +/- 3.5	>0.05
Time to afebrile state after treatment (days)	6.4 +/- 2.3	5.2 +/- 4.1	>0.05
Duration of chest drainage (days)	5.8 +/- 4.5	9.2 +/- 8.8	>0.05
Surgical therapy	10%	20%	>0.05
Complication (pneumothorax)	20%	10%	>0.05

Table-2: Comparison between the two groups

But there was significant improvement in the volume of pleural fluid drained and radiographs in the group that was administered with streptokinase.¹³ In a study conducted by Diacon et al in the year 2004 found higher success rates in the streptokinase group with few indications for surgery. However during a follow up period of 6 months, there were no significant radiological differences observed in the placebo and the intervention group.²⁰ In a metaanalysis conducted by Cameron et R, they concluded that although streptokinase helps in reducing the hospital stay along with visible radiological improvements but these trials do not provide an insight to the efficacy of fibrinolytics in reducing the mortality and need for surgery.²¹ The use of these fibrinolytics amongst children is still limited such that their actual efficacy cannot be established. There has been various case series evaluating the use of streptokinase, urokinase or tissue plasminogen, all of them have shown successful results without the use of surgery.²²⁻²⁵ In a randomised controlled trial conducted by Thompson et al amongst 60 children, they found that use of urokinase resulted in shortened hospital stay compared to placebo.¹⁰ In a study conducted by ulku et al⁶ amongst 78 children to determine the efficacy of intrapleural fibrinolytic agents like streptokinase and urokinase in different stages of effusion or empyema, they concluded that treatment with fibrinolytics provides significant benefit in patients of stage

2 empyema but no significant effect was observed amongst stage 3 cases. According to the present study, the mean hospital stay in conventional group was 19.3 +/-5.7 days and in streptokinase group was 18.9 +/-4.8. The mean duration of hospital stay after surgery was 9.6 +/-2.1 and 8.5 +/- 3.5 in the conventional and streptokinase group respectively. Duration of afebrile state after surgery was 6.4 +/- 2.3 and 5.2 +/- 4.1 in the conventional and streptokinase groups respectively. The mean duration of chest tube drainage in conventional group was 5.8 +/- 4.5 days and in streptokinase group was 9.2 +/- 8.8 days. There were 4% in drainage group and 8% in streptokinase group that resorted to surgery. Pneumothorax as a complication was seen in 8% subjects in conventional group and 4% subjects in streptokinase group. There was no significant difference in the variables between the two groups as the p value was more than 0.05. In another retrospective study conducted by Barnes et al, amongst 100 subjects suffering from stage 2 or stage 3 empyema found that surgical intervention was required only in 2% of the cases.²⁶ In a meta analysis reported by Avansino et al, the use of fibrinolytics provided with no added advantage over the non operative conventional therapy of using antibiotics and thoracocentesis.²⁷ The major limitations of our study was the retrospective design and smaller sample size. Stage specific results were also not obtained in our study which

was another major drawback of our study.

CONCLUSION

From the above study it is clear that addition of intrapleural streptokinase along with the conventional therapy provides no additional advantage. Fibrinolytics can be used as an adjunctive therapy without any significant advantage over the conventional group. In complicated cases fibrinolytics can be used as additional therapy.

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