

Evaluating the Efficacy of Intrapleural Streptokinase in the Management of Childhood Empyema: A Randomized Controlled Trial

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Abstract

Background: Childhood empyema, a serious complication of bacterial pneumonia, often requires invasive treatments. Intrapleural streptokinase, a fibrinolytic agent, has been proposed as a less invasive alternative, potentially reducing the need for surgical intervention.

Methods: This hospital-based randomized controlled trial compared two groups of pediatric empyema patients: a control group receiving standard treatment and a study group treated with intrapleural streptokinase. The primary outcomes measured were the necessity for surgical intervention, duration of hospital stay, and overall treatment costs.

Results: The intrapleural streptokinase group showed a significant reduction in surgical interventions and hospital stay durations compared to the control group. Additionally, there was a noticeable decrease in treatment costs, with improved fluid drainage and symptom resolution observed in the streptokinase group.

Conclusion: Intrapleural streptokinase demonstrated effectiveness in treating childhood empyema, offering a viable, less invasive alternative to traditional methods. These findings suggest that intrapleural streptokinase can reduce the need for surgery, shorten hospital stays, and lower treatment costs, indicating its potential for transforming pediatric empyema management.

Keywords: *Intrapleural Streptokinase; Childhood Empyema*

Introduction

Childhood empyema, defined as the accumulation of pus in the pleural space, has long been a recognized medical condition, dating back to the time of Hippocrates. It's commonly associated with significant morbidity, especially in pediatric patients where pulmonary infections are a major cause of hospital admissions. Empyema typically follows acute bacterial pneumonia in children, presenting with respiratory failure or hypoxia. This condition evolves from a simple exudative parapneumonic effusion into a more complex, multiloculated purulent form characterized by low pH and high lactate dehydrogenase levels.

Globally, childhood empyema occurs at a rate of 0.7 to 3.3 per 100,000 population. The infection can arise from both iatrogenic causes and primary empyema, which occurs without pneumonia. Historically, the management of thoracic empyema has been challenging, often resisting evidence-based approaches. This is partly due to the expanding pool of potential candidates for empyema thoracis as a result of increased life expectancy, improved survival from malignant diseases, and extended operability criteria in thoracic surgery.

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The management of thoracic empyema in children has been a topic of controversy for decades, with treatment options ranging from antibiotics alone or in combination with thoracentesis, tube thoracostomy, intrapleural fibrinolytics, thoracoscopy, to open decortication. This diversity in therapeutic approaches across different centers highlights the lack of consensus and substantial evidence in establishing the ideal treatment. This variability often leads to treatments being influenced by institutional traditions, personal experiences, and biases rather than solid clinical evidence.

The debate over the role of surgical decortication in the management of empyema, which involves a thoracotomy to remove the inflamed, thickened pleura with fibrinous deposits, is not a recent development. The practice varies significantly, with the rate of this procedure in reported series ranging from 1% to 90%. This variability in practice has been highlighted by recent publications from tertiary centers advocating early open decortication, citing excellent clinical outcomes. However, open decortication is notably invasive, causing significant postoperative pain and leaving a thoracotomy scar. In contrast, thoracoscopic decortication is less invasive but still requires multiple smaller incisions and prolonged general anesthesia.

Current accepted management generally includes systemic antibiotics and drainage of the pleural cavity, achieved either through medical chest tube drainage or surgery. Several studies have explored the efficacy and safety of intrapleural fibrinolytics in treating pleural effusion and empyema. These fibrinolytic agents, when used early in loculated effusions, can break down loculations and early pleural peel, thereby facilitating drainage of the pleural space. This approach of using intrapleural fibrinolytic agents to dissolve fibrinous clots and membranes, thereby improving drainage and reducing hospital stay, fever intensity, and the need for chest tube drainage, was first described over fifty years ago. Despite these advancements, there remains a lack of sufficient data and evidence to fully support the use of fibrinolytic therapy in managing empyema cases.

This background sets the stage for the present study conducted at a tertiary care center, aiming to determine the advantages of intrapleural instillation of streptokinase compared to conventional therapy in managing childhood empyema.

Methodology

This study was a hospital-based, randomized controlled, non-blinded trial conducted over 18 months at a tertiary care center's pediatric department. The study aimed to evaluate the effectiveness of intrapleural streptokinase in managing childhood empyema. Forty children, aged 6 months to 15 years, with a confirmed diagnosis of empyema, were enrolled. They were randomized into two groups using a 4-block randomization method:

- Group A: Streptokinase group.
- Group B: Non-streptokinase group.

Inclusion and exclusion criteria: Inclusion criteria comprised children of either gender within the specified age range, diagnosed with empyema (loculated or non-loculated), with or without underlying pneumonia. Parents or legal guardians provided informed consent. The exclusion criteria included children with pneumonia/pleural effusion without empyema, those with tuberculous empyema, and cases where informed consent was not given. Children with other comorbid lung conditions like bronchiectasis, chronic lung disease, congenital lung anomalies, asthma, or comorbid illness of other systems like cerebral palsy or nephrotic syndrome were also excluded.

Study protocol: Upon approval from the institutional ethics committee and obtaining written informed consent from the patients' guardians, children presenting with symptoms suggestive of empyema were evaluated. Diagnosis was confirmed using chest X-ray and ultrasonography (USG) of the thorax, performed by an experienced radiologist. In some cases, CT thorax was conducted as per the USG report to confirm the diagnosis. Pleural fluid taps were analyzed for microscopy, cells, sugar, protein, pH and culture. All patients with confirmed empyema had an intercostal drainage (ICD) tube placed with water seal drainage.

In the streptokinase group, intrapleural streptokinase was administered at a dose of 15000 units/kg via a syringe pump. The infusion lasted one hour, followed by clamping for four hours. After this period, the clamp was removed to allow free drainage. This treatment was repeated daily for three days. The first follow-up USG thorax was done on day 4. Depending on the resolution observed on USG, intrapleural streptokinase was administered for up to two additional days. A second check USG thorax was performed on day 7, and a CT thorax was conducted if required. Intravenous antibiotics and supportive management were continued as per standard protocols for empyema. The chest drain was removed based on clinical and radiological improvement, typically when fluid drainage was less than 20 mL per day. A repeat USG was conducted one week post-drain removal to assess empyema resolution.

Response and follow-up: Response to treatment was defined as a reduction in respiratory distress, decrease in fever, improvement in clinical findings (such as better air entry) and improvements observed in chest X-ray and USG findings. Complete or near-complete disappearance of opacity on chest X-ray and insignificant fluid in the pleural space on USG were considered as resolution.

Children were followed until discharge, and outcomes in terms of survival or transfer to surgery were recorded.

Statistical analysis: Quantitative data were presented as mean and standard deviation. Comparisons between study groups were made using unpaired t-tests as per normality test results. Qualitative data were represented as frequency and percentage. The association among the study groups was assessed using Fisher's test, Student's t-test, and Chi-Square test. A 'p' value of less than 0.05 was considered statistically significant.

Results

The study's results are crucial in evaluating the effectiveness of intrapleural streptokinase in managing childhood empyema. The trial involved 40 children, randomized into two groups - Group A (Streptokinase group) and group B (Non-streptokinase group).

Age and gender distribution: The mean age of children in group A was 4.87 ± 4.50 years, and in group B, it was 4.01 ± 2.78 years. This difference was not statistically significant ($p > 0.05$). Regarding gender distribution, in group A, there were 13 (65%) males and 7 (35%) females, while group B had 12 (60%) males and 8 (40%) females.

Clinical observations: Clinical parameters were closely monitored in both groups. The study assessed key indicators such as the duration of defervescence (the time taken for fever to resolve), the duration of respiratory distress, the duration of chest tube drainage, the requirement of surgery, and the overall hospital stay duration.

Response to treatment: Treatment response was defined based on several factors: the reduction of respiratory distress, decrease in fever, improvement of clinical findings (like better air entry), and the improvement observed in chest X-ray and USG findings. The resolution of empyema was considered based on the complete or near-complete disappearance of opacity on chest X-ray and insignificant fluid in the pleural space on USG.

Significant findings: The use of intrapleural streptokinase in group A showed a notable impact on the study's primary outcomes. The duration of defervescence was significantly shorter in the streptokinase group compared to the non-streptokinase group. Additionally, children in the streptokinase group experienced a quicker resolution of respiratory distress and required shorter durations of chest tube drainage.

Moreover, the requirement for surgical intervention was markedly lower in the streptokinase group. This reduction in the need for surgery underscores the therapeutic potential of intrapleural streptokinase in managing childhood empyema. The overall duration of hospital stay was also significantly reduced in the streptokinase group, indicating not only clinical effectiveness but also potential benefits in terms of healthcare resource utilization.

Duration of chest tube drainage: A significant observation was the difference in the duration of chest tube drainage between the two groups. Group A, which received intrapleural streptokinase, showed a shorter average duration of chest tube drainage (5.85 days) compared to group B (9.44 days). This reduction in drainage duration is indicative of the efficacy of intrapleural streptokinase in facilitating fluid clearance from the pleural space.

Requirement of surgery: The requirement for surgical intervention was notably lower in group A (Streptokinase group) than in group B (Non-streptokinase group). In group A, only 3 out of 20 children required surgery, whereas in group B, 7 out of 20 children underwent surgical procedures. This finding highlights the potential of intrapleural streptokinase in reducing the need for more invasive surgical interventions in the management of childhood empyema.

Hospital stay and costs: The duration of hospital stays was significantly different between the two groups. The mean duration of hospital stay was shorter in the streptokinase group (Group A) at 10.3 days, compared to 15.55 days in the non-streptokinase group (Group B), with a p-value of $1E-4$, indicating a high level of statistical significance. This reduced hospitalization duration not only signifies a quicker recovery but also suggests a more efficient use of healthcare resources.

Moreover, there was a notable difference in the cost of hospital stays between the two groups. The mean cost for group A was substantially lower at 525.29, compared to 775.55 in group B, with a p-value of $1E-4$. This significant cost reduction implies that intrapleural streptokinase therapy could offer a more cost-effective approach to managing childhood empyema, potentially leading to economic benefits for healthcare systems.

These results collectively underscore the effectiveness of intrapleural streptokinase in the management of childhood empyema. The therapy not only contributed to improved clinical outcomes, as evidenced by shorter durations of chest drainage and reduced need for surgery, but also presented advantages in terms of reduced hospital stay durations and associated costs. These findings hold substantial implications for the treatment protocols and resource allocation in pediatric healthcare settings dealing with empyema.

Discussion

The study's findings have significant implications in the context of childhood empyema treatment, particularly concerning the use of intrapleural streptokinase. The reduction in the need for surgical intervention in the streptokinase group compared to the non-streptokinase group is a pivotal outcome. This aligns with existing literature suggesting the efficacy of intrapleural fibrinolytics in reducing surgical requirements in empyema patients [1,2]. The study contributes to this growing body of evidence, emphasizing the potential of intrapleural streptokinase as a non-invasive treatment alternative.

The significantly shorter duration of hospital stays in the streptokinase group not only suggests clinical efficacy but also indicates a potential reduction in healthcare resource utilization. This is especially relevant in pediatric healthcare, where minimizing hospitalization duration can reduce patient and family distress and lower healthcare costs. This finding is consistent with previous studies demonstrating the cost-effectiveness of intrapleural fibrinolytic therapy [3,4].

Furthermore, the study showed that children in the streptokinase group experienced quicker resolution of respiratory distress and shorter durations of chest tube drainage. These outcomes highlight the efficiency of intrapleural streptokinase in improving patient

comfort and accelerating recovery, which is critical in pediatric care. The efficacy in fluid clearance and symptom resolution corroborates with other studies which have observed similar benefits with intrapleural fibrinolytics [5,6].

However, it is important to consider the limitations of the study. The sample size, while adequate for a preliminary investigation, warrants larger-scale studies for broader generalization. Moreover, being a hospital-based study, the results might not be entirely representative of broader pediatric populations. Future research should aim to include a more diverse patient demographic to validate these findings across different healthcare settings.

Despite these limitations, the study's findings are a valuable addition to the literature on pediatric empyema management. The reduced need for surgery, shorter hospital stays, and potential cost savings advocate for intrapleural streptokinase as an effective treatment modality, especially in resource-limited settings where healthcare resources are scarce.

The study's results regarding the effectiveness of intrapleural streptokinase in managing childhood empyema also extend to the realms of patient safety and healthcare efficiency. The reduced requirement for invasive surgical procedures in the streptokinase group underlines the safety aspect of this treatment. This is particularly important in pediatric care, where less invasive procedures are favored to minimize trauma and speed up recovery. These outcomes align with the recommendations of the pleural disease guideline group of the British Thoracic Society, which emphasizes the importance of medical management in pleural infections [7].

Moreover, the shorter duration of chest tube drainage in the streptokinase group suggests an expedited recovery process, leading to enhanced patient comfort and reduced risk of hospital-acquired infections, a crucial factor in pediatric patient care. This finding is consistent with other studies that have observed the benefits of intrapleural fibrinolytics in improving drainage efficiency and reducing the duration of chest tubes [4,8].

The economic implications of these findings cannot be overstated. The significant reduction in hospital stay duration and associated costs in the streptokinase group indicates that intrapleural streptokinase could offer a cost-effective treatment strategy. This is particularly relevant in healthcare systems with limited resources, where cost-effective treatments can greatly impact patient care and resource allocation.

However, it is crucial to recognize the potential risks associated with intrapleural streptokinase, including allergic reactions and bleeding complications. While these risks were not significantly observed in the study, they remain a concern in clinical practice and should be considered when opting for this treatment.

In conclusion, the study's findings advocate for the inclusion of intrapleural streptokinase in the standard treatment protocols for childhood empyema. Its ability to reduce the need for surgical interventions, shorten hospital stays, and lower treatment costs, all while maintaining patient safety, makes it a valuable treatment option. Future studies with larger sample sizes and diverse patient demographics are needed to further validate these findings and explore the long-term outcomes of this treatment approach [9-19].

[Next, a conclusion will be provided, summarizing the key findings and implications of the study].

Conclusion

The study conducted on the effectiveness of intrapleural streptokinase in the management of childhood empyema provides valuable insights into non-invasive treatment options for this condition. The significant findings of the study include a marked reduction in the need for surgical interventions, shorter hospital stays, and decreased overall treatment costs in the streptokinase group compared to the

non-streptokinase group. These results highlight the potential of intrapleural streptokinase as an effective, less invasive alternative to traditional surgical methods in treating childhood empyema.

Importantly, the study underscores the role of intrapleural streptokinase in improving patient outcomes, enhancing recovery speed, and reducing the burden on healthcare resources. While the study faced limitations such as a limited sample size and being hospital-based, its findings are consistent with existing literature and contribute significantly to the ongoing discourse on pediatric empyema management.

In summary, the study advocates for the consideration of intrapleural streptokinase as a standard treatment option for childhood empyema, particularly in settings where reducing healthcare costs and minimizing invasive procedures are priorities. Future research should focus on larger-scale studies to confirm these findings and explore the long-term implications of this treatment approach, ensuring that pediatric patients with empyema receive the most effective and efficient care possible.

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