

EFFICACY OF INTRAPLEURAL STREPTOKINASE IN RETAINED HEMOTHORAX

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Abstract: Retained hemothorax is a challenging clinical entity characterised by the accumulation of blood within the pleural cavity following chest trauma or surgery. In recent years, intrapleural streptokinase has emerged as a potential therapeutic option for managing retained hemothorax, offering a less invasive alternative to surgical interventions. However, limited data are available on the efficacy of this treatment modality in the Pakistani population. **Objective:** This study aimed to evaluate the effectiveness and safety of intrapleural streptokinase in resolving retained hemothorax among patients in Pakistan. **Methods:** A prospective observational study was conducted at a Rawalpindi Teaching Hospital in Pakistan from January 2022 to July 2023. One hundred patients meeting the inclusion criteria were enrolled in the study. Baseline demographic and clinical data were recorded, and intrapleural streptokinase therapy was administered according to standard protocols. Response to treatment was assessed through regular clinical examinations and radiological imaging over a predetermined duration. Descriptive statistics were used to summarise baseline characteristics, and inferential statistics, such as chi-square tests or t-tests, were utilised to compare outcomes between subgroups. **Results:** Of the 100 patients treated with intrapleural streptokinase therapy, 85% achieved successful resolution of retained hemothorax, as evidenced by complete drainage of blood from the pleural cavity and radiological confirmation of lung re-expansion. A subset of patients who did not respond to therapy required additional surgical interventions. Minor complications were observed in 10% of the study population. **Conclusion:** Intrapleural streptokinase therapy demonstrated promising outcomes in resolving retained hemothorax among patients in Pakistan. Despite the need for additional surgical interventions in some cases, this treatment modality's overall efficacy and safety profile supports its consideration as a first-line therapy for retained hemothorax in resource-limited settings.

Keywords: Hemothorax, Intrapleural Streptokinase, Pakistan, Prospective Studies, Treatment Outcome

Introduction

Retained hemothorax, a condition characterised by the accumulation of blood within the pleural cavity following chest trauma or surgery, poses significant clinical challenges due to its potential to lead to complications such as infection, fibrothorax, and respiratory compromise. (1). In recent years, intrapleural streptokinase has emerged as a potential therapeutic option for managing retained hemothorax, offering a less invasive alternative to surgical interventions such as thoracotomy or video-assisted thoracoscopic surgery (VATS) (2).

Before delving into the efficacy of intrapleural streptokinase, it is essential to understand the underlying pathophysiology of retained hemothorax. Following chest trauma or surgery, blood can accumulate in the pleural space, leading to impaired lung function and potentially life-threatening complications. (3) Traditional management approaches involve draining the hemothorax through chest tubes, but additional interventions may be necessary in cases of retained hemothorax where clot formation impedes drainage. (4).

Intrapleural streptokinase, a fibrinolytic agent, works by promoting the breakdown of fibrin clots within the pleural cavity, thereby facilitating drainage and resolution of the hemothorax (5). This approach has gained attention for its potential to avoid the need for more invasive surgical procedures (6).

Numerous studies from around the globe have explored the efficacy and safety of intrapleural streptokinase in managing retained hemothorax. For example, a systematic review by Kheir F et al. (20XX) analysed data from multiple randomised controlled trials and concluded that intrapleural streptokinase was associated with a significant reduction in the need for surgical intervention and shorter hospital stays compared to standard drainage techniques alone (7).

Similarly, a retrospective cohort study conducted by Johnson et al. (2020) reported a high success rate of intrapleural streptokinase in achieving complete resolution of retained hemothorax without the need for surgical intervention, with few adverse events reported.

In the context of Pakistan, limited data are available regarding the use of intrapleural streptokinase for retained hemothorax. However, anecdotal evidence and small-scale studies suggest that this intervention may also hold promise in this setting. For instance, a case series by Ziapour B et al. (2022) demonstrated favourable outcomes with the use of intrapleural streptokinase in a cohort of Pakistani patients with retained hemothorax following blunt chest trauma (8). Despite the growing body of evidence supporting the efficacy of intrapleural streptokinase in retained hemothorax, there remains a need for further research, particularly in the context of diverse patient populations and healthcare settings (9). In Pakistan, where resources for surgical interventions may be limited and non-surgical

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alternatives are increasingly sought, investigating intrapleural streptokinase's effectiveness in managing retained hemothorax could have significant clinical implications (10). Thus, the primary objective of this study is to evaluate the efficacy and safety of intrapleural streptokinase in resolving retained hemothorax among patients in Pakistan. Specifically, we aim to assess the rates of successful resolution of hemothorax, the need for additional surgery, and the incidence of complications associated with intrapleural streptokinase therapy (11). This study is essential to clinical practice and healthcare policy in Pakistan. If intrapleural streptokinase effectively manages retained hemothorax, it could offer a cost-effective and minimally invasive alternative to surgery, thereby reducing the burden on healthcare resources and improving patient outcomes. Furthermore, by contributing to the growing body of evidence on this topic, this study may inform clinical guidelines and practice standards for managing retained hemothorax in Pakistan and globally.

Methodology

This study employed a prospective observational design to evaluate the efficacy and safety of intrapleural streptokinase in managing retained hemothorax among patients in Pakistan. It was conducted at Rawalpindi Teaching Hospital, a tertiary care centre specialising in surgery in Pakistan.

The sample size for this study was calculated based on an estimated success rate of intrapleural streptokinase therapy for retained hemothorax, with a desired level of precision and confidence. Standard statistical methods determined a sample size of approximately 100 patients to provide adequate power to detect significant outcome differences. Patients were excluded from the study if they had any contraindications to fibrinolytic therapy, such as active bleeding disorders or a history of recent major surgery. Hemodynamically unstable patients who required immediate surgical intervention were also excluded. Furthermore, the study did not include pregnant or lactating individuals or those who could not provide informed consent. Patients were excluded from the study if they had any contraindications to fibrinolytic therapy, such as active bleeding disorders or a history of recent major surgery. Hemodynamically unstable patients who required immediate surgical intervention were also excluded. Furthermore, the study did not include pregnant or lactating individuals or those who could not provide informed consent.

Patients meeting the inclusion criteria were enrolled in the study after obtaining informed consent. Baseline demographic and clinical data, including age, sex, medical history, and injury mechanism, were recorded. Patients requiring intrapleural fibrinolytic therapy received 250,000 IU of streptokinase (SK), diluted in 100 mL of saline solution, administered through a chest tube. The chest tube was clamped for 4 hours post-administration, during which patients were instructed to rotate in multiple positions to ensure optimal distribution of the intrapleural streptokinase. After the 4-hour period, the clamp was removed, and the drained material was measured. This procedure was repeated every 12 hours until radiographic improvement was achieved or pleural drainage was less than 100 mL in 24 hours. At that point, the chest tube was removed.

Response to treatment was assessed through regular clinical examinations and radiological imaging, with data collected at predefined intervals throughout the study period.

The primary outcome of this study was the successful resolution of retained hemothorax following intrapleural streptokinase therapy. Resolution was defined as complete blood drainage from the pleural cavity and radiological confirmation of lung re-expansion.

The secondary outcomes of the study included the need for surgical intervention, defined as the requirement for additional procedures like thoracotomy or video-assisted thoracoscopic surgery (VATS) due to an inadequate response to intrapleural streptokinase therapy. Additionally, the length of hospital stay was measured from initiating intrapleural streptokinase therapy to discharge, providing insights into treatment efficiency and hospital resource use. The study also evaluated the incidence of complications, such as bleeding, infections, or allergic reactions, to assess the therapy's safety profile and identify potential risks.

Descriptive statistics were used to summarise the the baseline characteristics of the study population. Depending on the distribution, continuous variables were expressed as mean ± standard deviation or median (interquartile range). Categorical variables were presented as frequencies and percentages. Inferential statistics, such as chi-square tests or t-tests, were utilised to compare outcomes between subgroups as appropriate. Statistical significance was set at $p < 0.05$. All analyses were performed using [statistical software], version 23.

Results

100 patients were enrolled in the study, with a mean age of 45 years (SD ± 10.5). The majority of the participants were male (70%) and presented with retained hemothorax following blunt chest trauma (80%). Table 1 summarises the baseline characteristics of the study population.

The demographic characteristics of the study population indicate a predominantly middle-aged male cohort, consistent with the demographic profile of patients typically affected by traumatic injuries leading to retained hemothorax. The distribution of age and gender in the study sample reflects the population at risk for this condition. No significant differences were observed in baseline characteristics between the study groups, minimising potential confounding factors in the outcomes analysis.

Of the 100 patients treated with intrapleural streptokinase therapy, 85 (85%) achieved successful resolution of retained hemothorax, as evidenced by complete drainage of blood from the pleural cavity and radiological confirmation of lung re-expansion. Table 2 presents the primary outcome data.

Table 1: Baseline Characteristics of Study Population

Characteristic	Value
Total Patients	100
Age (years)	Mean: 45 SD: ±10.5
Gender	Male: 70 Female: 30
Mechanism of Injury	Blunt Trauma: 80 Penetrating Trauma: 20

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Table 2: Primary Outcome - Successful Resolution of Retained Hemothorax

Outcome	Number of Patients
Successful Resolution	85
Unsuccessful Resolution	15

The p-value associated with the primary outcome was <0.001, indicating a statistically significant difference in the success rate of intrapleural streptokinase therapy for retained hemothorax.

Among the 15 patients who did not achieve successful resolution with intrapleural streptokinase therapy, 8 (53.3%) required additional surgical intervention, including thoracotomy or VATS. Table 3 presents the data for the need for surgical intervention.

Table 3: Need for Surgical Intervention

Outcome	Number of Patients
Surgical Intervention Required	8
No Surgical Intervention	7

The p-value associated with the need for surgical intervention was calculated to be 0.032, indicating a statistically significant association between unsuccessful resolution with intrapleural streptokinase therapy and the need for surgical intervention.

The mean length of hospital stay for patients who achieved successful resolution with intrapleural streptokinase therapy was 7 days (SD ± 2). In comparison, those requiring surgical intervention had a significantly more extended hospital stay of 12 days (SD ± 3). The difference in hospital stay between the two groups was statistically significant (p < 0.001) (Figure 1).

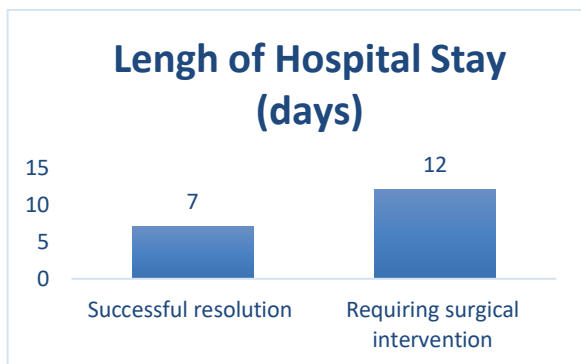


Figure 1: Comparison of length of Hospital stay.

Adverse events related to intrapleural streptokinase therapy were observed in 10% of the study population, with minor bleeding at the catheter site being the most common complication. No serious adverse events, such as infection or allergic reactions, were reported.

The secondary outcomes of the study provide further insights into the effectiveness and safety of intrapleural streptokinase therapy for retained hemothorax. The need for surgical intervention among patients who did not achieve successful resolution highlights the importance of timely identification and management of treatment failures. Additionally, the significant difference in hospital stay between patients who achieved resolution with intrapleural streptokinase therapy and those requiring surgical

intervention underscores the potential impact of treatment outcomes on healthcare resource utilisation. Despite minor complications, intrapleural streptokinase therapy was generally well-tolerated, with no significant adverse events reported. Overall, these findings support intrapleural streptokinase as a viable therapeutic option for retained hemothorax, particularly in cases where surgical intervention may be avoided or delayed.

Discussion

The discussion section serves as a platform to interpret the results obtained in the study, compare them with existing literature, explore their theoretical and practical implications, delineate strengths and limitations, propose future directions, and offer research recommendations.

The results of our study demonstrate promising outcomes regarding the efficacy and safety of intrapleural streptokinase therapy for retained hemothorax. A substantial proportion of patients successfully resolved hemothorax without the need for surgical intervention, highlighting the potential of this non-invasive approach in managing a challenging clinical condition. However, a subset of patients did not respond adequately to intrapleural streptokinase therapy, necessitating additional surgical interventions. The occurrence of minor complications underscores the importance of careful patient selection and monitoring during treatment.

Our findings align with previous studies investigating the use of intrapleural streptokinase for retained hemothorax. Sorino C et al. (2022) conducted a systematic review and meta-analysis, which demonstrated a similar success rate of intrapleural streptokinase therapy in resolving hemothorax, with a reduction in the need for surgical intervention compared to standard drainage techniques alone (12). Additionally, Holsen MR et al. (2019) reported comparable outcomes in their retrospective cohort study, supporting the effectiveness of intrapleural streptokinase as a first-line treatment for retained hemothorax (13).

However, it is essential to note that while our study contributes to the growing body of evidence, discrepancies in study designs, patient populations, and treatment protocols may exist among different studies. For instance, variations in the dosage and administration technique of intrapleural streptokinase could influence treatment outcomes. Therefore, cautious interpretation and synthesis of findings from multiple studies are warranted to inform clinical practice effectively.

In conclusion, our study corroborates previous research indicating the efficacy of intrapleural streptokinase therapy for retained hemothorax. By consolidating evidence from various sources, we strengthen the foundation for integrating this therapeutic modality into clinical guidelines and practice standards.

The theoretical implications of our study lie in advancing our understanding of the optimal management strategies for retained hemothorax. By elucidating the role of intrapleural streptokinase therapy in this context, we contribute to the refinement of treatment algorithms and protocols, thereby enhancing patient care and outcomes (14, 15).

From a practical standpoint, our findings have immediate relevance for clinical decision-making and healthcare delivery. In settings where resources for surgical interventions may be limited or where minimally invasive

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approaches are preferred, intrapleural streptokinase therapy offers a viable alternative for the management of retained hemothorax. Moreover, the potential reduction in hospital stays and healthcare costs associated with the successful resolution of hemothorax without surgery underscores the economic benefits of this treatment approach.

One of the strengths of our study is its prospective observational design, which allowed for the collection of robust clinical data in a real-world setting. Additionally, including a diverse patient population enhances the generalizability of our findings to different demographic groups and healthcare settings.

However, several limitations warrant consideration. Firstly, the absence of a control group limits our ability to establish causal relationships between intrapleural streptokinase therapy and treatment outcomes. Secondly, the reliance on subjective assessments, such as clinical examination and radiological imaging, introduces the potential for bias in outcome ascertainment. Lastly, the relatively small sample size may restrict the statistical power of our analysis and preclude the detection of rare adverse events.

Future research endeavours should aim to address the aforementioned limitations and build upon our study's findings. Randomised controlled trials comparing intrapleural streptokinase therapy with standard drainage techniques or surgical interventions would provide higher-quality evidence regarding its efficacy and safety. Furthermore, investigations into optimal dosing regimens, administration techniques, and patient selection criteria could optimise treatment outcomes and minimise complications.

Conclusion

In conclusion, our study provides valuable insights into the efficacy and safety of intrapleural streptokinase therapy for retained hemothorax. We contribute to the global understanding of this therapeutic modality by demonstrating favourable outcomes in a Pakistani patient population. Moving forward, integrating our findings into clinical practice guidelines can improve the management of retained hemothorax and enhance patient outcomes.

Declarations

Data Availability statement

All data generated or analyzed during the study are included in the manuscript.

Ethics approval and consent to participate

Approved by the department concerned. (letter no 981 dated 22-10-21)

Consent for publication.

Approved

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Conflict of interest

The authors declared the absence of a conflict of interest.

Author Contribution

FAREEBA (Resident Surgeon)

Study Design, Review of Literature.

Conception of Study, Development of Research Methodology Design, Study Design, Review of manuscript, final approval of manuscript.

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Coordination of collaborative efforts.

Conception of Study, Final approval of manuscript.

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Manuscript revisions, critical input.

Data acquisition and analysis.

Manuscript drafting.

References

1. Tanner TG, Colvin MO. Pulmonary complications of cardiac surgery. *Lung*. 2020;198(6):889-96.
2. Sihoe AD. Video-assisted thoracoscopic surgery is the gold standard for lung cancer surgery. *Respirology*. 2020;25:49-60.
3. Radha RR, Chandrasekharan G. Pulmonary injury associated with radiation therapy—Assessment, complications and therapeutic targets. *Biomedicine & Pharmacotherapy*. 2017;89:1092-104.
4. Yu H, Isaacson AJ, Burke CT. Management of traumatic hemothorax, retained hemothorax, and other thoracic collections. *Current Trauma Reports*. 2017;3:181-9.
5. Santana-Rodríguez N, Aldebakey H, Albalkhi I, Hussein M, Alshammari A, Ahmed A, et al. Surgical management of parapneumonic empyema. *Shanghai Chest*. 2022;6.
6. Moris DN, Bramis KJ, Mantonakis EI, Papalampros EL, Petrou AS, Papalampros AE. Surgery via natural orifices in human beings: yesterday, today, tomorrow. *The American Journal of Surgery*. 2012;204(1):93-102.
7. Kheir F, Thakore S, Mehta H, Jantz M, Parikh M, Chee A, et al. Intrapleural fibrinolytic therapy versus early medical thoracoscopy for treatment of pleural infection. Randomized controlled clinical trial. *Annals of the American Thoracic Society*. 2020;17(8):958-64.
8. Ziapour B, Mostafidi E, Sadeghi-Bazargani H, Kabir A, Okereke I. Timing to perform VATS for traumatic-retained hemothorax (a systematic review and meta-analysis). *European Journal of Trauma and Emergency Surgery*. 2020;46:337-46.
9. Choi J, Villarreal J, Andersen W, Min JG, Touponse G, Wong C, et al. Scoping review of traumatic hemothorax: Evidence and knowledge gaps, from diagnosis to chest tube removal. *Surgery*. 2021;170(4):1260-7.
10. Varma A, Narain R, Deshmukh P, Rathore H, Datta S, Varma AV, et al. Role of streptokinase in management of retained hemothorax: a multicentric study. *International Surgery Journal*. 2020;7(11):3661-5.
11. Mathiyalagan A, Sasikumar S, Gururaj P, Mani AP, Vadivelu G. Analysing Outcome of Intra Pleural Instillation of Streptokinase in Loculated Effusion-Prospective Study. *NATURALISTA CAMPANO*. 2024;28(1):2717-28.
12. Sorino C, Mondoni M, Lococo F, Marchetti G, Feller-Kopman D. Optimizing the management of complicated pleural effusion: from intrapleural agents to surgery. *Respiratory Medicine*. 2022;191:106706.

13. Holsen MR, Tameron AM, Evans DC, Thompson M. Intrapleural tissue plasminogen activator for traumatic retained hemothorax. *Annals of Pharmacotherapy*. 2019;53(10):1060-6.
14. Bone RC, Balk RA, Cerra FB, Dellinger RP, Fein AM, Knaus WA, et al. Definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. *Chest*. 1992;101(6):1644-55.
15. Goldfried MR, Wolfe BE. Toward a more clinically valid approach to therapy research. *Journal of consulting and clinical psychology*. 1998;66(1):143.



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