

## Original Research Article

# Role of streptokinase in management of retained hemothorax: a multicentric study

Ankur Varma<sup>1</sup>, Ravikant Narain<sup>1</sup>, Parag Deshmukh<sup>1</sup>, Himmat Rathore<sup>1</sup>,  
SGS Datta<sup>1</sup>, Aditi V. Varma<sup>2\*</sup>, Pawan Sharma<sup>3</sup>, Jebin Joseph<sup>4</sup>

<sup>1</sup>Department of Surgery, 151 Base Hospital, Guwahati, Assam, India

<sup>2</sup>Department of Radiology, 151 Base Hospital, Guwahati, Assam India

<sup>3</sup>Department of Trauma Surgery, AFMC, Pune, Maharashtra, India

<sup>4</sup>Department of Surgery, INHS Sanjeevani, Kochi, Kerala, India

**Received:** 04 August 2020

**Revised:** 19 September 2020

**Accepted:** 24 September 2020

### \*Correspondence:

Dr. Aditi V. Varma,

E-mail: [ankurvarma2@gmail.com](mailto:ankurvarma2@gmail.com)

**Copyright:** © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

## ABSTRACT

**Background:** Enzymatic debridement of the pleural cavity for retained haemothorax is a frequently overlooked option.

**Methods:** A retrospective, multicentre study was carried out using intrapleural streptokinase was carried out in 15 patients with retained or clotted haemothorax.

**Results:** Thirteen of fifteen patients (86%) with retained pleural collections underwent successful enzymatic debridement and tube drainage with streptokinase injections in our study. The average increase in chest tube output following streptokinase injections was 160%. No significant adverse reactions occurred. Two patients required thoracotomy when streptokinase therapy failed. No deaths were reported in the study.

**Conclusions:** Intrapleural streptokinase is a safe, effective means of removing retained proteinaceous collections in the pleural space. It is a useful adjunct to chest tube drainage and may obviate the need for more invasive procedures.

**Keywords:** Clotted haemothorax, Streptokinase, Fibrinolytic drug

## INTRODUCTION

In majority of cases, tube thoracostomy is adequate for the initial management of a haemothorax in most instances however, failure of tube thoracostomy and clotted haemothorax is seen in 5% to 30% of cases.<sup>1</sup> Insufficient care of post-traumatic clotted haemothorax and repeated thoracentesis are a major risk for secondary bacterial infection leading to sepsis and persistent broncho-pleural fistula.<sup>2-4</sup> So, early detection and management of haemothorax is of greatest importance.<sup>5,6</sup> Most authors recommend Video assisted thoracoscopic surgery (VATS) as the management of retained or clotted haemothorax as VATS provides direct visualization of the pleural cavity with has the ability to give full vision of the pleural cavity with the scope for manipulation of chest tube, elimination

of retained clot and avoidance of bacterial infections within the thoracic cavity.<sup>5,6</sup> Thoracotomy and VATS are invasive procedures. Although VATS is the gold standard for management of retained haemothorax, its availability in smaller centres is limited. One of the alternative methods to VATS is the use of fibrinolytic therapy within the pleura.<sup>7-9</sup> We assessed the efficacy of Streptokinase (SK) administration intrapleurally to enhance the dissolution of clotted haemothorax in the patients' pleural spaces for accelerate the resolution response of clot.

### *Pathogenesis*

Bleeding into the pleural space can occur due to disruption of the tissues of the chest wall and pleura or the intrathoracic structures. Blood that enters the pleural

cavity is exposed to the motion of the diaphragm, lungs, and other intrathoracic structures. This results in some degree of defibrination of the blood leading to incomplete clotting. Within several hours of cessation of bleeding, lysis of existing clots by pleural enzymes begins. However, when this lysis is incomplete or bleeding is relatively large, clot formation is inevitable.

Once the clot has been allowed to organize, it adheres to the lung and pleura, making it difficult to remove. The complications of untreated haemothorax result from fibrin threads formation on the surface of pleura, accompanied by proliferation of fibroblastic and angioblastic cells.<sup>7</sup> Consequently, the haemothorax transforms to fibrothorax due to inflammatory exudates covering visceral and parietal pleura, reducing the ability of lung ventilation.<sup>8-10</sup> SK is an anti-thrombotic agent that acts on the fibrinolytic system. SK is obtained naturally from Beta haemolytic streptococci. It is utilized to break down clots in some cases of myocardial infarction, pulmonary embolism, and arterial thrombo-embolism by injection into a vein.<sup>4</sup> The pathological features of haemothorax suggest that a clot within the pleural space should be evacuated as early as possible to prevent downstream complications.

### Objective of the study

To evaluate the role of intrapleural fibrinolysis in retained haemothorax or loculated pleural collections, a retrospective, multicentre trial was carried out in three hospitals in India.

## METHODS

### Study design and objective

To evaluate the role of intrapleural fibrinolysis in retained haemothorax or loculated pleural collections, a retrospective, multicentre trial was carried out in three hospitals in India, 151 Base Hospital, INHS Sanjeevani, Base Hospital Delhi Cantt over a period of 06 months from March 2020 to August 2020.

### Selection Criteria

Patients aged 16-80 years were included in the study if they had clotted haemothorax, that did not resolve with closed thoracotomy.

Individuals younger than 16 years; those with known bleeding disorder, recent stroke or recent anticoagulant therapy, or administration of SK in the previous 2 years were excluded from the study.

### Therapeutic regimen

All patients had determination of coagulation parameters, liver function tests, and creatinine before and after intra pleural streptokinase.

SK, 250,000 IU, was diluted in 100 mL of saline solution and administered through chest tube. The chest tube was clamped for 4 hours, and patients were asked to rotate in several positions to allow for better distribution of intra pleural streptokinase. After the 4 hours, the clamp was removed, and the drained material was measured. The procedure was repeated 3-6 times or till radiographic improvement was achieved or until pleural drainage was less than 100 mL in 24 hours. At that time, the chest tube was also removed.

All patients received standardized broad-spectrum antibiotics initially that were later adjusted to the microbiological culture results.

### Criteria for effectiveness

We quantified the amount of pleural drainage and the radiologic improvement after administration of intrapleural SK. The criteria for improvement were defined as follows: complete response (normal or near-normal chest radiograph); partial response (a clearance of 30 to 80% of pleural opacities); no response (<30% of clearance of pleural opacities).

### Ethical approval

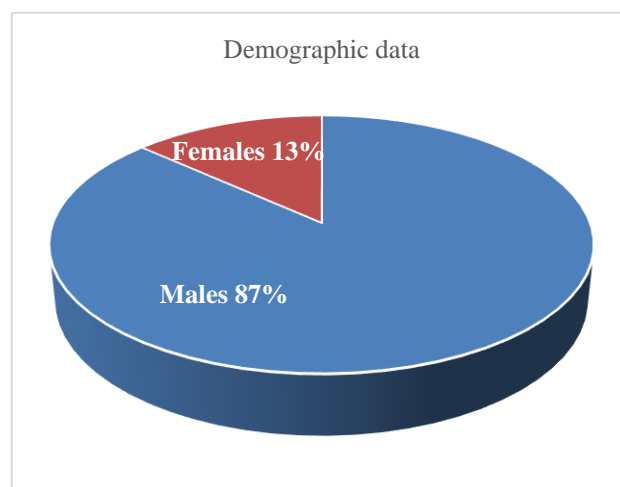
The study was approved by the Institutional Ethics Committee.

### Statistical analysis

Statistical package for social sciences (SPSS) 26 software was used for statistical analysis.

## RESULTS

This study was conducted on 15 clotted haemothorax patients who fulfilled the above criteria after chest tube thoracostomy with mean age of 35 years. There were 13 males and 2 females included in the study.



**Figure 1: Gender distribution.**

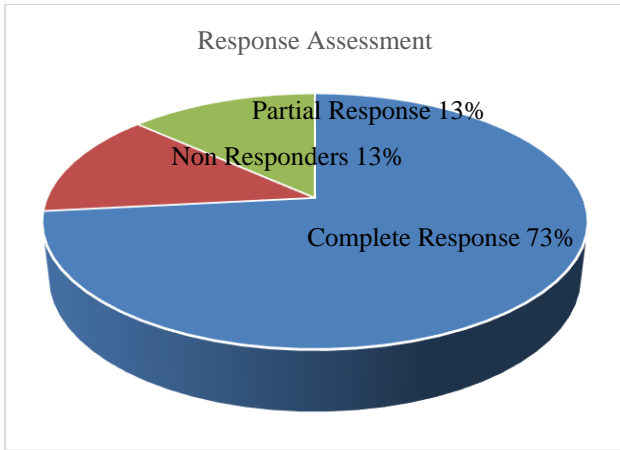


Figure 2: Response assessment.

Table 1: Outcomes of hospital days.

Median outcomes in hospital days	Number	p value
Chest tube duration	4-11	0.200
Hospital length of stay	9-19	0.355
Referral for surgery	2/15 (13)	0.121
<b>Complications</b>		
Re-admission	13 (87)	0.741
Bleeding	1 (6)	0.043
Tube dislocation	0	-

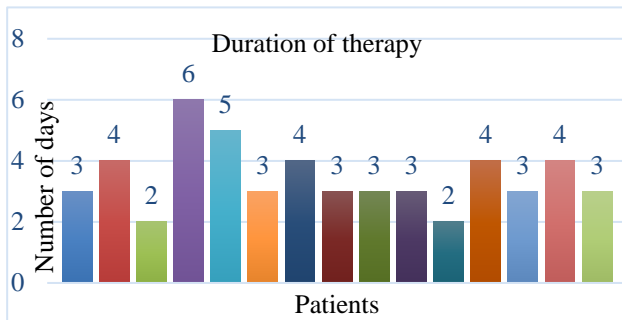


Figure 3: Drug therapy.

The total number of SK instillations ranged from 3 to 6 (mean 3.4).

All patients were subjected to complete blood count, plain chest X-ray and computed tomography scan of the chest. Haematological studies including haemoglobin, platelet count, Prothrombin time (PT), International normalized ratio (INR), and Activated partial thromboplastin time (APTT) were taken before every dose of SK instillation.

Complete response, represented by relief of symptoms and complete resolution of radiological findings, occurred in 11 patients (73%). Partial response, represented by relief of symptoms and partial resolution on radiological examination, occurred in 2 patients (13%). Two patients were non-responders (13%) as they needed VATS and

decortication. The mean duration of thrombolytic treatment was 7 days (3 to 8).

The overall intrapleural SK effectiveness in achieving complete drainage of pleural collections was 13 of 15 cases (86%). Of 13 patients with successful outcome, 3 patients (23%) had residual mild pleural opacities (<10% of haemothorax) and accepted as successively treated cases.

There were no serious complications related to intrapleural SK treatment.

**DISCUSSION**

The results of this multi-centric study suggest that intrapleural fibrinolysis is useful in the treatment of persistent, loculated haemothorax. A significant increase in the drainage of chest tube with clot lysis with improvement from the clinical, and radiologic parameters suggests that intra-pleural streptokinase is an effective alternative of surgical decortication in a significant number of patients.

Haemothorax frequently occurs after a chest trauma leading to a clotting of the intrapleural blood followed by a thin layer of fibrin and cellular elements coating the pleural surface. This covering develops into a progressively thicker membrane on the visceral and parietal surfaces and forms a sac like structure containing the haemothorax.<sup>13,14</sup> There is a general agreement that early treatment of patients with traumatic haemothorax includes chest tube drainage.<sup>14,15</sup> Computed tomography (CT) scan has been used for evaluation of trauma to the thorax for three decades. More detailed findings are attained with CT scan than with plain X-ray or physical examination.

The reported complication rates of VATS in large series are around 10%.<sup>16</sup> The most common complications of VATS are transient hypoxaemia or reversible arrhythmia. Surgical complications such as chest wall bleeding or iatrogenic lung injury have also been reported. Insertion or levering on the trocars can result in intercostal neuritis. However, intrapleural fibrinolysis therapy is also not immune to complications. Although, the use of intra pleural fibrinolysis generally causes no systemic coagulation effects there is a report of a single case of a major haemorrhage following intrapleural SK instillation, attributed to systemic absorption of the agent.<sup>17-19</sup> Other systemic side effects with intrapleural SK are arthralgia, nausea, malaise, headache, fever and pleural pain.<sup>19,20</sup>

Anaphylaxis and acute hypoxemic respiratory failure, although very uncommon, have also been reported.<sup>14,15</sup> Hypoxaemia most likely results from a direct effect of the products of fibrinolysis on the pulmonary circulation. In addition, streptokinase may be associated with allergic reactions, although these are uncommonly seen nowadays, due to the availability of purified forms of SK.

Our study shows a significant difference in the total amount of drainage in the chest pre and post SK injection for treating of clotted haemothorax. The clotted haemothorax should be eliminated within a week after injury to avoid the complication of fibrothorax and empyema. Many published studies advise fibrinolytic therapy or VATS can be performed in assessment and treatment of clotted haemothorax with good prognosis.<sup>7,8,9,14</sup> The presented study showed a significant decrease in clotted haemothorax among most patients after the period of treatment with SK injection. Therefore, intrapleural SK is applied in the treatment of haemothorax and empyema.<sup>8,15</sup>

### Limitations

Study has following limitations: SK was the only fibrinolytic used as it was readily available and cost effective while newer fibrinolytics are available lack of comparison among several streptokinase dose regimens, long term follow up with respiratory function tests needs to be done before replacing an excellent and time tested surgical option and small set of patients with varying comorbidities participated in this study.

### CONCLUSION

In conclusion, intrapleural administration of SK has the ability for liquify clots of traumatic haemothorax due to its fibrinolytic action and subsequently prevented of fibrinous adhesion of the pleural layers. So, SK should be considered an excellent alternative to more invasive procedures for patients with mild to moderate clotted haemothorax. Intrapleural fibrinolysis should be added to the algorithm for management of clotted haemothorax before proceeding to VATS, mini-thoracotomy or thoracotomy as seen in similar studies. Finally, the cost of intrapleural thrombolysis was less than half that of VATS.

*Funding: No funding sources*

*Conflict of interest: None declared*

*Ethical approval: The study was approved by the Institutional Ethics Committee*

### REFERENCES

1. Navneet S, Damian G, Zubayr Z, Fracs R, Fracs CP. A novel treatment option in the management of traumatic haemothorax. *Journal of Trauma and Acute Care Surgery*. 2019;86(2):374-5.
2. Stiles PJ, Drake RM, Helmer SD, Bjordahl PM, Haan JM. Evaluation of chest tube administration of tissue plasminogen activator to treat retained haemothorax. *Am J Surg*. 2014;207:960-3.
3. Meyer DM, Jessen ME, Wait MA, Estrera AS. Early evacuation of traumatic retained hemothoraces using thoracoscopy: a prospective, randomized trial. *Ann Thorac Surg*. 1997;64:1396-400.
4. Ahmed N, Jones D. Video-assisted thoracic surgery: state of the art in trauma care. *Injury*. 2004;35:479-89.
5. Oguzkaya F, Akcali Y, Bilgin M. Video thoracoscopy versus intrapleural streptokinase for management of post traumatic retained haemothorax: a retrospective study of 65 cases. *Injury*. 2005; 36:526-9.
6. Navsaria PH, Vogel RJ, Nicol AJ. Thoracoscopic evacuation of retained posttraumatic haemothorax. *Ann Thorac Surg*. 2004;78:282-5.
7. Joseph D, Kenji I, Demetrios D, Thomas SM, James C, Jay M et al. AAST Retained Hemothorax Study Group Management of post-traumatic retained haemothorax: A prospective, observational, multicentre AAST study, *The Journal of Trauma and Acute Care Surgery*. 2012;72(1):316-7
8. Marder VJ, Sherry. Thrombolytic therapy - current status. *N Engl J Med*. 1988;318:1512-20.
9. Thomas TR, Follis F, Kessler RM, Pea SS, Wenly JA. Intrapleural fibrinolysis. *Chest*. 1996;110:102-6.
10. Aye RW, Froese DP, Hill LD. Use of purified streptokinase in empyema and haemothorax. *Amer J Surg*. 1991;161:560-2.
11. Bergh NP, Ekroth R, Larsson S. Intrapleural streptokinase in the treatment of hemothorax and empyema. *Scand J Thor Cardiovasc Surg*. 1977;11:265-8.
12. Stiles PJ, Drake RM, Helmer SD, Bjordahl PM, Haan JM. Evaluation of chest tube administration of tissue plasminogen activator to treat retained hemothorax. *Am J Surg*. 2014;207:960-3.
13. Oguzkaya F, Akçali Y, Bilgin M. Videothoracoscopy versus intrapleural streptokinase for management of post traumatic retained haemothorax: A retrospective study of 65 cases. *Injury*. 2005;36:526-9.
14. Goehring WO, Grant JJ. Allergic reaction to streptokinase streptodornase solution given intrapleurally. *JAMA*. 1953; 152: 1429-30.
15. Cangir AK, Yuksel C, Dakak M. Use of intrapleural streptokinase in experimental minimal clotted hemothorax. *Eur J Cardiothorac Surg*. 2005;27:667-70.
16. Rahman NM, Maskell NA, West A. Intrapleural use of tissue plasminogen activator and DNase in pleural infection. *N Engl J Med*. 2011;365(6):518-526.
17. Krasna MJ, Deshmukh S, McLaughlin JS. Complications of thoracoscopy. *Ann Thorac Surg*. 1996;61:1066-9.
18. Berglin E, Ekroth R, Teger-Nilsson AC, William-Olsson G. Intrapleural instillation of streptokinase. Effects on systemic fibrinolysis. *Thorac Cardiovasc Surg*. 1981;29:124-6.
19. Davies CW, Lok S, Davies RJ. The systemic fibrinolytic activity of intrapleural streptokinase. *Am J Respir Crit Care Med*. 1998;157:328-30.
20. Rosen H, Nadkarni V, Theroux M, Padman R, Klein J. Intrapleural streptokinase as adjunctive treatment for persistent empyema in paediatric patients. *Chest*. 1993;103:1190-3.

21. Geha AS. Pleural empyema. Changing etiologic, bacteriologic, and therapeutic aspects. *J Thorac Cardiovasc Surg.* 1971;61:626-35.

**Cite this article as:** Varma A, Narain R, Deshmukh P, Rathore H, Datta SGS, Varma AV. Role of streptokinase in management of retained hemothorax: a multicentric study. *Int Surg J* 2020;7:3661-5.