Clinical Science

Evaluation of chest tube administration of tissue plasminogen activator to treat retained hemothorax

P. J. Stiles, M.D.a, Rachel M. Drake, M.Ed.a, Stephen D. Helmer, Ph.D.a,b, Paul M. Bjordahl, M.D.a, James M. Haan, M.D.a,c,*

aDepartment of Surgery, The University of Kansas School of Medicine–Wichita, 929 North Saint Francis Street, Room 3082, Wichita, KS 67214, USA; bDepartment of Medical Education, Room 3082, cDepartment of Trauma Services, Room 2514, Via Christi Hospital on Saint Francis, 929 North Saint Francis Street, Wichita, KS 67214, USA

KEYWORDS:
Trauma; Retained hemothorax; Intrapleural; Fibrinolysis; Tissue plasminogen activator

Abstract

BACKGROUND: When retained hemothorax occurs, video-assisted thoracoscopic thoracotomy is performed, but recently, tissue plasminogen activator (tPA) has been used. This study evaluated intrapleural tPA use for retained traumatic hemothoraces.

METHODS: A retrospective review was conducted of trauma patients treated with intrapleural tPA for retained hemothorax. Data included demographics, past medical and surgical histories, injury details, treatment details, and outcomes.

RESULTS: Seven patients (median age = 47 years, male = 6, blunt trauma = 6) met study criteria. All patients received a chest tube. Six patients later received computed tomography-guided drains for tPA infusion. Number of tPA treatments per patient varied from 1 to 5. Median total tPA dosage was 24 mg. Median time from injury to chest tube placement was 11 days and from chest tube placement to first tPA treatment was 4 days. No patients required a video-assisted thoracoscopy; however, 1 patient required thoracotomy. There were no deaths or bleeding complications attributed to intrapleural tPA.

CONCLUSION: Although future studies are needed to identify optimum treatment guidelines, intrapleural tPA appears to be a safe and efficacious treatment option.

The true incidence of retained hemothoraces is unknown, but the literature reports rates ranging from 5% to 30%.1,3 The presence of retained hemothorax after chest tube placement is a known risk factor for 2 serious complications: fibrothorax/trapped lung and empyema.3

Retained hemothorax is a problem in trauma patient care and there is debate regarding the best practice for treatment.4 Historically, treatment involved thoracotomy to drain the residual blood and today this remains the gold standard against which other treatments are measured. Recently, video-assisted tube thoracoscopic (VATS) has proven to be safe, effective, and less invasive than thoracotomy for treatment.

Hemothorax because of chest trauma is a common surgical emergency and occurs in 38% of patients sustaining chest trauma.1 Simple tube thoracostomy is effective in draining most hemothoraces.2 Occasionally, undrained blood remains after chest tube placement resulting in retained hemothorax.3

The authors declare no conflicts of interest.


* Corresponding author. Tel.: +1-316-268-5538; fax: +1-316-291-7892.
E-mail address: James.Haan.Research@viachristi.org

Manuscript received July 19, 2013; revised manuscript August 2, 2013

0002-9610/$ - see front matter © 2014 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.amjsurg.2013.08.052

of retained hemothoraces. VATS is currently the most common treatment used, although optimal timing of the procedure is still debated. Other treatments include observation only, another tube thoracostomy, or image-guided catheter drain placement. The newest treatment option is use of intrapleural fibrinolysis.

Intrapleural fibrinolysis is accomplished by placing tissue plasminogen activator (tPA) through either a chest tube or an image-guided catheter drain. tPA functions to liquefy the clotted hemothorax to induce drainage. This approach is less invasive than either VATS or thoracotomy. However, there exists limited data on the safety and efficacy of this treatment. The purpose of this study was to evaluate efficacy of intrapleural tPA use in the treatment of retained traumatic hemothoraces.

**Patients and Methods**

A retrospective review was conducted of all patients treated with intrapleural tPA for retained hemothorax at an American College of Surgeons verified level 1 trauma center between March 1, 2009 and August 31, 2011. Patients were identified and data were retrieved from the trauma registry, as well as from patient medical records. Patient data included age, sex, medical comorbidities, history of lung disease, prior chest operations, and anti-coagulation medications. Injury data included mechanism of injury, injury severity, presence of hemothorax, all other injuries sustained, international normalized ratio, and partial thromboplastin time. Treatment regimens including all chest tubes placed, time frame in which they were placed, dose of tPA, and number of doses given were collected. Outcome measures included length of time chest tube was required, need for a VATS or thoracotomy, hospital length of stay, bleeding complications, and mortality.

Bleeding complications were defined as a decrease in hemoglobin of 4 g/dL, new onset intracranial hemorrhage, an increase in the hemothorax volume radiographically, or any other visualization bleeding post-treatment. The protocol for tPA treatments was the same for all patients. The patient was placed on their side with the affected side up. Every 10 min the patient was switched laterally for 30 total minutes.

This study was approved for implementation by the Institutional Review Board of Via Christi Hospitals Wichita, Inc. Data were summarized using SPSS Version 19.0 (IBM Corp, Somers, NY).

**Results**

Seven patients were identified with retained hemothorax that was treated with tPA. Six were male and median age was 47 years (Table 1). At baseline, 2 patients had diabetes, 2 had hypertension, 1 had coronary disease, 1 had liver disease (hepatitis), and 1 had renal disease. Only 1 patient had both prior thoracic surgery and underlying pulmonary disease (sarcoidosis). The most common comorbidity was smoking (n = 4). Six patients sustained blunt trauma and 1 penetrating trauma. The most common injury was rib fracture (n = 5). Only 1 patient had coagulopathy as evidenced by an international normalized ratio of 6.1. All patients received a 36- or 40-French chest tube. All patients had traumatic hemothoraces with serosanguinous chest tube output. Initial chest tube output ranged from 55 to 1,400 mL (mean ± standard deviation = 599.3 ± 538 mL). Six patients later had computed tomography (CT)-guided drains (12- to 14-French chest tube) placed by radiology through which the tPA was administered.

Number of tPA treatments varied from 1 to 5 total treatments per patient and the median total tPA dosage given was 24 mg (Table 2). Median time from injury to chest tube placement was 11 days (range 0 to 21) and from chest tube placement to first treatment was 4 days (range 0 to 12). Median length of time patient's required a chest tube was 13 days. No patients required a VATS. One patient required a thoracotomy, but this patient was later found to have pulmonary myeloid sarcoma which contributed to her retained hemothorax. No patients had bleeding complications attributed to intrapleural tPA. Median hospital length of stay was 14 days (range 5 to 23). The patient with pulmonary myeloid sarcoma died of causes unrelated to the tPA treatment, resulting in an all-cause mortality rate of 14%.

Three patients presented immediately after their trauma and were found to have retained hemothorax early in their hospital course. One of the patients who presented immediately after the trauma was a 15-year-old male who fell from a tree stand. He was found to have a T7 burst fracture with bilateral lower extremity neurologic deficits and posterior rib fractures. Initially, CT of the chest did not show evidence of a hemothorax. On hospital day 2, he underwent repair of his spinal fractures utilizing an anterior approach and was found to have a large hemothorax prompting placement of a 36-French chest tube. He subsequently developed a retained hemothorax. An image-guided catheter was placed on hospital day 12 and he received 2 doses of 8 mg of tPA. His hemothorax resolved over the next 5 days.

Four out of the 7 patients presented in a delayed fashion >10 days from their trauma. The mechanisms included a single fall, a moped accident, an assault, and an all-terrain vehicle accident. In the delayed presentation group, all patients received 40-French chest tubes immediately upon presentation. All 4 patients demonstrated retained hemothoraces as seen on chest X-ray over the next 1 to 3 days. Each subsequently received early image-guided catheters and were treated with tPA within 1 day of their image-guided catheter placements. All 4 had clinical resolution of their hemothoraces and were discharged home between hospital days 5 and 14. None were readmitted or suffered sequelae related to their hemothoraces.

One patient in this group was an 89-year-old woman with a prior history of a thoracotomy and sarcoidosis who had crashed her all-terrain vehicle into a tree 3 weeks before her presentation. She presented with respiratory distress. Chest X-ray on admission revealed a large hemothorax and...
multiple rib fractures. She had minimal drainage when a 40-French chest tube was placed. This chest tube was then followed by placement of an image-guided catheter on the same day. Three days later she was given 2 doses of 12 mg of tPA. She improved clinically and was discharged home on hospital day 5. She represented to the emergency department tPA-related bleeding complications. Jerges-Sanchez et al13 studied 23 patients with retained traumatic hemothorax who were treated with intrapleural tPA and reported that only 1 patient required decortication (4%). In a study by Inci et al14 of 24 trauma patients with retained hemothorax, 15 (63%) had complete response, 7 (29%) had partial response, and 2 (8%) required decortications. Moreover, Kembrell et al16 treated 25 trauma patients with intrapleural tPA and reported that 23 had clinical resolution, with no need for additional therapy and absence of bleeding complications. As with prior studies, our study provides evidence that intrapleural fibrinolysis should be added to the treatment algorithm for retained traumatic hemothoraces. However, it should be noted that none of the previously mentioned studies evaluated optimal treatment regimens, including dosing and frequency of administration. Our study included the use of a wide range of doses and frequencies, yet we had good resolution of clotted blood without any hemorrhagic complications.

Unfortunately, there is no consensus regarding where and how intrapleural fibrinolysis fits into a treatment algorithm, and not all studies agree that intrapleural fibrinolysis fits well into the treatment algorithm for clotted hemothoraces. Oguzkaya et al17 compared VATS with intrapleural fibrinolysis for managing post-traumatic retained hemothorax. They found VATS to be superior to intrapleural fibrinolysis, reporting less need for open surgery, shorter hospitalization stays, and a lower rate of empyema. A recent multicenter American Association for the Surgery of Trauma study also addressed this question. They evaluated 328 patients, comparing 6 different initial treatments including thoracotomy, VATS, second chest tube, thrombolytics, image-guided drain placement, and observation alone.7 Among the 328 patients in the study, 15 received thrombolytics and 10 of the 15 required a second intervention after thrombolytics. Seven of these 10 patients received an image-guided percutaneous drain, while the remaining 3 patients required VATS. They concluded that VATS should be the initial treatment of choice if CT evaluation

Table 1  Summary of patient demographics, comorbidities, mechanism of injury, and injury characteristics

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>7</td>
</tr>
<tr>
<td>Age (y)*</td>
<td>53.3 ± 23.7/47 (43, 74)</td>
</tr>
<tr>
<td>Male</td>
<td>6 (86%)</td>
</tr>
<tr>
<td>Preinjury anticoagulation (aspirin)</td>
<td>1 (14%)</td>
</tr>
<tr>
<td>History of lung disease (sarcoidosis)</td>
<td>1 (14%)</td>
</tr>
<tr>
<td>Blunt injury</td>
<td>6 (86%)</td>
</tr>
<tr>
<td>Rib fracture</td>
<td>5 (71%)</td>
</tr>
<tr>
<td>Coagulopathy (elevated INR)</td>
<td>1 (14%)</td>
</tr>
<tr>
<td>Chest tube placed</td>
<td>7 (100%)</td>
</tr>
<tr>
<td>Traumatic hemothorax with serosanguine chest tube output</td>
<td>7 (100%)</td>
</tr>
<tr>
<td>Radiologic-guided catheter drain</td>
<td>6 (86%)</td>
</tr>
</tbody>
</table>

INR = international normalized ratio.
*Data are represented as mean ± standard deviation/median (25th and 75th percentiles).

Table 2  Summary of patient tissue-plasminogen activator dose and treatment, chest tube requirements, need for video-assisted thoracic surgery or thoracostomy, bleeding complications, and hospital length of stay

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of tPA treatments</td>
<td>2.4 ± 1.3/2 (2, 3)</td>
</tr>
<tr>
<td>tPA dose (mg)</td>
<td>62.4 ± 105.6/24 (14, 50)</td>
</tr>
<tr>
<td>Interval from injury to chest tube placement (d)</td>
<td>9.6 ± 9.3/11 (0, 20)</td>
</tr>
<tr>
<td>Interval from chest tube placement to tPA treatment (d)</td>
<td>5.9 ± 4.7/4 (3, 12)</td>
</tr>
<tr>
<td>Chest tube requirement (d)</td>
<td>12.4 ± 6.6/13 (7, 17)</td>
</tr>
<tr>
<td>Need for VATS</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Need for thoracostomy (myeloid sarcoma)</td>
<td>1 (14%)</td>
</tr>
<tr>
<td>tPA-related bleeding complications</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Hospital length of stay</td>
<td>13.6 ± 6.8/14 (7, 20)</td>
</tr>
</tbody>
</table>

Data are represented as mean ± standard deviation/median (25th and 75th percentiles) or number (percent).
*Data are represented as mean ± standard deviation/median (25th and 75th percentiles).
**Data are represented as mean ± standard deviation/median (25th and 75th percentiles) or number (percent).

Comments

Our study demonstrates that intrapleural tPA is both safe and effective. Intrapleural fibrinolysis has been shown to be effective in studies among nontrauma patients for the treatment of various complex pleural processes such as empyema, loculated pleural effusions, parapneumonic effusions, and hemothoraces.9–12 However, the literature in trauma patients is limited to small retrospective studies and case series.13–16 As with our study, these prior studies all documented excellent outcomes with no hemorrhagic complications. Jerges-Sanchez et al13 studied 23 patients with retained traumatic hemothorax who were treated with intrapleural tPA and reported that only 1 patient required decortication (4%). In a study by Inci et al14 of 24 trauma patients with retained hemothorax, 15 (63%) had complete response, 7 (29%) had partial response, and 2 (8%) required decortications. Moreover, Kembrell et al16 treated 25 trauma patients with intrapleural tPA and reported that 23 had clinical resolution, with no need for additional therapy and absence of bleeding complications. As with prior studies, our study provides evidence that intrapleural fibrinolysis should be added to the treatment algorithm for retained traumatic hemothoraces. However, it should be noted that none of the previously mentioned studies evaluated optimal treatment regimens, including dosing and frequency of administration. Our study included the use of a wide range of doses and frequencies, yet we had good resolution of clotted blood without any hemorrhagic complications.

Unfortunately, there is no consensus regarding where and how intrapleural fibrinolysis fits into a treatment algorithm, and not all studies agree that intrapleural fibrinolysis fits well into the treatment algorithm for clotted hemothoraces. Oguzkaya et al17 compared VATS with intrapleural fibrinolysis for managing post-traumatic retained hemothorax. They found VATS to be superior to intrapleural fibrinolysis, reporting less need for open surgery, shorter hospitalization stays, and a lower rate of empyema. A recent multicenter American Association for the Surgery of Trauma study also addressed this question. They evaluated 328 patients, comparing 6 different initial treatments including thoracotomy, VATS, second chest tube, thrombolytics, image-guided drain placement, and observation alone.7 Among the 328 patients in the study, 15 received thrombolytics and 10 of the 15 required a second intervention after thrombolytics. Seven of these 10 patients received an image-guided percutaneous drain, while the remaining 3 patients required VATS. They concluded that VATS should be the initial treatment of choice if CT evaluation...
determined that there was >300 mL of retained hemothorax. They recommend thoracotomy if there is concern for a diaphragm injury or if CT estimates indicate >900 cc of retained blood. Finally, observation alone is appropriate if CT estimates volumes <300 mL in selected patients. They did not include intrapleural tPA in their algorithm.

Our results identified a niche for intrapleural fibrinolysis in the management of retained post-traumatic hemothorax. We recommend using intrapleural fibrinolysis for patients with a delayed presentation. The literature recommends evacuating clotted blood before 7 to 10 days; however, after 7 to 10 days there is an increased risk of developing fibrothorax and empyema. Four of our study population presented in a delayed manner, and 3 out of 4 had clinical resolution of their hemothorax, while the 4th patient’s course was complicated by pre-existing pulmonary myeloid sarcoma. Additionally, we recommend using intrapleural fibrinolysis in patients with significant medical comorbidities such as older patients, or in those with multiple other severe injuries. These patients may not tolerate a thoracotomy or VATS and also may have less physiologic reserve with which to tolerate a complication such as empyema or fibrothorax.

Conclusions

In conclusion, intrapleural tPA is both safe and effective and should be included in the physicians’ armamentarium for treating traumatic retained hemothoraces. We recommend using intrapleural tPA in patients who present late, or in patients with low physiologic reserves and who would have difficulty tolerating a thoracic operation. In the future, more prospective studies looking at optimal treatment regimens and optimal patient selection are warranted.

References