Tissue plasminogen activator in the treatment of empyema in children

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Introduction: Complex empyema or complicated parapneumonic effusions may develop in up to 1/3 of patients with parapneumonic effusions. Treatment options include instillation of fibrinolytic agents or surgical approaches such as thoracoscopy, thoracotomy, and video assisted thoracic surgery. As fibrinous debris is deposited on the pleural surface creating loculations that prevent tube drainage of the fluid, there is a theoretical rational for the use of fibrinolytic agents to lyse these adhesions and allow for effective clearance of the loculations. Of the available fibrinolytic agents, the use of streptokinase in children is limited because of the potential for allergic phenomena and the period of unavailability of urokinase has led to a decrease in its use. Therefore, the most appealing agent in children appears to be tissue plasminogen activator (TPA). To date, there are limited reports evaluating the efficacy of TPA in aiding in the resolution of empyema. We retrospectively review our experience with the use of TPA in Pediatric ICU patients with empyema.

Methods: This retrospective chart review was approved by the hospital's IRB. The pharmacy records were reviewed and patients identified who had received TPA for the treatment of empyema. Demographic data included age, weight, and gender. Information regarding the pleural effusions from the initial drainage procedure (thoracentesis or catheter placement) included cell count, protein, glucose, culture, and volume collected. Pleural fluid was drained by either a chest tube or an 8.5 French pigtail catheter (Cook Catheter, Bloomington, Indiana). TPA (2-5mg) was reconstituted in saline (5mL/kg). The solution was then infused through a stopcock on the pigtail catheters or via a catheter tip syringe through the chest tubes. The solution was left in the pleural space for 4-6 hours. During this period, the patient was repositioned every 30 minutes in 4 different positions: Trendelenburg, reverse Trendelenburg, left lateral decubitus, and right lateral decubitus. The treatment was repeated every 12-24 hours until either the chest x-ray demonstrated disappearance of the effusion or the therapy was no longer beneficial (volume of fluid out equaled the volume of the fluid in). The chest tube was removed when there was less than 10-20 mL of drainage in 24 hours. Adverse effects during therapy were noted. The volumes of fluid that drained before and after TPA were compared by a paired, two-tailed t-test.

Results: A total of 25 doses of TPA (3-5 per patient) were administered to 6 patients ranging in age from 2 to 13 years. A bacterial etiology was identified in 2 of the six cases as *Streptococcus pneumoniae* while no etiology was identified in the other 4 patients. Reasons for initiating TPA included persistent fever, decreasing chest tube output, and residual fluid after placing drainage systems. For the 6 hours before TPA, there was a total of 22.5 mL ± 18.4 mL of chest tube drainage which increased to 141.7 mL ± 28.3 mL ($p<0.0001$) after TPA. After TPA, 5 of the 6 patients became afebrile within 48 hours. Patient #6 had a more complicated course of therapy, requiring additional chest tubes to be placed. This patient presented to our hospital after a 2-3 week course of illness and may have already advanced to phase 3 (formation of an organized pleural peel). This patient's length of stay was longer than the other patients; however, after placement of additional chest tubes, thrombolytic therapy was sufficient and surgical intervention was not necessary. Three of the six patients receiving TPA therapy demonstrated a change in the color of the pleural drainage after initiation of TPA. The pleural fluid was not grossly bloody, but rather tinged with blood. This may have resulted from bleeding from the initial insertion site of the catheter or alternatively from the inflamed pleural surface. These patients' hematocrits were followed and no change was noted. One patient developed a low serum albumin (1.2 gm/dL) with edema and ascites. This patient was 2 years old and weighed 11.6 kg. The loss of albumin was likely from the large amount of pleural fluid drained rather than a direct effect of TPA therapy. No other adverse effects were observed.

Conclusion: We found that TPA was successful in the treatment of complex empyema in 5 of 6 patients and may have benefited the sixth patient. TPA therapy increased pleural fluid output by a factor of 6-7. An additional benefit of TPA may be the ability to drain complicated pleural effusions through a smaller drainage catheter. Five of the 6 patients in the current series were effectively drained using an 8.5 French drainage catheter that can be placed using the Seldinger technique. A prospective clinical trial comparing TPA therapy to other thrombolytic agents &/or surgical approaches would be worthwhile as well as trials comparing different doses of TPA.