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The role of tissue plasminogen activator in the management of complex intra-abdominal abscesses in children

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Abstract

Objective: The objective of this study is to assess the safety of fibrinolytic therapy using tissue plasminogen activator (tPA) in children with complex intra-abdominal abscesses.

Summary Background Data: Intra-abdominal abscesses are common in children. Antibiotics and percutaneous drainage are the mainstays of treatment, but drainage may be less effective when the fluid is thick or septated. Fibrinolytic therapy using tPA is effective in a rat model of intra-abdominal abscesses, has recently been reported for the treatment of intra-abdominal abscesses in adults, and is commonly used in the treatment of empyema in children.

Methods: This is a retrospective review of all patients over a 10-year period who had intra-abdominal collections managed with tPA abscess drainage.

Results: Sixty-four children had a total of 66 drains placed and 92 doses of tPA. Appendicitis was the cause of the abscesses in 52 of 64 children. Mean length of stay pre-tPA was 11.7 ± 7.63 days, mean time from drain insertion to tPA was 4.3 ± 3.78 days, and mean time from tPA to discharge was 8.6 ± 8.85 days. Thirty patients underwent an operation before tPA administration. No patients experienced bleeding complications, anastomotic or appendiceal stump leak, or wound dehiscence after the administration of tPA, and no patients had abnormalities in coagulation studies related to tPA administration. One child died of sepsis.

Conclusions: Tissue plasminogen activator is safe for the management of thick or septated intra-abdominal abscesses in children. A prospective controlled study will be needed to evaluate the efficacy of this technique.

Intra-abdominal abscesses occur frequently in pediatric patients. Although most are associated with appendicitis, several other inflammatory or mechanical causes exist [1-3].

Although some intra-abdominal abscesses in children can be effectively managed with antibiotics alone, most are now treated with percutaneous drainage using image-guided techniques [4-6]. However, these drains may be ineffective if the abscesses are complex or the purulent fluid within the abscesses is very thick.

Fibrinolytic therapy was first described as an intravenous treatment for ischemic stroke, pulmonary embolism, and

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catheter thrombosis [7,8]. However, many authors have now described the use of fibrinolytic agents for the treatment of extravascular conditions such as empyema, purulent pericarditis, and peritoneal catheter-related peritonitis [9-13]. Although most of this experience has been in adults, multiple studies have now documented their use in children [14-18]. Tissue-type plasminogen activator (tPA) cleaves plasminogen into active plasmin through fibrin-specific mechanisms and thus can prove beneficial in the dissolution of fibrinous deposits as part of an abscess [19-23].

There are, however, some risks to fibrinolytic therapy with streptokinase and urokinase, such as hypotension, hypersensitivity reactions, apnea, and bleeding [24,25]. In children, treatment with streptokinase is occasionally associated with an allergic reaction especially in patients exposed to a recent streptococcal infection [26]. Tissue-type plasminogen activator has a lower complication rate than streptokinase and urokinase and has become the predominant fibrinolytic agent in clinic use in recent years.

Based on the success achieved using tPA for the management of empyema at our center and other centers, we began using this technique for the management of complex intra-abdominal abscesses in children [16]. The purpose of this study was to evaluate the safety of this technique in a larger group of children.

1. Methods

1.1. Patient selection and technique of tPA use

The diagnosis of intra-abdominal abscess was suspected clinically and confirmed by radiologic studies, either computed tomography or ultrasound. An abscess was diagnosed when a hypoechoic or heterogeneous well-defined collection was seen on ultrasound or when a well-defined hypodense walled off collection was seen on computed tomography. Drain insertion, after informed consent was obtained, was carried out by our interventional radiologists [4].

The decision to use tPA was made on a case-by-case basis, after collaborative discussion between the attending surgeon (n = 8) and interventional radiologist (n = 5), and was based on failure of the abscess to resolve with routine drain management (ie, flushes with saline and gravity drainage). There was heterogeneity in approaches by the individual surgeons and radiologists, and the decision to treat with tPA was also individualized according to the patient's clinical status and course of disease. Parents were informed about the potential risks of tPA, based on our previous experience in children with empyema. Tissue-type plasminogen activator was instilled if the catheter was in a satisfactory position, but there was minimal drainage despite documented residual collection on imaging or if the collection appeared viscous or complex in nature and therefore unlikely to spontaneously drain. The requirement of satisfactory catheter position was to ensure that inadequate drainage was not simply because of a suboptimally positioned catheter or because of an undrained second abscess [27]. Subsequent abscesses found on imaging were treated with additional drainage catheters and not simply tPA. Tissue-type plasminogen activator was diluted in 8 to 10 mL of 0.9% saline, instilled into the drainage catheter, and capped for 1 hour before returning to gravity drainage. The patient was encouraged to move about to assist with distribution of the tPA within the cavity. If there were multiple catheters, then the tPA dose was divided among them. In some patients, tPA was given on several occasions to achieve complete drainage of the abscess cavity despite adequate positioning of the drainage catheter. Both the surgical service and the interventional radiologists were responsible for tPA administration. Patients were monitored closely post-tPA administration for hemodynamic instability, increasing abdominal pain, bleeding, and coagulation parameters (PTT and international normalized ratio).

Regular 8-hourly flushing with 5 mL of sterile saline solution was performed to ensure drain patency. Patients with drains were followed up clinically, and the drains were removed when drainage was considered minimal, approximately less than 10 mL/d of serosanginous fluid.

Patients were treated with appropriate intravenous antibiotic therapy in hospital while the drain was in situ. Children who were on full oral feeding and otherwise stable for discharge but required ongoing antibiotic therapy were switched to oral antibiotics or discharged with a peripherally inserted central catheter line and home administration of intravenous antibiotics.

1.2. Patient population

A retrospective review was carried out of inpatient surgical and image-guided therapy records, to identify those children who underwent insertion of a drain for abdominal abscesses and subsequent instilment of tPA between January 2000 and January 2010. This included patients with multiple drains and those with multiple doses of tPA.

Patients would not have been considered for tPA if they had pancreatic abscess that were not bacterial in nature, coagulation impairment, known central nervous system tumor or abscesses, arteriovenous malformation, aneurysm or history of central nervous system bleeding, hypersensitivity to tPA, recent administration of an investigational drug, pregnancy, breast-feeding, or fulminant hepatic failure. These criteria were chosen because they are the accepted standard exclusion criteria for the vascular use of tPA. It was our belief that similar standards should be used for intracavitary use of tPA [28].

Demographic information was collected including age and weight at drain insertion and comorbidities (please refer to Table 1). Data on length of stay, length of time with drain, tPA administration, complications, and contraindications