Efficacy of Chest Drain and Fibrinolytic Therapy for Paediatric Empyema: A Single-Centre Retrospective Review

Ahmed Hassan [a-b*], Nick Lansdale [a-c], Robert Peters[a], Maher El Dessouky[b], Ahmed Khairi[b], Mohamed Shamseldin[b], David Wilkinson[a-c]

[a] Department of Paediatric Surgery, Royal Manchester Children Hospital, Manchester, United Kingdom.

[b] Department of Paediatric Surgery, Faculty of Medicine, Alexandria University, Alexandria, Egypt.

[c] Department of Paediatric Surgery, Faculty of Biology Medicine and Health, Manchester University, Manchester, United Kingdom.

Abstract

Background: Managing paediatric empyema sparks controversy in the literature, with the debate centered on chest drain with fibrinolytic therapy versus Video-Assisted Thoracoscopic Surgery (VATS).

Objectives: Retrospective evaluation of the management of paediatric empyema with chest drain and fibrinolytic therapy in relation to success of the intervention, total hospital stays and readmission rate.

Patients and methods: All children less than 16 years diagnosed with empyema between January 2015, and January 2020 admitted to our centre and received primary intervention in the form of chest drain with fibrinolytic therapy were identified from the hospital database. patient records were retrospectively reviewed to obtain patient demographics, days of symptoms before admission, preoperative inflammatory markers (WBC and CRP), chest x-ray and chest ultrasound scan, oxygen requirement before intervention, hospital stay before intervention. Overall outcome (we defined success of the primary intervention by being curative with no need for secondary intervention), Hospital stay and readmission rate. Patients with other comorbidities, those with bleeding disorders and those who received primary intervention in their local hospital or received VATS were excluded from our study.

Results: In total 63 children underwent chest drain insertion with urokinase administration as a primary intervention for empyema during the study period with overall success rate 84.1% (53/63). The median for the total hospital stay was 12.0 (7.0-36.0) days, and the readmission rate was 4.8 % (3/63). Using smaller size chest drain was not associated with increased risk of requiring secondary intervention or prolonged hospital stay in comparison with bigger size drains.

Conclusion: Despite the ongoing debate among different paediatric surgery centres regarding the management of paediatric empyema, our study indicates that chest drain insertion with fibrinolytic therapy is a reasonable and less invasive approach with a high success rate. Further analysis is needed to identify prognostic factors that might favour primary VATS.

Keywords: Empyema; VATS; Fibrinolytics; Chest drain; Children.

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***Correspondence**: Dr.ahmed.sobhy.89@gmail.com

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Introduction

Parapneumonic effusion is an exudative pleural effusion due to the spread of an active infective or inflammatory process from the lungs. The condition usually starts with pleural inflammation and subsequent migration of fluids, proteins, and leukocytes into the pleural cavity. As the disease progresses, bacteria can migrate into the cavity, and the effusion becomes more organized, resulting in empyema. Parapneumonic effusion can complicate 2–12% of children diagnosed with pneumonia. **(Byington et al., 2002)** Parapneumonic effusion progresses through 3 phases: The exudative phase, characterized by an increase in capillary permeability, leads to simple effusion (sterile). The fibrinopurulent phase is characterized by the invasion of bacteria into the pleural space and the deposition of fibrin in the pleural space resulting in the formation of loculations. The organization phase is characterized by the formation of the pleural peel due to the growth of fibroblasts on both the visceral and parietal pleura causing impairment of lung inflation. **(Rodgers and McGahren, 2005)** Clinical presentations include fever, loss of appetite, cough, chest pain, decreased air entry and dullness to percussion, and sometimes septic shock. As with any infection, there is an increase in inflammatory markers, including white blood cells (WBCs) and C-reactive protein (CRP). A chest x-ray typically reveals obliteration of the costophrenic angle and the meniscus sign and may show a mediastinal shift and/or scoliosis and sometimes complete white out of the affected hemithorax. **(Balfour-Lynn et al., 2005)**

Ultrasound scan is usually preferred, especially in children with moderate-to-large effusions. It confirms the diagnosis and accurately detects loculations within the effusion. Also, determine the optimum spot for chest tube insertion. **(Yang et al., 1992)** CT, although not routinely used in all centres, can add value by identifying the anatomy and delineating the underlying lung pathology. **(Islam et al., 2012)**

In the early stages of effusion children usually have small effusions, and there are no manifestations of respiratory distress; they can be treated as outpatients with analgesics, antipyretics, oral antibiotics, and close follow-up. In cases of more significant effusions or respiratory distress, management will include hospital admission, analgesics, antipyretics, parenteral antibiotics, intravenous fluids as needed, and the possibility of inserting a chest drain or, in rare cases, thoracocentesis.**(Bradley et al., 2011)** As the condition progresses, the effusion may develop septations and an organization phase, necessitating more aggressive interventions such as intrapleural fibrinolytic therapy or surgical procedures (VATS up to a thoracotomy). **(Griffith et al., 2018)** The primary intervention for the advanced disease remains debatable between paediatric surgery centres and through the literature.

The aim of our study is to assess the outcome of primary chest drain with fibrinolytic therapy in terms of the need for secondary intervention, hospital stay and readmission.

Patients and methods

After obtaining the institutional approval we conducted a retrospective study on all children that were admitted to Royal Manchester Children's Hospital with the diagnosis of paediatric empyema from January 2015 till January 2020.our inclusion criteria included patients under the age of 16 years, diagnosed confirmed by chest x ray and US or CT scan confirming empyema and patients received primary intervention in the form of chest drain and fibrinolytic therapy.**(Fig 1,2,3)** We excluded all patients who received intervention (in the form of chest drain or thoracentesis) before referral, Patients with other comorbidities (malignancy, immunodeficiency, renal or cardiac problems), Patients with bleeding or coagulation disorders, patients who received VATS as a primary intervention.

Upon admission, full resuscitation was done and IV antibiotics were started (if not already started before transfer) according to the hospital policy. The hospital records were checked for each patient obtaining the following data:

Before intervention: Days of symptoms before admission, Inflammatory markers (WBC and CRP), degree of oxygen requirement (Self-ventilating in air, Non-invasive ventilation or Invasive ventilation), chest x ray, chest ultrasound scan, days of hospital stay before intervention.

After intervention: Post-intervention ICU/HDU admission, days of hospital admission after the intervention, need and type of secondary intervention and readmission in the 6 months following discharge. Chest x-ray was to be obtained in our centre and to be reported by paediatric radiology consultant. No staging system for the effusion or the mediastinal shift was used. The presence or absence of any degree of mediastinal shift was recorded. A chest ultrasound scan was done by a paediatric radiology consultant, and again, no staging system was used. Confirmation of loculation and maximum depth of the collection was to be measured and reported.

The choice of the primary intervention is usually made after agreement between the paediatric respiratory team and the paediatric surgery team. The decision is based on the clinical condition of the patient, imaging performed, the availability of resources, and active discussion with the parents. However, we included only patients with chest drain and fibrinolytic therapy.

Chest drain insertion: After adequate resuscitation of the patient and obtaining the consent. Chest drains were inserted under general anaesthesia under both ultrasound scan and fluoroscopy guidance using Seldinger's technique. wide range of chest drains sizes were used throughout the study period according to surgeon preferences. Local anaesthesia is injected and the region is prepped with drapes. A large-bore needle connected to a sterile syringe is advanced into the pleural space while aspirating on the syringe. The presence of returning fluid indicates that the position is proper which is also confirmed with fluoroscopy. On initial drainage of 20 ml/kg of fluid, the chest drain is usually clamped to minimise the risk of re-expansion pulmonary oedema. Then the chest drain can be unclamped within the next 4 hours according to the clinical condition and with close monitoring of the output.

For children 1 year of age and older, Urokinase 40,000 units in 40 ml of 0.9% saline should be administered twice daily for three days (a total of six doses); for younger children, Urokinase 10,000 units in 10 ml of 0.9% saline should be administered. The chest drain is to be clamped for 4 hours after administration of the urokinase. In our study, failure of the primary intervention is defined by the need for secondary intervention.

Hospital records were reviewed to collect the requested data, followed by a comprehensive statistical analysis of both preoperative and postoperative parameters. The mean and median values for these various parameters were then calculated and succinctly presented **(Table 1)**.

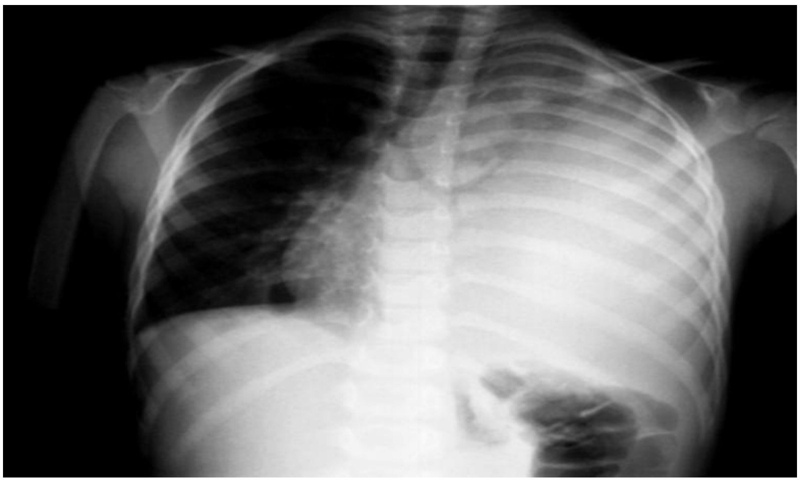

Fig 1. Chest x ray showing large left pleural effusion with whiteout of the left hemithorax & mediastinal shift to the right.

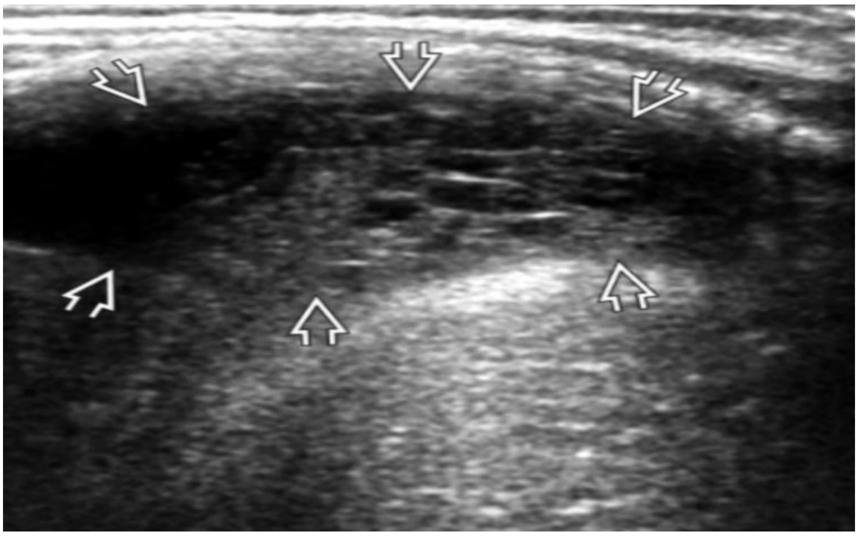

Fig 2. Chest ultrasound view of a 7 years old child showing pleural effusion containing echogenic debris and multiple loculations (white arrows).

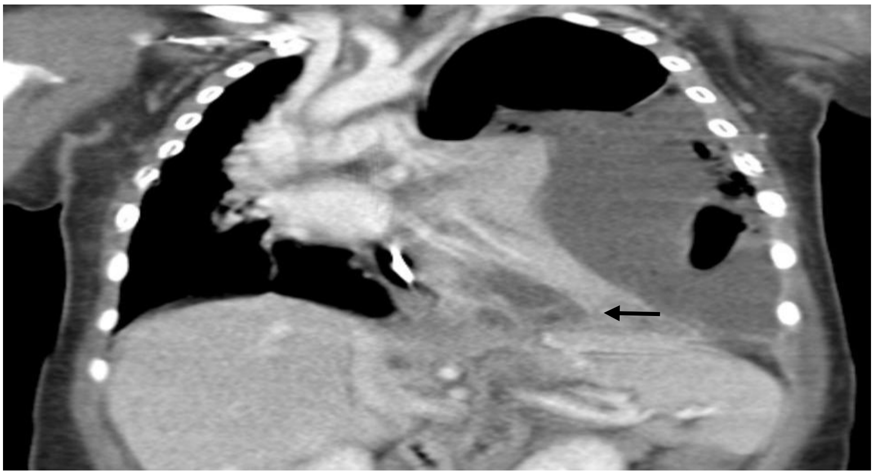

Fig 3. CT Chest (coronal view) showing left extensive empyema (black arrow) with mediastinal shift to the right side.

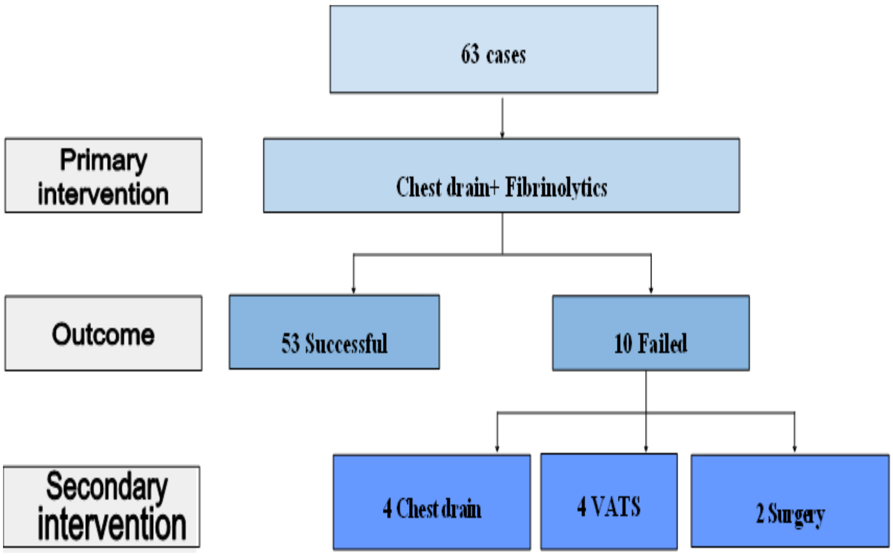

Fig 4. Flow chart of the outcome of primary chest drain with fibrinolytic therapy.

Results

Our study included 63 patients who underwent chest drain insertion with fibrinolytic therapy as a primary intervention. Upon reviewing the demographic data, we found that the median age was 4 (0 – 15) years. The median duration of symptoms before admission was 7.0 (2.0-14.0) days. The median hospital stay before the intervention was 1 day. Preintervention inflammatory markers were also reviewed in our study, with a median WBC of 19.10 (3.50-50.20) and a median CRP of 201.0 (8.0-464.0). Regarding postoperative HDU/ICU admission, the mean postoperative HDU/ICU stay was 1.44 ±2.58 days, and the mean total hospital stay was 13.51 ± 5.71 days. **(Table 1)**.

The chest drain and fibrinolytic therapy approach were curative and successful as a primary intervention in 84.1% of the cases. Only ten cases needed a secondary intervention (4 cases needed another chest drain insertion, 4 cases needed VATS, and 2 cases needed an open thoracotomy and decortication). Readmission within 6 months after the initial discharge was noted in 3 cases where they required another course of intravenous antibiotics, and one of them required subsequent chest drain insertion. **(Figure 4)**.

Table 1. Summary of the preoperative and post operative data analysis

Age on admission	
Mean ± SD.	4.34±3.70
Median (Min. – Max.)	4.0(0.0-15.0)
Days of symptoms	
Mean ± SD.	8.35±3.72
Median (Min. – Max.)	7.0(2.0-14.0)
Hospital stay before primary intervention	
Mean ± SD.	2.11±2.71
Median (Min. – Max.)	1.0(0.0-16.0)
WBC (x 10^3 mm^3)	
Mean ± SD.	21.52±10.31
Median (Min. – Max.)	19.10(3.50-50.20)
CRP (mg/dl)	
Mean ± SD.	209.92±109.08
Median (Min. – Max.)	201.0(8.0-464.0)
Oxygen requirement	
Before intervention	
SVIA	39(61.9%)
NIV	21(33.3%)

IV	3(4.8%)
Post intervention	
SVIA	38(60.3%)
NIV	17(27.0%)
IV	7(11.1%)
OPTIFLOW	1(1.6%)
Patients required IV post-operative not before	4(6.3%)
Patients no change post intervention	45(71.4%)
CXR (presence of mediastinal shift)	18(28.6%)
Chest US max depth (cm)	
Mean ± SD.	2.88±1.27
Median (Min. – Max.)	2.70(0.70-9.0)
HDU/ICU	
Mean ± SD.	1.44±2.58
Median (Min. – Max.)	0.0(0.0-11.67)
Hospital stay after primary intervention	
Mean ± SD.	11.40±5.75
Median (Min. – Max.)	10.0(6.0-36.0)
Total hospital stay	
Mean ± SD.	13.51±5.71
Median (Min. – Max.)	12.0(7.0-36.0)
Primary intervention (Failed)	10(15.9%)
Readmission	3(4.8%)

Discussion

This is a retrospective study aiming to assess the outcome of primary chest drain with fibrinolytic therapy in treatment of paediatric empyema. As parapneumonic effusion can occur in different phases with a variable rate of progression between the phases, there are different treatment modalities for the corresponding phases. **(Jaffé and Balfour-Lynn, 2005)**.

The optimum timing and type of drainage and surgical intervention (especially with the advancement in thoracoscopy) remain controversial. While some publications showed no difference in outcome between VATS and chest drain with fibrinolytic therapy focusing on the total hospital stay and cost of the intervention. Other publications have documented better clinical outcomes achieved with the minimally invasive technique since Kern et al. first described VATS for treating paediatric empyema in 11993. **(Kern and Rodgers, 1993)**

The advantages of VATS include the capacity to decorticate the lung, mechanically disintegrate fibrous septae, and both drain and irrigate the pleural cavity to facilitate lung expansion. In our study group, the size of the chest drain used was subjected mainly to the main surgeon's surgical preference, and a wide range of chest drains were used throughout the study, including 10, 12, 14, 16, and 20 Fr, with 12 Fr being the most commonly used in our study.

Since the optimal drain size is still being debated, a multicentric randomized study found that using small surgical drains (mean size 10.5 Fr) is associated with a shorter hospital stay than using larger percutaneous catheters (mean size 20.1 FG) **(Thomson et al., 2002)**. Also, small chest drains cause less pain and do not obstruct the mobilization of the child, which enhances a faster recovery.

On dividing the patients in the chest drain with the fibrinolytics group into subgroups according to the chest drain size, There was no statistical difference between the different subgroups according to age, CRP, presence of a mediastinal shift in the preoperative x-ray, duration of hospital stay after the chest drain insertion and the need for secondary intervention, with success rates of 81.3% in the 10 Fr subgroup and 83.3% in the 16 Fr subgroup. Reinforcing that the use of small chest tubes is as effective as the bigger chest drains.

On reviewing the relevant literature comparing both interventions we noted different approach being adapted in different centres and detailed look is essential if we want to build our decision on which intervention to choose.

Sonnappa et al. (2006) performed a prospective randomized trial on 60 patients under the age of 16 with radiological evidence confirming empyema, including chest x-ray and ultrasound (30 patients underwent chest drain insertion with fibrinolytic therapy, and 30 underwent VATS).There was no significant statistical difference in the hospital stay after primary intervention in both groups, with a median of 6 days (range 3–16 days) in the VATS group and a median of 6 days (range 4–25 days) in the chest drain group. Chest drains were removed one day earlier in the VATS group when the number of days with a chest drain in place was compared between the two groups. This difference was statistically marginal ($p = 0.055$). However, because it had no effect on the length of hospital stay following the intervention, this was not clinically significant. Primary VATS was successful in 25/30 patients (83.3%). Four out of thirty patients in the VATS group had to be converted to mini-thoracotomy, and one out of thirty underwent another VATS procedure later. The failure rate for the chest drain was 17.8%, with no statistically significant difference observed between both groups. It is worth mentioning that in 4/30 patients (13.3%) of the chest drain group, the chest drain came out, and they had to be reinserted, but the author did not consider this as a failure despite the need for secondary intervention. At the end of the study, it was suggested that intrapleural fibrinolytic therapy should be the primary intervention of choice as it is considered cheaper and has more or less a similar outcome to VATS.

Khalil et al. (2007) performed a retrospective study that included 17 patients with chest drain and fibrinolytic therapy (40.000 units twice daily for three days through a small pore chest drain) and nine patients who underwent VATS. There was no statistical difference between the two groups in relation to age and days of symptoms before admission. There was no statistical significance between both groups in relation to hospital stay after the primary intervention, with a median of 10 days in the chest drain with the fibrinolytic therapy group and a median of 9 days in the VATS group. This result was exactly the same in our study. Three out of seventeen patients who had had a chest drain and urokinase underwent secondary intervention (1 needed a thoracotomy, and two needed VATS). They recommended a small-pore chest tube with fibrinolytic therapy as a first-line management option, with VATS as a reasonable second-line choice.

Pacili and Nataraja (2019) published a systematic review and meta-analysis regarding the management of paediatric empyema. They found that the VATS group had a considerably lesser need for re-intervention (RR 0.55 [CI: 0.34-0.88], p = 0.01) and that hospital stay was significantly lower in the VATS group (SDM 0.45 [CI: 0.78 to 0.12], p = 0.007).They concluded that VATS might be a better option for reducing the length of hospital stay without causing any additional morbidity in centres with expertise in minimally invasive surgery, especially in children with advanced complex empyema. At the same time, the chest drain with a fibrinolytic therapy approach is effective in about 75% of such cases.

Derderian et al. (2020) published a retrospective study in 2020 that included patients under the age of 18 from multiple centres (583 underwent primary VATS, 2649 received chest drain and fibrinolytics (tPA, urokinase, or streptokinase).Twenty nine percent of children in the chest drain group received fibrinolytic therapy for longer than three days; the average number of fibrinolytic doses was 3.29 ± 2.01 days. One hundred ninety-three patients from the chest drain with fibrinolytic therapy group (7%) required secondary intervention in the form of VATS.

Although we did not include the cost of the treatment in our study, it has been previously contradicted in the literature. One study stated that VATS costs 35% more than fibrinolytic therapy. **(St Peter et al., 2009)**

On the other hand, a retrospective multicentric study showed that the average hospital cost for each group was comparable ($32,136 for VATS and $36,618 for chest tubes and fibrinolysis, p=0.401). The higher need for further treatments and more extended hospital stays in the chest drain group with fibrinolytic therapy outweighed the expense of VATS. **(Shah et al., 2010)**.

Conclusion

Despite the ongoing debate among different paediatric surgery centres regarding the management of paediatric empyema, our study indicates that chest drain insertion with fibrinolytic therapy is a reasonable and less invasive approach with a high success rate. Further analysis is needed to identify prognostic factors that might favour primary VATS.

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