Title
What is the best treatment option for empyema requiring drainage in children?

Scenario
A 4 year old girl attends with a three day history of cough, breathlessness and fever. She is started on antibiotics but fails to improve over the subsequent 48 hours. A chest x-ray and ultrasound of the thorax reveals a large, loculated pleural effusion amenable to drainage.

Structured Clinical Question
In managing children with a large empyema (patient), does a pleural drain with fibrinolytics or primary video-assisted thoracoscopic surgery (VATS) (intervention) result in better treatment outcome (outcome)?

Search
There are currently no applicable reviews in the Cochrane database. The PubMed Index was searched with the following strategy: "(paediatric OR pediatric OR child) AND empyema AND (VATS OR thoracoscopic) AND (drain OR thoracostomy) AND (urokinase OR fibrinolysis OR fibrinolytics)". This revealed 36 articles. All abstracts were reviewed; four prospective randomised studies were identified. We did not consider studies that compared VATS with chest drain without fibrinolytics[1], or national surveillance studies[2]. All references in these papers were reviewed, and no further relevant papers were found. These papers are summarised in Table 1.

Summary

Citation	Study Group	Study Type	Primary Outcome	Key Result	Comments
Sonnappa et al. (2006)	60 <16 year olds with radiographic evidence of empyema and indication for drainage. Randomsied to VATS (30) or percutaneous chest drain + intrapleural urokinase (30).	Randomised, prospective, single-centre	Median length of stay in hospital after intervention.	VATS: 6 days (range 3-16) Urokinase: 6 days (range 4-25) p=0.311	UK study. 5 patients in VATS arm required further surgery. 2 patients in urokinase arm went on to require VATS. VATS arm 25% more costly than urokinase arm.
St. Peter et al. (2009)	36 <18 year olds with empyema confirmed on CT or ultrasound. Randomised to VATS(18) or chest drain + tissue plasminogen activator(18).	Randomised, prospective, single-centre	Median length of hospital stay after intervention.	VATS: 6.9 ± 3.7 days Fibrinolysis: 6.8 ± 2.9 days. p=0.96	American study. 3 patients in fibrinolysis arm went on to require VATS. Cost of VATS significantly higher than fibrinolysis ($11.7k compared to $7.6K)
Cobanoglu et al. (2011)	54 cases of empyema confirmed on CXR, ultrasound and CT. Randomised to either VATS (27) or chest tube + streptokinase (27)	Randomised, prospective, single-centre	Duration of hospital stay (DOHS), Duration of symptoms after intervention (DOSI)	DOHS: VATS – 7.41 days Fibrinolyisis: 10.37 days (p=0.0001) DOSI: VATS – 3.78 days Fibrinolysis: 6.78	Turkish study. Higher treatment failure rates than other studies. Fibrinolysis cost significantly lower than VATS ($387 vs. $957). No discussion of how

				days (p=0.0001)	symptoms measured.
Marhuenda et al. (2014)	103 <15 year olds with effusion requiring drainage confirmed on USS. Randomised to VATS debridement (53) or chest drain +intrapleural urokinase (50).	Prospective, randomised, multi-centre trial.	Median length of hospital stay after intervention.	VATS: 10 days (IQR 7-13) Urokinase: 9 days (IQR 8-12) p=0.45	Spanish study. 6 centres recruited patients. Chest tube retained for longer in urokinase group compared to VATS group. (6 days compared 4 days p=<0.001). Complication rates similar.

Table 1: Summary of papers

Commentary

The incidence of empyema in children in the developed world appears to be increasing[3]. A simple parapneumonic effusion may progresses from the exudative stage with anechoic non-septated fluid (stage 1), through hyperechoic fluid with fibrinous septation (stage 2) to an organisational stage with hyperechoic loculations with or without thick pleural peel (stage 3). Many treatment options are available, from intravenous antibiotics alone, to chest drain insertion with or without fibrinolytics, to surgical options. Indications for intervention include large effusions, effusions associated with loculations, or effusions associated with symptoms that are worsening or not improving[4]. The main aims of treatment for empyema are to sterilize the pleural cavity, reduce duration of fever and to ensure full expansion of the lung and thus returning pulmonary function to normal.

There is currently no standardized treatment regimen for childhood empyema, and patient management is dependent upon local practices and guidelines, as well as physician preference. Part of the issue stems from a lack of paediatric population-based evidence. Although VATS is the most commonly performed surgical pleural drainage procedure, its availability as a local procedure often dictates how early it is used in management.

Intrapleural interventions have been associated with significantly shorter hospital stays when compared to intravenous antibiotics alone, while instillation of intrapleural fibrinolytics offers additional benefits beyond simple chest tube drainage shortening length of hospital stay[5,6]. Unfortunately, there is little evidence in children to suggest the optimal fibrinolytic agent between streptokinase, urokinase or alteplase. In animal models there is little difference between agents, although in adults there are concerns over allergic reactions to streptokinase. Often local availability of agents dictates choice[4].

Sonnappa et al.[7] compared either chest drain with instillation of urokinase every 12 hours or VATS for children with stage 1 to 3 empyema. They found no difference in median length of stay, treatment failure rates and radiological outcome at six months between the groups. Similarly, St. Peter et al.[8] compared chest drain insertion with intrapleural alteplase therapy every 24 hours or VATS in stage 2 to 3 empyema. They again found no difference in length of stay between the two groups, or in duration of increased oxygen requirement, duration of fever, analgesia, or treatment failure. Marhuenda et al.[9] examined patients with a confirmed septated empyema (stage 2 or 3 on ultrasound scan) who received either chest drain and intrapleural urokinase every 12 hours or VATS. Again, this group found no significant differences between the two groups in length of stay, duration of fever or treatment failure/adverse event rate. The only significant difference found was in the length of chest tube placements, which was longer in the chest drain and urokinase group compared to the VATS group.

Conversely, Cobanoglu et al.[10] compared chest drain insertion and streptokinase every 24 hours via a large bore drain or VATS. The study is more difficult to interpret, comprising children with potentially more advanced disease (31 of 54 with stage 3 disease), and the outcomes are markedly different to other studies. Compared to chest drain and streptokinase, the VATS patients had a shorter duration of symptoms after intervention and a shorter hospital stay in total (7.41 days vs. 10.37 days). Treatment failure rates were markedly higher than other studies with 30% of the chest drain group progressing to VATS (one required thoracotomy as well), while 22% in the VATS group progressed to thoracotomy. Other clinical parameters such as total fluid drained; lung function; duration of oxygen support and time until afebrile after procedure showed no significant difference between the two groups.

The one area of clear difference between VATS and chest drain with fibrinolysis is health economics, where chest drain with fibrinolysis appears superior. Sonnappa et al.[7] found the VATS group had significantly higher mean costs compared to the chest drain and urokinase ($11,379 compared to $9,127), and they concluded that based on cost (despite similar clinical outcomes) chest drain with fibrinolysis therapy was preferable to VATS. Similarly St. Peter et al. [8] reported significant cost implications of VATS over drain and alteplase, and they also concluded that based on cost, drain and fibrinolysis was the preferable first-line treatment. The costs in the study reported by Cobanoglu et al.[10] were noticeably lower, but again cost of VATS was significantly greater than tube and streptokinase ($957 versus $387 per patient). Marhuenda et al.[9] did not perform a cost analysis on their data set.

It is suggested that the use of VATS as primary treatment has increased over the past decade[11]. However the evidence at present suggests there is no significant difference in outcomes between chest drain with intrapleural fibrinolytics or VATS as the primary treatment modality for childhood empyema. Median length of hospital stay, duration of symptoms and treatment failure rates appear to be similar for both options. The only significant consideration between the two is cost, and it can be argued that in an age of 'prudent healthcare', chest drain and intrapleural fibrinolytics offer the same clinical benefit at a lower price. Furthermore availability of VATS is not uniform across the UK and will not be accessible in some centres. The American Paediatric Surgical Association asserts there is sufficient high quality evidence to support the use of chest tube and fibrinolysis as the primary treatment modality in childhood empyema, with VATS procedures being reserved for difficult cases where fibrinolysis has failed[4]. Therefore chest drain and intrapleural fibrinolysis should be considered the primary management option for children presenting with empyema requiring drainage.

Clinical Bottom Lines

- There is little national consensus on the best treatment option for childhood empyema (Grade C)
- Chest drain insertion with intrapleural fibrinolytics and VATS have similar clinical outcomes (Grade D)
- VATS is a technically more difficult and expensive procedure than insertion of chest drain and fibrinolytics (Grade B)

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10: Cobanoglue, U et al. (2011) Comparison of the methods of fibrinolysis by tube thoracostomy and thorascopic decortications in children with stage II and stage III empyema: a prospective randomized study. *Pediatric Reports* Vol. 3(29) pp 114-118
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