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COMPARATIVE STUDY OF CHEST TUBE DRAINAGE WITH INTRAPLEURAL UROKINASE VERSUS THORACOSCOPIC DRAINAGE FOR FIBROPURULENT EMPYEMA IN PEDIATRIC AGE GROUP

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Abstract

Background: Various treatment options exist for fibropurulent empyema including intravenous antibiotics with repeated thoracocentesis, chest tube drainage, fibrinolytic therapy, video-assisted thoracic surgery (VATS) and thoracotomy with decortication.[4,5] Present study was aimed to compare chest tube drainage with intrapleural urokinase versus thoracoscopic drainage for fibropurulent empyema in pediatric age group at a tertiary hospital. **Material and Methods:** Present study was single-center, prospective, comparative study, conducted in patients under the age of 12 years, with clinical and radiographic evidence of empyema (i.e., pleural fluid on chest X-ray) with sonographic findings of hyperechoic fluid with or without thin septation. Block randomisation scheme was used with equal allocation of subjects to urokinase group and VATS group & each group had fifteen patients. **Results:** In present study, pleural effusion collapse consolidation was common finding on chest X ray in Urokinase as well as VATS group. Mean period of hospitalisation in thoracostomy group was 9.3 days vs 8.4 days in VATS group but not proved to be statistically significant. We observed that frequency of hospitalization days was 6-7 days (6patient) in VATS gr and 9 days (4 patients) in thoracostomy group. Mean duration of ICD (in days) of study participants belonging to Urokinase group and VATS group was 8.2±3.10 and 6.8±3.2 respectively & there was no statistically significant difference in the mean duration of ICD. **Conclusion:** Parameters of clinical outcome between intrapleural urokinase and VATS for the treatment of childhood empyema were comparable. Urokinase is a more economic treatment option compared with VATS and should be the primary treatment of choice.

Keywords: intrapleural urokinase, VATS, childhood empyema, chest tube drainage

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Introduction

Empyema thoracis' is the presence of pus within the pleural space and is associated with significant morbidity like development of scoliosis and restrictive lung disease.[1] Parapneumonic effusion and empyema have an incidence of 3.3 per 100 000 children.[2,3,4] Parapneumonic effusions and empyema are more common in boys than girls and are more frequently encountered in infants and young children.[2] In the pediatric population, parapneumonic effusion complicates pneumonia in 36 to 57% of cases.[5]

Empyema thoracis is among the few conditions where the management depends much on the appropriate timing of treatment in the course of the disease. Chest x-ray, ultrasonography and computed tomography have been helpful in delineating the nature and degree of underlying parenchymal disease, but not so predictive of the presence of pleural peels. The principles of management of empyema thoracis are prompt initiation of appropriate antibiotics, the complete evacuation of the purulent fluid/material and preservation/ restoration of lung expansion. [4,5]

Various treatment options exist including intravenous antibiotics with repeated thoracocentesis, chest tube drainage, fibrinolytic therapy, video-assisted thoracic surgery (VATS) and thoracotomy with decortication.[4,5] Present study was aimed to compare chest tube drainage with intrapleural urokinase versus thoracoscopic drainage for fibropurulent empyema in pediatric age group at a tertiary hospital.

Material And Methods

Present study was single-center, prospective, comparative study, conducted in department of Surgery, at Government Medical College and Hospital, Nagpur, India. Study duration was of 2 years (October 2010 to October 2012). Study approval was obtained from institutional ethical committee.

Inclusion criteria

- Patients under the age of 12 years, with clinical and radiographic evidence of empyema (i.e., pleural fluid on chest X-ray) with sonographic findings of hyperechoic fluid with or without thin septation.
- Indications for drainage were persistent fever of 38°C (100° F) or greater after more than 24 h of parenteral antibiotic treatment or respiratory distress (tachypnea and/or oxygen requirement) caused by the pleural collection
- Parents willing to participate in present study

Exclusion criteria

- Thoracocentesis or chest drain insertion performed or attempted.
- Cases of organized empyema diagnosed on the basis of duration and radiographic and sonographic evidence of well-formed loculations.
- Known immunodeficiency.
- Recurrent empyema.
- Patients with associated known complications like bronchopleural fistula.
- Patients above 12 years of age.
- Patients with low platelets or abnormal coagulation profile.

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Study was explained to patients in local language & written consent was taken for participation & study. Each patient was assessed for symptoms of fever, cough, breathlessness, chest pain. Each of the symptoms was assessed in detail laying emphasis on exact duration of that symptom. This was a major aspect of our study as the empyema was staged according to the duration of illness which corresponds to the pathogenesis of empyema.

Parents or caregivers were specifically questioned regarding the presence of any risk factors such as repeated lower respiratory tract infections, tuberculosis, contact with tubercular patients and immunodeficiencies. Any treatment history (antibiotic therapy, prior hospital admission and any interventions like aspiration or drainage) was inquired.

Thorough physical examination was done and weight of child was recorded. Investigations like Complete blood count, Bleeding Time, Clotting Time, Pleural fluid for routine microscopy, culture sensitivity, Blood culture, X-ray chest and Ultrasonography of thorax were performed in every patient.

Diagnostic thoracocentesis was done in all children. A written informed consent was taken from the parents or caregivers prior to the procedure. Massive effusions were drained from the posterior axillary line in the fifth intercostal space whereas smaller or loculated effusions were drained with ultrasound guidance.

The pleural fluid sample was examined for its gross appearance and sent for

a) Biochemical analysis
b) Primary smear for gram staining
c) Culture sensitivity

A diagnosis of empyema thoracic was made in these children either by aspirating frank pus with WBC count > 500/µl and increased polymorphs i.e. > 50% or by demonstrating exudative nature of the pleural fluid according to Light's criteria or by demonstrating organisms by Gram's staining or by culture. (Light's criteria- PH < 7.2 Glucose level < 40 mg / dl, LDH > 300 IU /ml, Protein level > 2.5 g /dl)

Block randomisation scheme was used with equal allocation of subjects to urokinase group and VATS group & each group had fifteen patients.

- Urokinase group were subjected to tube thoracostomy with intrapleural urokinase instillation.
- VATS group were subjected to video assisted thoracoscopic drainage technique.

INTERCOSTAL DRAINAGE WITH INTRAPLEURAL UROKINASE - Chest tube drain insertion was done under general anaesthesia or local anaesthesia with IV sedation. General anaesthesia was preferred option for unco-operative children. The position of the tip of the chest tube was aimed basally for the drainage of pleural fluid. The drain was secured after insertion by a stay suture to prevent falling. The chest drain was connected to an underwater seal bottle which was kept below the level of the patient's chest at all times. A radiograph was taken to confirm proper placement of the drain after stabilization of patient. The respiratory swing of the fluid in the tube was used to assess tube patency and confirm the position of the tip of drain in the pleural cavity.

Urokinase was instilled twice daily (between 8am and 8pms) for three days (total 6 doses) starting immediately from postoperative period according to dose mentioned below. If inadequate response was obtained then further urokinase was instilled for two more days.

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Dose:

- <10kg weight - 10,000 units in 10ml 0.9% saline
- >10kg weight - 40,000 units in 40ml 0.9% saline

Video Assisted Thoracoscopic Surgery (VATS) - VATS was performed under general anaesthesia, with dual lung ventilation and with the patient in a lateral position. Two 5 mm ports were used in all patients. A primary port was placed through the fifth or sixth intercostal space (ICS) in the mid-clavicular line, through which a zero-degree wide angle scope was introduced. The CO2 insufflation pressure was maintained between 4-6 mm Hg at a flow rate of 1 litre/minute. The placement of a second port was based on thoracoscopic findings. Initial dissection and creation of space was achieved by CO2 insufflation and adhesions were released with the tip of the scope or tip of the suction cannula under vision. The fluid was sucked out and the peel was removed with a Maryland dissector. Sometimes long open surgical instruments were passed directly through the ports and aided in the removal of the peel. An ICD was placed through the camera port before closure of the ports. Postoperatively the patients were monitored in the recovery ward for 6-12 hours. A postoperative radiograph was carried out, to visualize the condition of the ipsilateral and contralateral lung after stabilization of patient.

Adequate pain management prevented splinting and more effective breathing, thereby preventing postoperative pneumonias and other pulmonary complications. Fibrinolytic therapy is usually not used following VATS or thoracotomy. Children with longer duration of illness with radiological features of hydropneumothorax, thick pleural peel, necrotic lung tissue, trapped lung and crowding of ribs were taken up for open thoracotomy with decortication and excluded from the study.

All patients had ICD insitu postop till full lung expansion which were maintained on low intermittent suction. All children were monitored clinically and with serial chest x-rays for improvement and lung expansion. In case of worsening distress or increase in effusion, repeat ultrasonography/CT scan was done. A second surgical procedure (thoracotomy+/decortication) was then considered.

Once the children were afebrile for 48 hours, with no drainage for a minimum of 24 hours, with radiological features of good lung expansion and no effusion, their chest tube were removed in both treatment groups. The antibiotics were continued according to the clinical condition and status of underlying pneumonia.

All patients were followed up on the OPD basis at 2 weeks, 4weeks and 3 months. On follow-up, detailed clinical examination and chest x-ray were done to assess lung expansion and to rule out residual effusion/ pneumonia.

Data was collected and compiled using Microsoft Excel, analysed using SPSS 23.0 version. Frequency, percentage, means and standard deviations (SD) was calculated for the continuous variables, while ratios and proportions were calculated for the categorical variables. Difference of proportions between qualitative variables were tested using chi-square test or Fisher exact test as applicable. P value less than 0.5 was considered as statistically significant.

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Results

In present study, total of 30 subjects belonging to age group 0-12 years attending the Surgery inpatient Department for management of empyema were enrolled and randomly allocated into two groups and operated.

Mean age, Laboratory parameters (Heamoglobin levels, TLC, PT-INR, Pleural fluid protein & Pleural fluid sugar), duration of ICD, duration to normalize fever, duration to normalize TLC, duration of oxygen need, analgesic required & duration to become asymptomatic were comparable among both groups & difference was statistically not significant ($p > 0.05$).

Table 1: General characteristics

	Urokinase Group (n=15)	**VATS Group (n=15)**	**P**
Mean age (in years)	3.9 ± 2.90	4.9 ± 3.58	.246 (NS)
Gender			
Male	11	13	
Female	4	2	
Laboratory parameters			
Heamoglobin levels	9.0 ± 1.66	9.4 ± 1.61	.513 (NS)
TLC	12213 ± 4372	13866 ± 4857	.268 (NS)
PT-INR	1.06 ± 0.14	1.07 ± 0.17	.849 (NS)
Pleural fluid protein	4.4 ± 1	4.2 ± 0.9	.540 (NS)
Pleural fluid sugar	35.9 ± 15.0	37.0 ± 8.4	.799 (NS)
Other			
Duration to normalize fever (in days)	3.9 ± 2.1	3.1 ± 2.3	.410 (NS)
Duration to normalize TLC (in days)	5.8 ± 2.3	6.5 ± 3.1	.513 (NS)
Duration of Oxygen Need (in days)	1.8 ± 0.91	1.9 ± 1.38	.882 (NS)
Analgesic Required (days)	5.2 ± 2.78	4.1 ± 1.99	.298 (NS)
Duration to become asymptomatic	4.2 ± 2.1	2.9 ± 2.2	.196 (NS)

NS: Not Significant

Pleural effusion collapse consolidation was common finding on chest X ray in Urokinase as well as VATS group.

Table 2: Chest X-Ray (CXR)

Finding	**Urokinase Group (%)**	**VATS Group (%)**
Pleural effusion collapse	5 (33.33 %)	3 (20 %)
Pleural effusion collapse consolidation	8 (53.5 %)	9 (60 %)
Pleural effusion consolidation	2 (13.33 %)	3 (20 %)

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On Ultrasonography Chest common findings were hyperechoic fluid, hyperechoic fluid/debris in fluid, hyperechoic fluid/loculation/debris in fluid & hyperechoic fluid/loculation,

Table 3: Ultrasonography Chest

Finding	Urokinase Group (%)	VATS Group (%)
Hyperechoic Fluid	4 (26.8 %)	3 (20 %)
Hyperechoic Fluid/Debris in fluid	4 (26.8 %)	4 (26.8 %)
Hyperechoic Fluid/Loculation/ Debris in fluid	7 (46.7 %)	4 (26.8 %)
Hyperechoic Fluid/Loculation	0	4 (26.8 %)

Mean period of hospitalisation in thoracostomy group was 9.3 days vs 8.4 days in VATS group but not proved to be statistically significant. We observed that frequency of hospitalization days was 6-7 days (6patient) in VATS gr and 9 days (4 patients) in thoracostomy group.

Table 4: Period of Hospitalization

Duration	Urokinase Group (%)	VATS Group (%)	P value
< 5 days	1 (6.6 %)	2 (13.2 %)	
5.1 to 10 days	10 (66.6 %)	11 (73.3 %)	
> 10 days	4 (26.8 %)	2 (13.5 %)	
Mean duration	9.3 ± 3.2	8.4 ± 4.2	.552 (NS)

In present study, both groups had majority (93.3 %) samples negative for blood culture.

Table 5: Blood Culture

Duration	Urokinase Group (%)	VATS Group (%)
Positive	1 (6.6 %)	1 (6.6 %)
Negative	14 (93.3 %)	14 (93.3 %)

Mean duration of ICD (in days) of study participants belonging to Urokinase group and VATS group was 8.2±3.10 and 6.8±3.2 respectively & there was no statistically significant difference in the mean duration of ICD.

Table 6: Duration of ICD

Duration	Urokinase Group (%)	VATS Group (%)	P value
< 5 days	4 (26.8 %)	7 (46.7 %)	
5.1 to 10 days	8 (53.5 %)	6 (40 %)	
> 10 days	3 (20 %)	2 (13.5 %)	
Mean duration	8.2 ± 3.1	6.8 ± 3.2	.273 (NS)

Hemmorhagic drain was observed in 3(20%) patients and pain during installation of urokinase observed in 3(20%) patients in thoracostomy group. 1(7%) patient of thoracostomy group develop recurrence of pyopneumothorax after 1 yrs. of initial completion of t/t and required repeated ICD insertion for the same. During initial ICD insertion and F/U for 3 months patient had good expansion of lung.

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Bronchopleural fistula developed in 2 (15%) patient of VATS group which was managed with continuous drainage of ICD and antibiotics. 1(7%) patient in VATS group develop subcutaneous emphysema after removal of ICD and required reinsertion of ICD for the same complaints.

No patient in either group had recurrence of effusions once the chest tube was re- moved during decided follow up period. No patient in each T/T group converted to open thoracotomy procedure due to worsening of symptoms

Table 7: Complications

	Urokinase Group (%)	**VATS Group (%)**
Hemorrhagic drain	3 (20 %)	0
Chest pain	3 (20 %)	1 (6.6 %)
Allergy	0	0
Pneumothorax	1 (6.6 %)	0
Lung abscess	0	0
Tension pyopneumothorax	0	0
Bronchopleural fistula	0	3 (20 %)
Subcutaneous emphysema	0	1 (6.6 %)

Discussion

The two most often used techniques of drainage of empyema are the thoracostomy with intrapleural urokinase technique and video assisted thoracoscopic drainage technique. In the progress of a thoracic empyema or complicated (persistent or loculated) parapneumonic effusion, viscous fluid with obstructing fibrinous debris and non-communicating fluid locules may develop; a single thoracic tube for drainage remains insufficient.[6,7] Insufficient treatment in the fibrinopurulent period causes pleural fluid organization and scar formation in the pleural cavity and the neighboring lung tissue.[6] In order to prevent this, and to clear out the fibrinous debris, numerous studies suggest video-assisted thoracoscopic decortication (VATS) or fibrinolytic treatment in the early stages.[1,8,9]

In our study, the mean age of children in urokinase group was 3.9±2.90 years and that in VATS group was 4.9±3.58 yrs. Hence, both groups were similar with respect to age (p=0.246). In the study conducted by Sonappa *et al.*,[10] median age of children was 3.57 yrs. in urokinase group and 3.07 yrs. in VATS group (p- 0.355).

In our study, majority of children were male. male: female proportion was 11:4 in urokinase group and 13:2 in VATS group Hence, both groups were similar with respect to gender (p=0.246) in our study. In the study conducted by Sonappa *et al.*,[10] male: female proportion was 17:13 in urokinase group and 16:14 in VATS group with a P value of 0.79 which was statistically insignificant.

In the only randomized prospective study in children comparing the instillation of urokinase through percutaneous chest drains to normal saline, the urokinase group had a significantly reduced hospital stay after intervention (7.4 d vs. 9.5 d; ratio of geometric means 1.28; confidence interval [CI], 1.16–1.41).[11] This study also found shorter hospital stay with small percutaneous chest drain insertion compared with large bore chest drains (7.2 d vs. 9.4 d). [11]

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In present study, dyspnea (93% in urokinase group and 86 % in VATS group), fever (80 % in urokinase group and 100 % in VATS group) and cough (66 % in urokinase group and 80 % in VATS group) were most common symptoms in both the groups. Chest pain was complained of by relatively a smaller number of children could be due to lower age group. Our findings are consistent with the observations of Arya *et al.*,[11] who reported fever (94%), cough (96%), breathlessness (48%) and chest pain (27%) as the presenting complaints. The most common findings on clinical examinations were crepitations (80%) and diminished respiratory movements (100%).

In the study of Baranwal AK *et al.*,[12] of 265 patients staphylococcus was considered to be the infecting organism in 162 (67%) patients. It predominated in all the age groups, more so among the under 5 years. The majority of S. pneumoniae were isolated from older children which are similar to our study. These results were slightly different than the microbiological data of previous study done by Sonappa *et al.*,[10] which showed Seven (23%) patients in each of the groups had positive blood or pleural fluid cultures. 47 (78%) of the pleural fluid samples were analyzed and cultured. Of these 27 (45%) were positive for fully penicillin-sensitive Streptococcus pneumonia.

Thoracostomy was performed under GA or IV sedation whereas all the VATS procedure were done under GA. Average mean duration of ICD insertion in our study was 25.3±8.9 (15 - 45) min compared to duration of VATS procedure was 72.6±29.0 (30 - 120) min. ($p < 0.001$), indicating that the difference in duration of surgery is statistically significant. As would be expected, the procedural time for VATS was longer, because more debridement and irrigation were performed.

In study by Rajesh R. Gandhi *et al.*[13] duration of VATS was slightly more i.e. 120 min.

In the study of Kent W Cocher *et al.*,[14] the mean (± SD) length of time in the operating room was 81 ± 19min. Shorter surgical time can have the effect of less stress for the family waiting for the child to return from the operating room. Though we used sedation with local anesthesia for some patients, which involves the use of opioid drugs and increases the chance of nausea and vomiting in the postoperative period.

Subramaniam R *et al.*,[15] reported a postoperative hospital stay of 4.63 d +_ 0.33 d (20), and Grewal *et al.*,[16] reported one of 4.9 d +_ 2.7 d (24). The only study in children to compare urokinase and early VATS was a retrospective review of clinical practice which showed that patients who received VATS had a significant reduction in total length of hospital stay.[7]

In study by Sonappa *et al.*,[10], VATS was compared with chest drainage and intrapleural fibrinolytic therapy and a failure rate of 16.6% was reported in each arm. They concluded that VATS was not recommended in children because it offered no therapeutic advantage over the simpler and cheaper alternative of chest drain and urokinase. While, Bishay *et al.*,[17], studied 114 children who underwent VATS performed by pediatric surgeons experienced in thoracoscopic surgery. They concluded that VATS has a very good outcome in childhood empyema and it has an important role in the management of this condition.

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Conclusion

Parameters of clinical outcome between intrapleural urokinase and VATS for the treatment of childhood empyema were comparable. Urokinase is a more economic treatment option compared with VATS and should be the primary treatment of choice.

Conflict of Interest: None to declare
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