INTRAPLEURAL FIBRINOLYSIS BY STREPTOKINASE AS ADJUNCTIVE TREATMENT OF LOCULATED EMPYEMA THORACIS

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Abstract

Objectives: To evaluate the effectiveness of intrapleural injection of streptokinase as a method of treatment for cases of loculated empyema thoracis that do not drain well with insertion of intercostal tube.

Patients & Methods: The study included 25 patients with loculated empyema that do not drain well with insertion of intercostal tube. 250,000 units of streptokinase are injected intrapleural via the chest tube. The chest tube is clamped for 3 hours. The chest tube de-clamped to drain in the under-water seal. The procedure repeated for another 2 days, for a total of 3 successive days.

Results: The study included 16 males (64%) and 9 females (36%), The duration of pleural drainage ranged from 4-12 days, with mean (SD) of 6.12 (±1.81), and the amount of total drainage ranged from 300-2150 ml, with a mean (SD) of 942 ml(±538.45), The cause of empyema in this study was not defined in (3) 12% of cases, complicated para-pneumonic effusion in (11) 44% of cases, post-traumatic in (10) (40%) of cases and post-operative in (one) (4%) of cases,. The results of the procedure were successful in 16 cases (64%) and failed in 9 (36%) cases.

Conclusion: Loculated empyema thoracis that do not drain well with insertion of intercostal tube, intrapleural injection of streptokinase in a dose of 250,000 units once daily for three successive days is an effective method of adjunctive treatment, and may avoid the need of open thoracotomy for decortication.

Keywords: Empyema thoracis, Intrapleural, Streptokinase

Introduction

Cardiothoracic surgery probably began with the management of empyema. (1) In 600 B.C. Hippocarates defined Empyema Thoracis as a collection of pus in the pleural cavity. (2) Weese defined it as a fluid with a specific gravity greater than 1018, a white blood cell count greater than 500/ml, or a protein level greater than 2.5g%. Vianna defined empyema as a pleural fluid with positive bacterial cultures or white blood cell count greater than 15,000/ml and a protein level above 3g%. Because many pleural effusions may meet these criteria, the most favoured definition is that of thick, purulent appearing pleural fluid. (3)

The most common cause of empyema thoracis is para-pneumonic, representing 40-60% of all cases. From 5% to 20% all para-pneumonic effusions become thoracic empyema. (4&5&6 &7) Thirty percent or less of all the adult cases originate from thoracic surgical procedures including: lung, esophageal, mediastinal or other intrathoracic procedures. (8) Another important cause of
Empyema is thoracic trauma.\(^9\) Other sources like non-operative esophageal, subdiaphragmatic and infected malignant pleural effusions are occasionally mentioned.\(^{10}\)

The diagnosis of empyema thoracis usually manifest by pulmonary manifestations (e.g. cough, tachypnea, sputum production, desaturations), radiographic studies include postero-anterior and lateral chest radiographs pleural space fluid, the pleural fluid analysis and radiological findings depends on the stage of empyema which is classified to 3 successive stages as follow:

- **Early/acute stage**, one or more of:
  - pH < 7.2
  - glucose < 40 mg/dL
  - LDH > 1000 IU/dL
  - protein > 2.5 g/dL
  - WBC > 500/µL
  - specific gravity greater than 1.018
  - Thin serous or cloudy fluid, generally sterile

- **Fibrinopurulent/intermediate stage**
  - Thicker, opaque fluid or fluid with positive cultures

- **Organizing/late stage**
  - An organizing peel with entrapment of the lung

Central to the staging schema is the development of restrictive pleural rinds or peels encasing the lung. Determination of the presence of this finding would be useful not only in staging the empyema process, but also in clinically guiding intervention. Layering of pleural fluid and the absence of pleural thickening or scoliosis on plain film radiographs may suggest an absence of the peel. Computed tomography and ultrasonography can delineate the nature and degree of parenchymal disease (such as the presence of underlying parenchymal abscesses) and the character of the pleural fluid or rind when complete opacification of the hemithorax is noted on plain films. Unfortunately, neither computed tomography nor ultrasonography has been uniformly predictive of the presence of pleural peels.\(^{11&12}\)

Despite improved antimicrobial therapy and multiple options for drainage of the infected pleural space, empyema thoracis continues to cause significant morbidity and mortality. Tube thoracostomy, image directed catheters, intrapleural thrombolytics, thoracoscopic drainage, decortication, and chronic open drainage have all been used as methods of treatment with success rates ranging from 10 to 90%.\(^{13&14}\)

The initial use of fibrinolytic enzymes for the treatment of haemothorax and post-pneumonic empyema was described in the 1950s.\(^{15}\)

Uncontrolled studies have suggested that intrapleural streptokinase may improve the drainage of infected pleural effusions by lysis of the intrapleural fibrinous adhesions.\(^{16}\)
Material and Methods

This is a non-randomized prospective study included 25 patients diagnosed as cases of loculated empyema, the study done in Benha University hospital, between January 2008 to January 2009 all patients were subjected to:

- History taking and clinical examination
- Chest X-ray and chest CT, ECG
- Chemical, Cytological and bacteriological examination of the pleural fluid.
- Sputum analysis with bacteriological examination.
- Blood culture.
- Full coagulation profile
- CBC, Liver function tests, and kidney function tests.

Exclusion Criteria for patients include:

- Patients with hemorrhagic blood disease.
- Patients with hemoptysis.
- Patients with broncho-pleural fistula.
- Patients with end-stage liver failure.
- Patients with renal failure or abnormal kidney functions
- Patients with chest wall deformities.
- Patients sensitive to streptokinase.

Technique of the Procedure:

- After diagnosis of loculated empyema and insertion of appropriate sized chest drain within the empyema loculus, and failure of complete drainage of the empyema loculus, with minimal daily drainage (≤50 ml/day) for at least 2 days.
- 250,000 units of streptokinase are diluted in 50 ml of normal saline and injected intrapleural via the chest tube, followed by injection of 50 ml of normal saline.
- The chest tube is clamped for 3 hours, while still connected to the under-water seal.
- The chest tube declamped to drain in the under-water seal.
- The process is repeated daily for another 2 days. So, the total injections are 3 injections (once daily for 3 successive days)
- Chest tube is removed after the drainage becomes clear and minimal (≤50 ml / day) for at least 2 successive days and chest CT showing disappearance of the empyema a loculus, and this is considered as successful case.
- If the empyema loculus still present in the CT film, with minimal drainage for at least 4 days this was considered failure of the procedure, and patient prepared for surgical intervention by doing decortication.
- The total period of drainage calculation started from the day of 1st injection, till the day of discharge from hospital in successful cases, and from the day of 1st injection till the day of decortication in failed cases.
Results

- The age range of the studied cases was 19 - 62 years with mean age of 43 ±13.8 years, the study included 16 males (64%) and 9 females (36%)
- 20 cases (80%) had right sided loculated empyema and 5 cases (20%) had left sided loculated empyema.
- The duration of pleural drainage ranged from 4-12 days, with mean (SD) of 6.12 (±1.81), and the amount of total drainage ranged from 300- 2150 ml, with a mean (SD) of 942 (±538.45). Fig. (1)

![Fig. (1): Amount of drainage](image)

- The cause of empyema in this study was not defined in (3) 12% of cases, complicated para-pneumonic effusion in (11) 44% of cases, post-traumatic in 10 (40%) of cases and post-operative in (one) 4% of cases, this post-operative case was not post-thoracic surgery.
- Sputum culture (table-1) was negative in 19 (76%) cases, staphylococcus isolated in 4 (16%) cases and Pseudomonas in 2 (8%) cases. pleural fluid culture (table-2) was negative in 16 (64%) patients, staphylococcus isolated in 5 (20%) cases, Pseudomonas in one (4%) case and mixed bacterial infection in 3(12%) cases.
- 14 (56%) cases were afebrile, while 11 (44%) cases had fever. Of those who had fever 5 (20%) cases had fever before and after the injection of streptokinase, and 6 (24%) developed fever after injection of the streptokinase.
- Only 3 cases (12%) complicated by bleeding, 2 of them the bleeding was in the form of changed color of the pus to be turbid reddish drainage and the coagulation profile of these 2 cases showed increased both INR and PTT of these cases to double value of the pre-procedural level, in both cases the color changes occurred after the third dose of streptokinase. The third case showed bleeding in the form of hematuria with no change in the coagulation profile, this case was 19 years old male with urological procedure
(percutaneous nephrolithotomy by supracostal approach) done 9 days before being referred to our department because of loculated empyema.

- The results of the procedure were successful in 16 cases (Fig. 2 & 3) and failed in 9 (36%) cases (36%) fig.(4)

![Pie Chart: Need for decortication](image)

**Fig. (4): Need for decortication**

**Statistical Method**

Statistical Package of Social Science (SPSS) version 11.0 was used for analysis of data.

**Discussion**

This study included 25 cases of empyema, in 10 of these cases the cause of the empyema was neglected trauma, in 11 cases the cause of empyema was infected para-pneumonic effusion, in 3 cases the cause was not clear, and in one case the empyema was post-operative for a urological operation (percutaneous nephrolithotomy by supracostal approach). Thoracic trauma was the cause of empyema in 40% of cases which is much than that reported by Mandal et al.\(^{(17)}\), who reported thoracic trauma to be the cause of empyema in 1.6% (87 of 5474 cases included in that study).

In all patients selected in this study, history of empyema is less than 4 weeks, as At 4 to 6 weeks after the development of the empyema fibrin layer becomes organized and forms a thick peel according to Lawrence et al.\(^{(18)}\)

In 18 cases the empyema was not loculated at the time of diagnosis, and chest tubes were inserted for drainage, and there were residual loculated pockets of empyema, while in 7 cases the empyema was loculated from the start.
Sputum and pleural fluid cultures were negative in most patients, as sputum culture was negative in 76% of cases and pleural fluid culture was negative in 64% of cases. And this may be due to the empirical antibiotics the patients were receiving before the culture, almost the same results regarding this point reported by Bouros et al.\(^{19}\), in that study which included 20 patients, in 17 patients the sputum culture was negative and in 15 patients the pleural fluid culture was negative.

In this study streptokinase was used in a dose of 250,000 units in 50ml normal saline followed by another 50ml normal saline injected through the chest drain once daily for three successive days, not twice daily as done by Maskell et al.\(^{20}\) who injected 250,000 units twice daily for three successive days. Also, in this study the chest drain clamped for three hours, and not four hours as suggested by Bergh et al.\(^{21}\) the reduction to three hours was to reduce possible adverse reactions without interfering with the fibrinolytic activity of streptokinase. As suggested by Aye et al.\(^{22}\)

Although Streptokinase is well tolerated and doses of up to 1.5 million units of Streptokinase have been shown to be safe in humans according to Davies et al.\(^{23}\) three of patients included in this study had bleeding and two of them showed increased PT and PTT, however, the bleeding was not sever, not necessitate any intervention nor blood transfusion, in the 3\(^{rd}\) case the bleeding was in the form of hematuria and the urology department was consulted for this patient as he had percutaneous nephrolithotomy by supracostal approach 9 days ago (this was the postoperative case), and they advise just observation for the hematuria which stopped after 48 hours.

The success rate in this study was 64% which is near to the results obtained by Masood et al.\(^{24}\) as in that study the success rate was 67% (30 cases out-of 45), and the results of this study is far away from that reported by Jerjes-Sdnchez et al.\(^{25}\) who reported overall success rate of 92%.

Even in cases who had decortication because of failure of streptokinase, the decortication was easier than usual.

**Conclusion**

This study shows that in cases of loculated empyema thoracis that do not drain well with insertion of intercostal tube, intrapleural injection of streptokinase in a dose of 250,000 units once daily for three successive days is an effective method of adjunctive treatment, and may avoid the need of open thoracotomy for decortication, as in more than 60% of the patients included in this study, decortication by open thoracotomy avoided by intrapleural injection of streptokinase.

**References**

2- **Adams F**: The genuine works of Hippocrates. Baltimore William and Wilkins Company. 1939; p51-2.


4- **Chapman SJ and Davies RJ**: The management of pleural space infections. Respirology 2004; 9:4-11.


Fig. (2): CT-scan of a case of loculated effusion before streptokinase

Fig. (3): CT-scan of the same case after streptokinase
### Sputum Culture

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Table (1): Results of sputum culture

### Pleural Fluid Culture

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Table (2): Results of pleural fluid culture