Intrapleural Fibrinolytic Instillation for the Treatment of Complicated Pleural Effusion: Our Experience at King Hussein Medical Centre
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Abstract

**Background:** management of empyema had evolved greatly since the administration of streptokinase which had resulted in improved outcome and great reduction in surgery rate. **Methods:** 57 patients were enrolled in a 2 year study, held in King Hussein Medical Centre, evaluating the efficacy of streptokinase instillation in multiloculated pleural empyema. **Results:** 36 male and 21 females were included in the study with median age of 32 years. Streptococcus pneumonia was the major pathogen followed by Staphylococcus aureus with 49% and 33% respectively. Drainage of empyema was between 50-750, 500-1000 and 250-600 ml for the first, second and third dose respectively. Chest pain and discomfort was the major complication (56.1%). Conclusion: streptokinase administration helps in resolving multiloculated empyema and can reduce the decortication surgery.

**Keywords:** Streptokinase, empyema, decortication, pleural effusion.

Introduction

Pleural effusion is one of the common problems in many medical specialities that will eventually seek the intervention by a thoracic surgeon for establishing diagnosis or as a definite management. The use of chest drainage techniques was well established for management of simple moderate and massive effusion [1]. Effusion complicated by empyema and failure of medical treatment and simple drainage warranted further management which might result in major surgery as decortication. Multiloculations of effusion and the start of early stages of empyema can be approaches with different strategies side by side with chest drain insertion. In the 1949 the instillation of fibrinolytic agent started by Sherry through the administration of streptokinase in the pleural cavity to open all the loculations [2]. After which the use of streptokinase was decreased due to its adverse reactions and side effects until a new purified streptokinase was introduced by Bergh and colleagues. The new purified form had great effect on loculations with very minimal adverse reactions [3].

**Material and Methods**

Between Nov, 2016 and Nov, 2018.57 patients were admitted to King Hussein Medical Centre with complicated pleural effusions due to different causes. All patient were treated initially medically with appropriate antibiotics and measurements according to hospital protocols. Patients who had failed the medical treatment and had a failed simple drainage or had complicated effusion proven by imaging studies on admission were included in this study.

Imaging techniques included chest ultrasonography, done either by the thoracic surgeon or the radiologist and showed Multiloculations and thick fluid, and chest CT scan which was also used to evaluate the lungs and the presence of loculations and pleural peel.

All patients initially had a chest drain inserted, different sizes were used according to the preference of the surgeon and according to clinical judgment and patient factors. 12 to 24 hour monitoring of the output of the drain regarding amount and nature. Failure to evacuate the effusion or an amount of less than 100 ml warranted the instillation of fibrinolytic agent (streptokinase).

Streptokinase was given in 2, 50,000 IU per dose. This dose was diluted in 50ml normal saline then installed through the chest tube catheter under a septic technique followed by immediate clamping of the
catheter for at least 4 to 6 hours in the first day and 6 to 8 hours in the second and third days. All patients were advice to change position periodically to enable good distribution of the material in the pleural cavity. Chest pain and discomfort, fever, cough and chest tightness were the complaints with which early unclamping was done.

We gave minimum of 3 doses and up to 6 doses according to response and radiological improvement. Bleeding disorder, allergy, pregnancy and post-delivery, liver and kidney disease patients were excluded from giving streptokinase.

Follow up was based on clinical improvements correlated with chest X-ray. If good drainage achieved then the chest X-ray is done at day 3. Chest tube removal is done 24 hours after the last dose with an acceptable chest X-ray

RESULTS

The administration of the fibrinolytic agent (streptokinase) has improved the drainage output in all the patients in overall. The mean age of the study group was 32 with range from 62 to 19 years. Almost Two thirds of the patients were males (63%). Result of cultures of the effusion had Streptococcus pneumoniae as the major pathogen (Table 1).

All patients received 3 doses over 3 days from the first instillation day. Output ranged from 50-750 ml per day for the first dose, 500-1000 on the second dose and 250-600 post the last dose. 35 patients (61.4%) had complete resolution of their empyema after 3 doses and were discharged on the 4th day post streptokinase. Whereas, 15 patients (26.3%) needed extra doses with up to 3 doses more to get acceptable results, and 7 patients (12.2%) underwent surgery for failure to achieve improvement (5 had VATS and 2 had open thoracotomy decortication).

Major complication of streptokinase instillation was chest pain and discomfort followed fever recorded as high as 38 °C (treated by simple paracetamol) Table 2.

All patients were discharged with acceptable chest X-ray. 2 week and 4 weeks outpatient clinic follow ups showed progressive radiological improvement. No further chest ultrasound or CT scan were needed or done.

<table>
<thead>
<tr>
<th>Pathogen isolated</th>
<th>Number of cases</th>
<th>Percentage of total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Streptococcus pneumonia</td>
<td>28</td>
<td>49</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>19</td>
<td>33</td>
</tr>
<tr>
<td>None</td>
<td>10</td>
<td>17</td>
</tr>
</tbody>
</table>

Table 2: Complications in patients after Streptokinase instillation

<table>
<thead>
<tr>
<th>Complications</th>
<th>Number of patients</th>
<th>Percentage of total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest Pain and discomfort</td>
<td>32</td>
<td>56.1</td>
</tr>
<tr>
<td>Fever</td>
<td>10</td>
<td>17.5</td>
</tr>
<tr>
<td>Haemorrhage</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Allergic Reactions</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

DISCUSSION

Failure of medical treatment of empyema post pneumonia warrant a multiteam management that involve more invasive methods. Chest tube drainage of simple effusions can lead to great results and improvements, still once complicated by loculations or the presence of pleural peel warrants further steps. Administration of fibrinolytic agent (streptokinase in our study) is the first step and surgery is the last resort.

In our study, the instillation of three doses of streptokinase (2,50,000 IU diluted in 50 ml normal saline) had shown great result in both clinical and radiological status of the patients with overall success rate of 87.7% (61.4% for 3 doses and 26.3% for further doses), which was comparable to that obtained in the randomized clinical trials by Aye[4] and Roupie [5].

Clamping of the chest drain in our study was 4–6 hours initially, which is slightly different from only 4 hours as in Bergh et al. [4]. We found that for the second dose a 6 hour clamp is the best timing for best drainage if tolerated by the patient. This was more convenient in our institution rather than less time (3 hours) as in Davies et al. [6], eliminating the need for surgery and decrease the morbidity and mortality resulting from decortication [7].

Timing of streptokinase instillation was optimal at 2–4 week from medical therapy initiation [8] and before the formation of pleural peel. Chest pain and discomfort followed by fever were evident in our study. No bleeding or allergic reaction episodes had occurred, mostly due to the purified streptokinase nature [8-10].

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CONCLUSION
Streptokinase administration through the chest drainage tube is safe and effective method in managing complicated para pneumonic effusion and can effectively alleviate the need for aggressive surgery.

REFERENCES