Original Article

A Five-Year Study of Intrapleural Fibrinolytic Therapy in Loculated Pleural Collections

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Abstract

Background. Pleural fluid loculations due to complicated parapneumonic effusion (CPE), empyema, tubercular effusion and traumatic hemothorax can be managed either by video-assisted thoracoscopic surgery (VATS) or intrapleural fibrinolytic therapy (IPFT). The former is more invasive, not easily available and is also more expensive. On the other hand, IPFT is less invasive, cheaper, easily accessible and if used early, in loculated pleural collections, break loculations and early pleural peel, thereby facilitating pleural space drainage.

Objective. To study the efficacy of IPFT in facilitating pleural space drainage in loculated pleural collections of diverse aetiologies.

Methods. A five-year retrospective, observational study of 200 patients, with loculated pleural collections and failed tube drainage and managed with IPFT was carried out. Responders were defined as those with significant volume of fluid drained and significant radiological resolution.

Results. There were 106 (53%) cases of CPE, 59 (29.5%) cases of tubercular effusion, 23 (11.5%) cases of empyema and 12 (6%) cases of hemothorax. Responders were 148 (74%) in number. The distribution of responders as per type of loculated pleural collection was as follows: CPE 88 (83%), tubercular 37 (62.7%), empyema 14 (60.8%) and traumatic hemothorax 11 (91.6%). The adverse effects were mild and included chest pain in six patients and low-grade transient fewer in three cases.

Conclusions. Intrapleural fibrinolytic therapy is a safe and cost-effective option in the management of selected patients with loculated pleural effusions. **[Indian J Chest Dis Allied Sci 2016;58:17-20]**

Key words: Loculated effusions, Complicated parapneumonic effusions, Intrapleural fibrinolytic therapy.

Introduction

When the chest tube is correctly positioned (as evidenced by postero-anterior and lateral chest radiographs) and there is a significant amount of pleural fluid, the major reasons for failed drainage are multi-plepleural space loculations or obstruction of the tube with thick and viscous fluid.[1] Pleural fluid loculations may occur in various aetiologies including complicated parapneumonic effusion (CPE), empyema, tubercular effusion and traumatic hemothorax. The various options for the management at this stage are: saline flushes, placing one or more catheters in loculi under image guidance, video-assisted thoracoscopic surgery (VATS), standard thoracotomy, drainage of empyema and decortication. The first two modalities are not so effective in improving drainage whereas last two surgical modalities are invasive, available only in specialised centres or are expensive. Fibrinolytic agents, if used early in loculated pleural collections, break loculations and resolve early pleural peel, thereby facilitating pleural space drainage. These agents possibly do not have significant liquefying effect on pus, and hence, may not be effective in the empyema stage.[2,3]

The agents that may be used for intrapleural fibrinolytic therapy (IPFT) include streptokinase (STK) and urokinase (UK). We have earlier reported our experience in loculated pleural collections related to CPE and empyema where we noted significant response without any significant adverse effects.[4] During the last few years we have been using IPFT in loculated pleural collections of other aetiologies too. The present study is a retrospective analysis of such cases.

Material and Methods

This is a retrospective study based on records of cases managed at two tertiary care chest centres of Armed

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Forces hospitals by different clinicians using the same protocol between January 2008 and December 2013. Loculated effusions of parapneumonic, empyema, tubercular and traumatic aetiologies belonging to any age group were selected for IPFT when intercostal tube drainage was less than 50mL in spite of the tube or pig tail catheter being properly positioned and functional. Imaging studies with either ultrasonography (USG) or commuted tomography (CT) were performed before the initiation of IPFT to assess the site and size of loculations and the extent of associated pleural thickening.

Contraindications to IPFT included presence of a bronchopleural fistula, major thoracic or abdominal surgery within past two weeks, coagulation defects, and previous STK administration by any route. The dosage used in adults was 2.5 lac IU of STK or 1 lac IU of UK 8 hourly. The dosing frequency of STK/UK in pediatric patients was similar with lower dosage as per the age group: STK: 100,000 IU (6-12 years), 50000 IU (1-6 years) and 25000 IU (less than 1 year); UK: 50000 IU (6-12 years), 25000 IU (1-6 years) and 10000 IU (less than 1 year). The drug was instilled through the intercostal drain by dissolving in 50mL of normal saline followed by flushing with 20mL saline in adults, in pediatric patients, the volume of fluid used was 20mL followed by flushing with 10mL saline). The tube or the catheter was clamped for two hours after each dose. Three doses of STK/UK constituted one cycle. The criteria for successful outcome were radiological resolution and the volume of pleural fluid drained. Chest radiology including USG was initially done 48 hours after one cycle of STK/UK therapy and subsequently depending upon the response to therapy. The criteria used for radiological resolution were as described by Sanchez *et al*.[5] These were: maximum (normal or near normal chest radiograph); moderate (a clearance of 50% to 80% of pleural fluid); minimal (<50% clearance); none (no change). The cumulative drainage was noted 48 hours after one cycle of STK/UK and thereafter till the removal of the chest tube. Fibrinolysis was repeated for more cycles of STK/UK in cases who had more than 100mL of cumulative drainage and minimal to moderate radiological improvement after 48 hours of the initiation of fibrinolytic therapy. Treatment was discontinued if 48 hours after first cycle of STK/UK, the cumulative drainage was less than 100mL and there was no radiological improvement. Responders to IPFT were defined as patients who had more than 500mL of cumulative drainage and maximum radiological resolution after one or two cycles of IPFT. The rest of the cases were defined as non-responders.

Results

There were total 200 patients. The demographic and clinical characteristics are presented in table. The oldest patient was 58 years old and the youngest one was one month old. The CPE was the most frequent aetiology. The average interval between the onset of loculated pleural collection and initiation of IPFT was 4.6±2.2 weeks. The STK was used in 90 (45%) cases and UK in 110 (55%) cases. One hundred and five patients (52.5%) received one cycle and 95 (47.5%) two cycles of STK/UK. Radiological resolution was maximum in 148 (74%), moderate in 34 (68%), and minimal in 18 (36%) cases. Mean cumulative drainage was 1081±187mL in 148 (74%) and 286±187mL in 52 (26%) cases. There were 148 (74%) responders. The distribution of responders as per the aetiology of loculated pleural collection was as follows: CPE–88 (83%), tubercular–37 (62.7%), empyema–14 (60.8%) and traumatic hemothorax–11 (91.6%). Response rate to the two agents was similar. Out of the 52 non-responders, the interval between the onset of loculated pleural collection and initiation of IPFT was more than 6 weeks in 39 (75%) patients. The only adverse effect observed were mild chest pain in six patients and low-grade transient fewer in three cases.

Table. Demographic and clinical characteristics

	No. (%)	Mean Age±SD
Gender		
Male	183 (91.5%)	
Female	17 (8.5%)	
Age (in years)		
Above 12	185 (92.5%)	31.7±8.4
Below 12	15 (7.5%)	6.4±2.4
Aetiology of pleural effusion		
CPE	106 (53%)	
Tubercular	59 (29.5%)	
Empyema	23 (11.5%)	
Traumatic hemothorax	12 (6%)	

Definition of abbreviations: SD=Standard deviation; CPE=Complicated parapneumonic effusions

Discussion

Sherry *et al*[6] first described the successful use of fibrinolytic agents in 1949 in 23 patients who had loculated empyema or hemothorax. Their patients received intrapleural instillation of both streptokinase and streptodornase, which was extracted from concentrated filtrates of streptococci of Lancefield group C. More reports appeared soon thereafter.[7,8] However, the initial enthusiasm waned because of significant systemic adverse effects in the form of fever, leucocytosis and general malaise. These effects were possibly due to an immunological reaction to impurities in the preparation of the agents. Bergh and colleagues[9] in 1977 used purified streptokinase and reported significant improvement in 10 of 12 patients with empyema without the need for any major surgical intervention and without any significant adverse effects.

In the last three decades or so there has been numerous case series[10] and controlled trials,[11-15] using STK/UK in CPE and empyema with significant results. Most of these studies[11-13] used the pleural fluid drainage and radiological improvement as primary outcome whereas some studies[13-15] used need for surgery, mortality, hospital stay and time for defervescence as primary outcomes. During the last 15 years or so, the intrapleural streptokinase has been used with encouraging results in our country as reflected in various case reports,[16,17] non-randomised trial[4] and randomised trials,[18,19] but with negative results in some study.[20] The IPFT has been used successfully in pediatric patients as reflected by various case reports[21,22] and a randomised control trial.[23]

A Cochrane Database systematic review (2008) comparing IPFT with placebo in adult patients with parapneumonic effusions and empyema found a significant reduction in the need for surgical intervention.[24] The most recent systematic review by Janda and Swiston[25] also observed significant reduction in the need for surgical intervention in IPFT group and also suggested a possible role in loculated effusions. The present study differed in that we used IPFT in loculated effusions of various aetiologies.

The overall success rate in all age groups in the present study was 74% almost similar to the other studies from other countries and India. The response rate of 83% and 60.3% in CPE and empyema, respectively, was also almost similar to previous studies from abroad[11-15] and India.[4,18,19] In developing countries like India, there are significant proportion of cases of loculated tubercular effusions (29.5% in the present study) and IPFT was effective in 60.8% of these cases. Use of IPFT exclusively in loculated effusion of tubercular aetiology has been studied with significant response in only previous Indian study.[18] Intrapleural fibrinolytic therapy with STK has been used in clotted hemothorax with a success rate of 91% to 93%.[26-28] In the present study, there were 12 (6%) patients of traumatic hemothorax and the percentage of responders (91%) was similar to the previously mentioned studies.[26-28]

Intrapleural fibrinolytic therapy has been recommended as a first-line therapy in traumatic hemothorax before proceeding to mini-thoracotomy or pleural decortications.[26] The number of dosages of STK/UK used in the present study ranged from 3-6, which is almost similar to other studies.[4,19]

The early initiation of fibrinolytic therapy, before the development of severe pleural adhesions, may lead to a more effective pleural drainage as has been demonstrated in an experimental study[30] and in a study by Boures *et al*.[31] In the present study, delayed treatment may be a reason in non-responders in our study since out of 52 non-responders, in 39 (75%) the interval between the onset of symptoms and the initiation of fibrinolytic therapy was more than six weeks. The same has been observed in our previous study.[4] There were no significant side effects observed during IPFT. This has been observed in majority of the previous studies too.

The comparative efficacy of STK and UK has not been studied systematically before but in the present study it was almost the same. Urokinase may be preferred over STK since the later is antigenic in nature.

Although tissue plasminogen activator (tPA) is being increasingly used in the west, its use in our country is precluded by its high cost and no evidence available regarding its efficacy better than STK/UK.

The present study has limitations. It was observational in nature and there was no control group. From the previous studies and our observations, it may be concluded that IPFT is a safe and cost-effective option in carefully selected patients in the management of loculated effusions.

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