ORİJİNAL MAKALE/ORIGINAL ARTICLE
J Turgut Ozal Med Cent 2015:22(2):99-102

Journal of Turgut Ozal Medical Center
www.jtomc.org

Intrapleural Fibrinolytic Treatment: Management of 85 Cases

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Abstract

Objective: Fibrous cortex developes over the lung in 7-10 days if the benign or malign pleural effusion consisting of blood, coagulum or empyema could not be drained. Thus, clinical conditions like trapped lung, restrictive lung disease, or dyspnea may appear as a result of fibrinous pleuritis. Both streptokinase and tissue plasminogen activator (tPA) are involved in the breakdown of proteins and fibrin. Hence, intrapleural fibrinolytic treatment (IPFT) may prevent invazive procedures by avoiding fibrous cortex develepment if it is applied at a proper time.

Materials and Methods: Eighty five cases undergoing IPFT by tube or catheter thoracostomies between 2003-2013 are evaluated retrospectively. Patients have been evaluated according to age, symptoms, diagnosis, and response to treatment.

Results: The mean age of the patients was 45.5 (65 males and 20 females). IPFT was performed in 30 patients with empyema, and in 20 and 13 patients due to postoperative or posttraumatic organised hematomas, respectively. Eleven patients underwent IPFT for loculated benign pleural effusions while 9 patients recieved the treatment for loculated malign pleural effusions. Complicated hydropneumothorax was the indication for IPFT in 2 patients. A total of sixty patients received tube thoracostomy while 25 patients underwent catheter thoracostomy. Tree patients had decortication and 4 underwent video assisted thoracoscopic (VATS) drainage due to failure of IPFT. Aseptic pleural space remained in 12 patients at the end of our study. One of the patients required blood transfusion and additional medical treatment for intrapleural hemorrhage secondary to the local absorption of the IPFT.

Conclusion: IPFT is a safe, effective treatment which can be performed prior to much invasive surgical procedures in patients with loculated empyema, clotted hemothorax, or postoperative hematoma, and benign or malign pleural effusions which can not be drained due to high fibrinous contents.

Key Words: Intrapleural; Streptokinase; Tissue Plasminogen Activator.

İntraplevral Fibrinolitik Tedavi Uygulamaları: 85 Olguluk Seri Sunumu

Özet:

Amaç: Komplike plevral efüzyonlarda sadece tüp ve katater torakostomi ile sıvıyı drene etmek her zaman mümkün olmaz. Drene edilemeyen kan, pıhtı, ampiyem, benign veya malign plevral sıvılarda 7-10 gün içinde akciğer üzerinden fibröz bir kabuk oluşmaya başlar. Bu durum ise tuzaklanmış akciğer ve akciğer restriksiyonu, sekonder ampiyem ve dispne ile sonuçlanır. Streptokinaz yada Tissue Plazminojen Activatörü (tPA), fibrin ve diğer bazı proteinleri parçalayarak etki etmekte olup uygun zamanda yapılan fibrinolitik tedavi ile bu süreç kesintiye uğratılıp, akciğer üzerinde fibröz kabuk gelişimi önlenerek hasta daha invaziv işlemlerden kurtarılabilir.

Gereç ve Yöntemler: Bu çalışmada 2003- 2013 yılları arasında tüp yada kateter torakostomisi ile intraplevral fibrinolitik tedavi (IPFT) uygulanan 85 olgu retrospektif olarak incelendi. Olgular yaş, cinsiyet, semptom, tanı ve tedaviye yanıt açısından değerlendirildi.

Bulgular: Olguların 65'i erkek, 20'si kadın, yaş ortalaması 45.5 idi. Otuz olguya ampiyem, 13 olguya travma sonrası gelişen organize hematom, 20 olguya postoperatif, 9 olguya malign plevral efüzyon, 11 olguya benign hastalıklara bağlı drene olmayan loküle plevral efüzyon ve 2 olguya hidropnömotoraks sonrası gelişen komplikasyonlar nedeniyle intraplevral fibrinolitik tedavi uygulandı. Olguların 25'sine kateter torakostomi, 60 olguya tüp torakostomi uygulandı. Olguların 7'sinde IPFT başarısız oldu, 4 olguya dekortikasyon, 3 olguya VATS (video-assisted thoracoscopic surgery) ile debridman uygulandı. Oniki olguda aseptik kısmi poş kaldı. Bir olguda lokal etkiye bağlı, kan transfüzyonu ve medikal tedavi ile kontrol altına alınan intraplevral kanama saptandı.

Sonuç: Loküle ampiyemlerde, pıhtılı hemotoraks ve postoperatif organize hematomlarda, yoğun fibrinli, drenajı olmayan malign plevral efüzyon ve benign plevral efüzyonlarda daha invaziv cerrahi girişimlerden önce uygulanacak IPFT güvenli, etkili, başarısı yüksek, yan etkisi az bir uygulamadır.

Anahtar Kelimeler: İntraplevral; Streptokinaz; Doku Plazminojen Activatör.

INTRODUCTION

Tube or catheter thoracostomy alone may not always be sufficient to drain fluid in complicated pleural effusions. Benign or malignant pleural effusions like blood, clots, or empyema that cannot be drained begins to form fibrinous layer on the lungs within 7-10 days which may cause trapped lung and lung restriction, empyema, and dyspnea. These cases may require decortication by thoracotomy or VATS. Streptokinase or tPA act by breaking down fibrin and certain proteins. Through timely fibrinolytic therapy, this cycle can be interrupted and help avoid development of fibrous shell on the lungs and, in turn, save the patient from undergoing more invasive procedures. In this study, we have evaluated the results of intrapleural fibrinolytic therapy (IPFT) in patients with pleural effusion who could not be treated with less complicated drainage methods such as tube or catheter thoracostomy.

MATERIALS and METHODS

To this end, we have retrospectively analysed 85 patients who underwent intrapleural fibrinolytic therapy with tube or catheter thoracostomy between 2003 and 2013 at Inonu University, Turgut Ozal Medical Centre, Thoracic Surgery Clinic. The patients were assessed according to age, sex, symptoms, diagnosis, type of treatment, amount of drainage, and complications.

RESULTS

65 of the patients (76.5%) were males and 20 (23.5%) were females; the mean age of the patients was 45.5 (5-86). The number of patients and the complications that required intrapleural fibrinolytic therapy were as follows: 30 (35.3%) patients for empyema, 13 (15.3%) patients for posttraumatic organised hematoma, 20 (23.5%) patients for postoperative hematoma, 9 (10.6%) for loculated pleural effusion due to malignant diseases that did not allow secondary drainage, 11 (12.9%) for loculated pleural effusion due to benign diseases that did not allow secondary drainage, and 2 (2.4%) patients for post-hydropneumothorax (Table 1).

Table 1. Reasons of IPFT administered.

Diagnosis	Number	%
Empyema	30	35.3
Posttraumatic hematoma	13	15.3
Postoperative hematoma	20	23.5
Malignant pleural effusion	9	10.6
Benign loculated pleural effusion	11	12.9
Hydropneumothorax	2	2.4

Twenty-five (29.4%) of the patients underwent catheter thoracostomy while 60 (70.6%) patients received tube thoracostomy therapy. For patients with loculated pleural fluid containing dense fibrin and, therefore, failed to have a complete drainage or radiological improvement, we planned intrapleural fibrinolytic therapy. 58 patients were administered 250000 IU fibrinolytic (streptokinase) in 100 cc SF through the pleural space. 27 patients received 5-10 mg/day of Tissue Plasminogen Activator (t-PA). The intrapleural agent was applied by catheter thoracostomy in a controlled manner into the intrapleural cavity for a period of 15-30 mins with the help of a 100 cc SF in Pleuracan set through 28 F chest catheter. After the application, according to the clinical status and type of the applied drug, we clamped the thoracostomy tube or catheter for 1 to 4 hours. In order to provide the optimal effect, the patients were encouraged to do posture exercises within the time the intrapleural fibrinolytic agent remained clamped. IPFT failed in 7 patients (8.2%). Our failure criteria were failure pleural drainage, impaired lung expansion or persistence of a large pouch. 4 patients underwent decortication while we applied debridement with VATS to 3 of our patients. Twelve (14.1%) patients were discharged with partial aseptic pouches but these pouches were fully resorbed during the follow-ups. Peroperative mortality was recorded in one of our patients who underwent VATS due to loculated malignant pleural effusion (lymphoma) with dense fibrins on the 16th day. Another patient with bilateral pleural effusion and SLE (Systemical Lupus Erythematosus) on the right side due to local effects was taken under control with blood transfusion and conservative treatment though the patient developed intrapleural bleeding. Therefore, we did not implement IPFT for this patient's loculated pleural fluid in the left side of the hemothorax but preferred debridement with VATS (Figure 1).

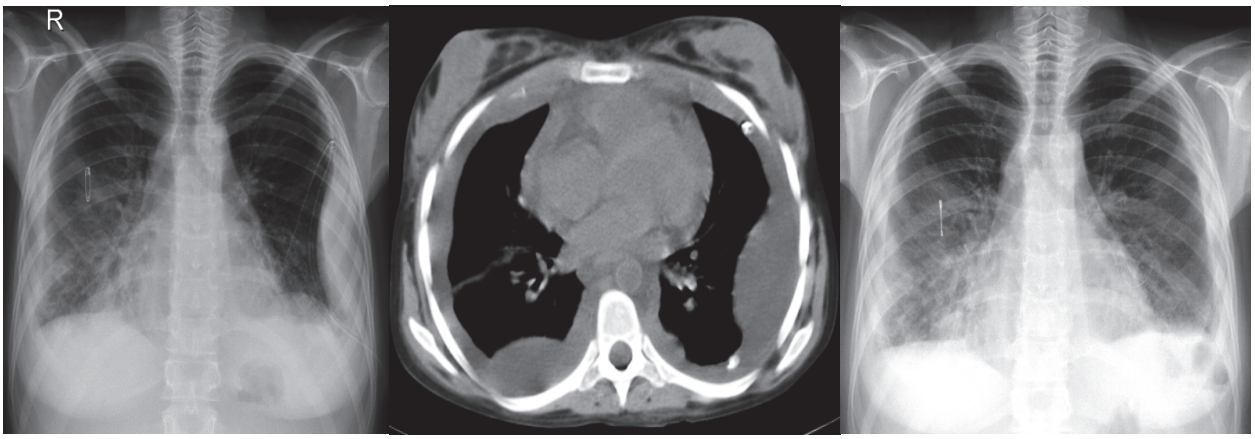

Figure 1. a) and **b)** Non-drainable pleural effusion despite catheter thoracostomy in the SLE case with bilateral pleural effusion; **c)** PA lung radiograph after IPFT.

We did not detect any reaction related to streptokinase or tPA. The intrapleural fibrinolytic application was limited to 5-7 days. In our series, the success rate of full drainage of pleural fluid with intrapleural fibrinolytic therapy was 91.8%. 8.2% of our patients did not fully respond to intrapleural fibrinolytic therapy and these patients required additional surgical intervention. All patients were monitored often by PA chest X-ray and occasionally by computed chest tomography (Figure 2).

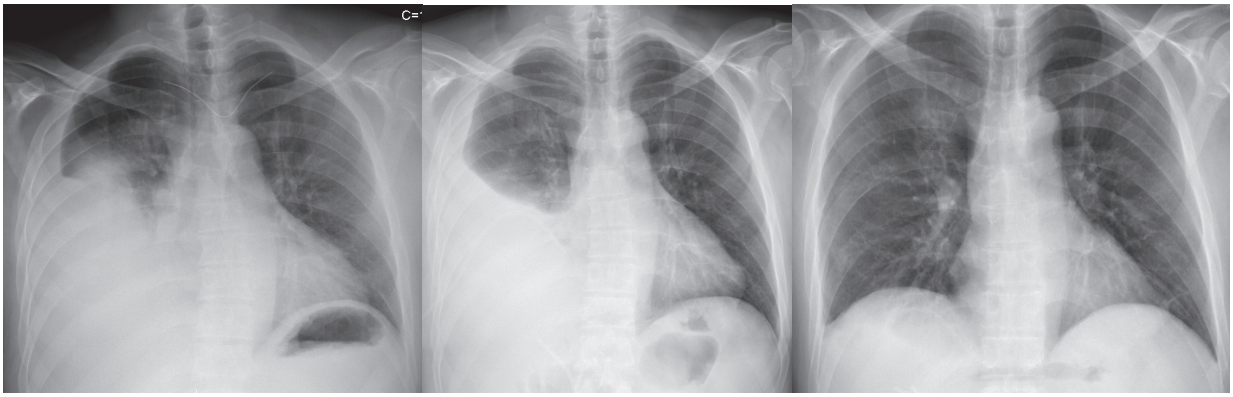

Figure 2. a) PA lung radiograph of the patient with parapneumonic pleural effusion; **b)** PA lung radiograph of the patient who could not achieve full drainage despite catheter thoracostomy; **c)** Post-IPFT PA lung radiograph of the same patient.

The radiological improvement of pleural effusion in the radiological view, achieving a daily fluid drainage of 150cc or below, and decline of the symptoms were considered a success. Sixty-one (71.7%) of the cases received intrapleural fibrinolytic therapy for three times while 19 (34.5%) patients received this therapy for four times. After the first application, the amount of drainage was reduced to 100-2000cc.

DISCUSSION

Despite many treatment options, complicated pleural effusion is still a significant reason behind morbidity and mortality today. Fibrinolytic therapy, one of the treatment options still in use since the 1950s, has been the subject of many studies concerning its effectiveness.

Although some studies take it for granted that fibrinolytic therapy increases the amount of pleural fluid drained daily while also enabling better lung expansion at discharge, it has still been put forward that it does not actually shorten healing period nor does it reduce surgical requirements or mortality rates (1, 2, 3, 4). In their study on 454 randomised patients, Maskell et al. have found out that there is no significant difference between streptokinase and placebo groups in terms of length of stay or hospital surgery requirements (5).

On the other hand, many studies report that IPFT was more successful than placebo treatment or surgical intervention alone in patients with effusion requiring fibrinolytic therapy. Thommi et al. have reached a success rate of 85% after applying tPA treatment to 120 patients with pleural effusion due to different etiologic factors. In the same study, the partial response to treatment was reported to be 8% (6). Misthos et al. have found a success rate of 67.1% and of 87.7% in patients who underwent tube thoracostomy and tube thoracostomy combined with streptokinase therapy, respectively. This latter study claims that streptokinase application significantly reduces the period of hospital stay and surgical intervention rate (7). We have come up with a similar result in our series and, using fibrinolytic agents, we have successfully treated 91% of patients who did not respond well to simple drainage methods.

The most important reason for the failure to get response to treatment in some of our patients was the fact that these patients had applied with chronic pleural effusion and already irreversible pleural thickening. The IPFT success rate varies between 44% and 100% in different series. This difference in success rates can be explained by the largely heterogeneous clinical picture of these patients and the assessment of chronic cases along with acute and subacute cases at the same time.

Studies show that effective dose range for tPA varies between 4mg/day and 100mg/day. The recommended dose for streptokinase is 250,000 U/day. Parallel to the recommended doses, we applied 250000 U/day of streptokinase and 5-10mg/day of tPA. The half-life of streptokinase is 15-30 mins; this is 4-8 mins for t-PA (8). Therefore, while we clamped the patients undergoing t-PA for 1-2 hours, we clamped the streptokinase treated patients for 2-4 hours. These are usually administered in three consecutive days. However, Diacon et al.'s study on randomised double-blind groups with streptokinase and saline solution has shown that there was a significantly higher success rate in the group that was treated with streptokinase after 7 days compared to the other groups that received the same therapy after 3 days (9). In our clinic, we continued the intrapleural fibrinolytic therapy for 1-7 days depending on the radiologic improvement of each patient.

It has been highlighted that minor complications can frequently be seen in IPFT. The most frequent complications are pain, dyspnea, and fever. These complications usually rear within the first two hours of the application and can be easily controlled with antipyretic, analgesic, and O2 treatment. However, other studies have also reported other major post-fibrinolytic therapy complications like massive bleeding, allergic reactions, respiratory failure, and cerebral air embolism (8, 10, 11, 12). In their 237-patient series, Abu Daft et al. have stated that 15 patients developed pleural bleeding and three of these patients required emergency thoracotomy (8). The incidence of bleeding was reported to be around 2-15% in numerous series (6, 13, 14). In our study, apart from minor complications, the only major complication was pleural haemorrhage in one

(1.2%) patient and this patient was treated with tPA. We controlled the bleeding with blood transfusions and fibrinolytic therapy in this patient. IPFT was even used in 2 pregnant patients developing non-drainable parapneumonic empyema safely. No complications related to the existing local treatments were observed in the mothers or infants after delivery (15). There was no IPTF-related mortality in our study.

According to studies, early surgical intervention (VATS or thoracotomy) can reduce complication rates and shorten healing process in the following clinical conditions: patients without clinical improvement despite tube drainage or tube and IPFT treatment; those with persistent fever and leukocytosis; patients with ongoing loculations in the imaging; and those without any improvement in the amount of pleural fluid (2, 3, 16, 17, 18). In our study, we applied decortication to 3 and VATS to 4 patients.

CONCLUSION

Fibrinolytic therapy is an effective method of draining the pleural space. Mechanical cleaning and debridement of the pleural space can largely be achieved with fibrinolysis. In short, intrapleural fibrinolytic therapy is a safe, effective, and successful method with fewer side effects in treating loculated empyema that cannot be drained with tube or catheter thoracostomy, clotted hemothorax and organised hematoma, and malignant or benign pleural effusions.

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Received/Başvuru: 29.08.2014, Accepted/Kabul: 24.09.2014

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For citing/Atıf için

Ulutas H, Celik MR, Kuzucu A. Intrapleural fibrinolytic treatment: management of 85 cases. J Turgut Ozal Med Cent 2015;22:99-102 DOI: 10.7247/jtomc.2014.2367