ORIGINAL ARTICLE

Role of Intrapleural Streptokinase in the Management of LoculatedParapneumonic Pleural Effusion

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ABSTRACT

Background: Para-pneumonic pleural effusions are quite common complication and add to further morbidity. Chest intubation has good role in drainage, but in few cases loculations may develop, requiring different maneuvers for drainage from medical therapy to surgical interventions. Intra-pleural streptokinase is considered as useful therapy to break the adhesions and accelerate the rate of recovery.

Methods: This study was conducted on 24 cases over the period of 2 years at ArAr region, Saudi Arabia having age 18 to 85 years with symptoms lasting for less than 2 weeks of duration. The exudative neutrophilic pleural effusion, irrespective of organism over culture, managed by ICT and not completely drained over 48 hours and having loculations on CT chest were included. Then in these cases streptokinase 250,000 units after diluting in 100 ml saline was injected and then chest tube was clamped for 4 hours. The fluid aspirated before and after instillation of SK was noted and these cases then underwent CT chest with IV contrast to see for complete drainage**.**

Results: In this study there were total 24 patients, out of which 16(66.67%) were males and 8(33.33%) females. The mean age was 40.81±13.79 years while the mean duration of symptoms was 6.30±2.75 days. The mean drain output before SK was 60.37±23.20 ml. After SK complete resolution was seen in 18(75%) out of 24 cases. The mean drain output after SK was 304.63±139.29 ml and mean time taken to resolution was 4.70±1.43 days. Eleven (68.75%) out of 16 males and 7(87.50%) out of 8 females got complete resolution (p=0.32). All 10 out of 10 cases in age group of 18 to 35 got complete resolution as compared to other groups with p value of 0.02. The cases with duration of symptoms 7 days or less had resolution in 16(94.12%) out 17 cases as compared to 2(28.57%) out of 7 with longer duration of symptoms (p=.003).There was significant association before and after SK in drain output (p=0.001). Side effects were seen in only 2 cases, one with pain and the other with mild hypersensitivity reaction.

Keywords: Streptokinase, pleural effusion,

INTRODUCTION

Pleural space is an un-usual but well reported site of infection leading to collection of free fluid labeled as pleural effusion. It is most commonly presented as a sequel of pneumonia and called as Para-pneumonic effusion. According to a study it is reported in almost 40% of the cases with pneumonia.[1]Para-pneumonic effusion can be simple exudation which may respond to antibiotics or may lead to thick and tenacious empyemathat needs intercostal drainage. The outcome is usuallygood and responds well to conventional therapies but sometimes the things get more complex.

In cases with complicated para-pneumonic effusions there is usually a high burden of disease causing organisms, leading to catastrophic reaction by neutrophils. These neutrophils metabolize the glucose and end up in acidic by product; hence leading to decrease in pH. Different markers like pro-calcitonin, pH and culture can be used to identify the bacterial infection and sometime specific orgarnism[2].The body usually shows a good immunological response to such infections in pleura, however response varied between the pathogenic organisms[3]. The pleural effusions usually present with multiple constitutional symptoms hence delaying in diagnosis. Moreover, the under-treatment interms of duration in such cases may also lead to delay in healing process. These along with other factors like DM, immunosuppression, malignancies, and drug resistance etc. conjugationally lead to active inflammatory process and fibroblast activation.[4]Thesefibroblast form adhesion in the form of strands which bind the parietal and visceral pleura and fluid is trapped in small to large pockets and called as loculated pleural effusion. This also results in deposition of a dense fibrin peel at visceral and parietal pleurae, and further delay in the expansion of the lung. Multiple agents like streptokinase,

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urokinase, alteplase and mucolytics have been used in the past for better drainiage[5,6].

MATERIALS AND METHODS

This study was conducted on 24 cases over the period of 2 years at ArArregion, Saudi Arabia from June 2014 to May 2016. The cases of age 18 to 85 years with symptomsof shortness of breath, cough, fever and chest pain lasting for less than 2 weeks having exudative neutrophilicpleural effusion caused by any organism over culture were taken. The loculations in the fluid were confirmed over CT scan chest with IV contrast. These cases were then managed by image guided intercostal chest drain (ICT) and observed for fluid drained. They were assessed after 48 hours by CT chest to look for residual fluid and loculations. The cases with complete resolution over CT chest were excluded. The cases with incomplete resolution, injection streptokinase (SK), 250,000 units after diluting in 100 ml saline was injected and then chest tube was clamped for 4 hours. The fluid drained before instillation of SK was noted and then patients were assessed on daily basis for the drain output and clinical improvement. The cases with clinical improvement underwent CT chest to see for complete drainage and absence of any fluid was labeled as complete resolution.

Statistical analysis;

This was a cross sectional study. The data was entered on SPSS version 17. The socio-demographic data like age, gender and other data like durationof symptoms, amount of fluid before and after SK were noted. The time taken for complete resolution was also noted. The mean and standard deviation were calculated for age, amount of fluid drained before and after SK, and time taken for complete resolution. Frequencies were calculated for gender, complete resolution over CT. Chi square test was used to see for significance and p value of ≤ 0.05 was taken as significant. Independent sample t test was applied to look for mean drain output before and after SK and values of≤ 0.05 was taken as significant.

RESULTS

In this study there were total 24 patients, out of which 16(66.67%) were males and 8(33.33%) females. The mean age was 40.81±13.79 years and maximum cases were in age group of 18 to 35 years having 10(41.67%) out of 24 cases. The mean duration of symptoms was 6.30±2.75 daysas shown in table 01. The mean drain output before SK was 60.37±23.20 ml. After SK complete resolution was seen in 18 (75%) out of 24 cases. The mean drain output was 304.63±139.29ml (Table 2) as compared to before SK with p= 0.0001. The mean time taken to resolution was 4.70±1.43 days. Eleven (68.75%) out of 16 males and 7 (87.50%) out of 8 females got complete resolution with insignificant p value of 0.32.

All 10 out of 10 cases in age group of 18 to 35 got complete resolution as compared to other groups with significant p value of 0.02. There was again significant association in patients presenting with duration of symptoms 7 days or less where resolution was seen in 16 (94.12%) out 17 cases as compared to 2 (28.57%) out of 7 with longer duration of symptoms (table 3). Side effects were seen in only 2 cases, one with intractable pain (4.17%) and the other with mild hypersensitivity reaction (4.17%) which was managed by a single dose of antihistamine and IV steroids

Fig. Side effect profile intrapleural streptokinase

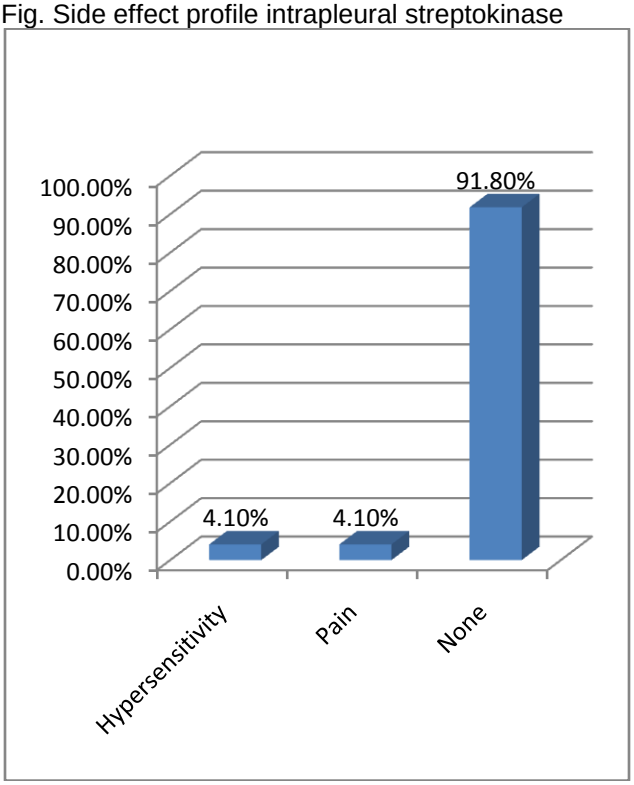


Table 1: study variables

	Mean	Range
Age	41.2+13.79	19 – 71 years
Duration of symptoms	6.46+2.75	3 – 13 days
Time taken to resolution	4.83+1.43	3 – 9 days

Table 2: Fluid output before and after streptokinase

	Mean	Range
Pre SK	60.83+23.20 ml	30 – 100ml
Post SK	312.50+139.29 ml	100 -700ml

P value 0.001

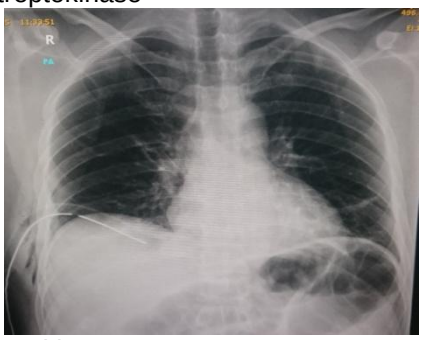
Table 3: Efficacy of SK with respect to different variables

Variables	Complete resolution		P value
	Yes	No	
Gender			
Male	11(68.75%)	5(31.25%)	0.31
Female	7(87.50%)	1(12.50%)	
Age groups			
18 - 35	10(100%)	0(00%)	0.02
36 - 50	6(75%)	2(25%)	
51 - 65	2(40%)	3(60%)	
66 - 80	0(00%)	1(100%)	
Duration of symptoms			
7 days or less	16(94.12%)	1(5.88%)	0.003
More than 7 days	2(28.57%)	5(71.43%)	

IMAGE PLATES OF PATIENTS

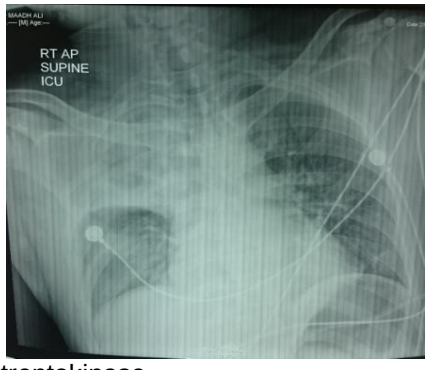
Case No.1:

Before Streptokinase



After Streptokinase

Case No. 2:



Before Streptokinase

After Streptokinase

DISCUSSION

In this study, the success rate was seen in 75% of the cases. Similar was noted by a study done by Abu-Daff S et al who found this success in cases of empyema in 85% of cases.[7]However in a study by MaskellNAet al the success rate was about 65%.[8]However in a meta-analysis where they compared with the placebo, they did not find any significant association.[9]Why the result of our study and from Abu-Daff were higher as compared to Maskell NA et al despite the same protocols of streptokinase? This might be because they used X ray chest for labeling complete resolution, which is not a good entity in cases of thick empyema, because of pleural thickening, it is unable to say it with surety about the presence or absence of further fluid. While in our study CT chest was used to assess this.

All 10 out of 10 cases in age group of 18 to 35 got complete resolution as compared to other groups with significant p value of 0.02. This was also observed by studies done by Chin NK et al and Amit B et al who also found that younger the age group, higher was the number to get early resolution[10,11].It can be explained by multiple ways. Younger population has better immunological response. Secondly, the co-morbidities like diabetes mellitus (DM) and malignancies in older age can also interfere with the healing process; hence decrease the time of resolution. Also the younger age group present early if they get any of the symptoms as compared to the older ones which linger on and correlate these symptoms as senile changes and ended up in fibrotic phase of the disease and led to decreased efficacy.

There was again significant association in patients presenting with duration of symptoms 7 days or less where resolution was seen in 16 (94.12%) out 17 cases as compared to 2 (28.57%) out of 7 with longer duration of symptoms. This was also note by DiaconAH et al and Lim TK et al who also found that the cases with earlier presentation got high success rates[12,13]. This strengthens the belief on

pharmacotherapy with the streptokinase and pathophysiology of the disease process that it works best when the adhesions are at earlier stages where fibrosis has not yet developed. At that point, this fibrinolytic therapy breaks the adhesion and in contrast if fibrotic bands are formed, then it has no role in full resolution.

Thedrain output before SK was 60.83±23.20 ml and after SK, 361.11±119.50 with significant p value of 0.001. This significant difference was also observed by studies done by Omar A et al and Abu-Daff S et al.[7, 14] The reason of this significant difference again joins back the pathophysiology. The cases with early adhesions after administration of SK revealed a very good outcome when after ahesionolysis, all free fluid was drained. However, in cases where the loculations were already fully established and there were pockets of collections of fluid, the SK was unable to break these and reach all the pockets and hence only limited area was drained where either one big pocket was present or few early septations were present.

Eleven out of 16 males and 7 out of 8 females got complete resolution with insignificant p value of 0.32. This was also seen by other studies done by RavagliaC et al and Coote N et al who also did not find any significant association.There were few limitation of this study as this did not elaborate the other co-morbidities like DM, HIV, malignancies which can affect the outcome and it also did not compare with other newer fibrinolytic agents.

CONCLUSION

Streptokinase is an effective fibrinolytic therapy in loculated pleural effusions. It is effective in every 3 out of 4 cases. It has significant association in efficacy in cases presenting within 7 days of symptoms, having age group less than 35 years and increase in drain output.

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