

Comparative Study between Medical Thoracoscope and Intrapleural Fibrinolytic Therapy in Complicated Parapneumonic Effusion and Empyema

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ABSTRACT

Background: patients with parapneumonic effusion and empyema must be managed probably to avoid surgery and decortication, the use of medical thoracoscope and instillation of streptokinase intra pleural through intercostal tube consider a modality of dealing with that medical situation.

Aim of study: it was to compare the therapeutic yield of medical thoracoscope and intrapleural fibrinolysis by streptokinase in complicated parapneumonic effusion and empyema.

Patients and methods: this study was conducted at Endoscopy Unit in Chest Department, Al- Hussin Hospitals, Al-Azhar University and Damanhur Chest Hospital in the period between May 2016 and May 2019. This study included 50 patients with complicated parapneumonic effusion and empyema. They were divided into 2 groups: Group A (25 patients): managed by medical thoracoscopy, Group B (25 patients): managed by intercostal tube drainage (ICT) plus intrapleural instillation of streptokinase as fibrinolytic agent.

Results: twenty three (92%) patients improved and 2(8%) failed in group A (thoracoscopic group) and 16(64%) patients improved and 9(36%) not completely improved in group B (Streptokinase group) with significant statistical difference.

Conclusion and Conclusion: we conclude that medical thoracoscope is very effective, successful and safe in management of such cases. Also, the use of streptokinase as fibrinolytic is safe and effective but not with the same degree of medical thoracoscope. Patients with parapneumonic effusion and empyema must be managed probably to avoid the risk of surgery and other complications.

Keywords: Medical thoracoscope, Streptokinase, Parapneumonic effusion, Empyema

INTRODUCTION

At least 40% of all patients diagnosed with pneumonia will have an associated pleural effusion, although the minority of these will require active intervention^(1,2). Parapneumonic pleural effusion refers to any effusion secondary to pneumonia or lung abscess Included patients had frank pus, pH< 7.20, positive Gram stain or culture It becomes 'complicated' when an invasive procedure is necessary for its resolution, or if bacteria can be cultured from the effusion⁽¹⁾.

Empyema is a term derived from the Greek verb empyein ('to suppurate') and literally refers to frank pus in the pleural space⁽²⁾. Complicated parapneumonic effusions and empyema are more common at both extremes of age^(2,3).

Patients will have an identifiable risk factor at presentation, which may include immunosuppressive states (most frequently HIV infection, diabetes mellitus and malnutrition), alcohol, intravenous drug abuse, poor dental hygiene or gastroesophageal reflux⁽²⁾. Intrapleural fibrinolytic therapy by streptokinase (STK) has shown benefit in various trials^(4,5).

Fibrinolytic therapy decreases viscosity, breaks loculations and pleural peel, resolves pleural sepsis, and decreases the need for invasive surgical intervention There are few case reports, and clinical trials reported from India. Intrapleural streptokinase

(STK) acts by lysing fibrin strands, thus opening pus pockets to drain^(6,7).

AIM OF WORK

The aim of this study is to compare the therapeutic yield of medical thoracoscope and intrapleural fibrinolysis by streptokinase in complicated parapneumonic effusion and empyema.

PATIENTS AND METHODS

This study included 50 patients with complicated parapneumonic effusion and empyema. Included patients had frank pus, pH <7.20 or positive Gram stain or culture. The patients were divided into 2 groups: Group A (25 patients); managed by medical thoracoscope and Group B (25 patients); managed by intercostal tube drainage (ICT) plus intrapleural instillation of streptokinase as fibrinolytic agent. All patients were subjected to full history, routine laboratory investigations, CXR, CT chest and sonar chest for evaluation and follow up.

All patients after giving written consent were subjected to the following:

- 1- Clinical history and examination.
- 2- Routine laboratory tests (CBC, liver and renal functions), CXR, chest ultrasound, CT chest, ABG, pleural fluid analysis, Biochemical analysis (pH,

proteins, LDH, glucose, total and differential white blood count "WBCs"), Microbiological assessment (Gram staining, culture and sensitivity, Ziehl Neelsen stain for AFB) and Cytological examination to exclude malignancy.

Exclusion criteria include:

Patients with tuberculus pleural effusion and patients with malignant effusion and para malignant effusion.

Ethical consideration and Written informed consent:

An approval of the study was obtained from Al-Azhar University academic and ethical committee. Every patient signed an informed written consent for acceptance of the operation.

Procedure:

Group A: managed by medical thoracoscope, the procedure was done in an especially equipped endoscopic suite in Chest department, in Damanhour Chest Hospital and Al-Hussin University Hospital. Ultrasound examination of the pleural cavity was done prior to the procedure to ensure adequate amount of effusion and proper site for insertion of the trocar.

The patient was positioned lying down in a lateral decubitus position with the affected side facing upwards to the operator, the probe of the ultrasound with its knob directed upwards is applied to the chest wall along the mid-axillary line with gel to identify the adequate dependent site for insertion of the trocar. The patient was positioned lying down in a lateral decubitus position with the involved side facing upwards. The entire lateral chest wall was scrubbed with iodopovidone conscious sedation (midazolam 5 mg) in an endoscopy room may need in some patient.

About 2 to 3 cm transverse skin incision was made by a scalpel parallel to the rib along the intercostal space chosen for trocar insertion in the wheal area form anesthesia. Blunt dissection of the intercostal tissues was performed by spreading straight clamp both parallel and perpendicular to the underlying muscles which were separated, and the parietal pleura was gently palpated by the index finger and was penetrated by the clamp.

The trocar was inserted through the incision, down the preformed tract, penetrating the pleural membrane into the pleural cavity. Cutting of adhesions and removal of pleural peels as much as possible using the Dissecting and Biopsy Forceps which was passed through channel in thoracoscope made the pleural cavity one cavity as possible opening of multiple

loculations were done by using forceps through forceps channel, lastly the pleural cavity was irrigated by normal saline.

Group B: managed by intrapleural instillation of streptokinase, 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 multiple pleural space loculations or tube obstruction by thick and viscous fluid.

The various modalities of treatment available at this stage are: saline flushes, placing one or more catheters in loculi under image guidance, thorascopic debridement, standard thoracotomy, drainage of empyema and decortication. The first two modalities are not so effective in improving drainage. The last two surgical modalities are more invasive, not easily available and, if available, are not affordable by majority of patients in the developing countries. The fibrinolytic agents, if used early in the CPE, break loculations and early pleural peel thereby facilitating pleural space drainage. undergoing intercostal tube drainage insertion in the pleural cavity, after 4hours of drainage, Streptokinase 250,000 U in 100 ml of normal saline solution was instilled through intercostal tube to the pleural cavity, tube was clamped for 8 hours then unclamped to continue drainage, this procedure was repeated daily for 4days.

Intercostal tube in both groups was left until fluid drainage becomes less than 50 ml/day. Patients of both groups received antibiotic therapy covering most likely possible organisms; third generation cephalosporin, respiratory quinolone, later readjusted according to the results of bacterial culture.

Statistical analysis

Statistical analysis was carried out using the SPSS computer package version 21.0 (SPSS Inc., Chicago, IL, USA).

The collected data were statistically managed as follows: For descriptive statistics: The mean \pm standard deviation (SD) was used for quantitative variables, the number and percentage were used for qualitative variables. For analytic statistics: The chi-squared test (X^2) was used to assess the differences in frequency for qualitative variables, while Fisher's exact test (FET) was applied if any expected cell values in a 2x2 table was <5 , while in quantitative variables, the Independent Samples t-test was used to compare between the means of both groups, the statistical methods were verified, assuming a significant level of $p < 0.05$.

RESULTS

Table (1): General characteristics of the studied groups

TVariables		Medical thoracoscopy group (n=25)		Intrapleural fibrinolysis group (n=25)		t /FET	P-value
		No	%	No	%		
Age (year)	Mean \pm SD Min – Max	52.0 \pm 7.19 33 – 67		50.88 \pm 6.01 36 – 64		0.60	0.553
Gender	Male	15	60.0	16	64.0	0.09	1.000
	Female	10	40.0	9	36.0		
Smoking habits	Smoker	15	60.0	13	52.0	0.33	0.776
	Non-smoker	10	40.0	12	48.0		
Co-morbidity	Yes	17	68.0	15	60.0	0.35	0.769
	No	8	32.0	10	40.0		

Table (2): Chest X-ray characteristics of the studied groups

CXR		Medical thoracoscopy group (n=25)		Intrapleural fibrinolysis group (n=25)		FET	P-value
		No	%	No	%		
Pre-procedure	Pleural effusion	25	100.0	25	100.0	-	-
Post- procedure 1st day	Complete improvement	2	8.0	0	0.0	2.08	0.490
	Partial improvement	23	92.0	25	100.0		
Post- procedure 5th day	Complete improvement	15	60.0	9	36.0	2.89	0.156
	Partial improvement	10	40.0	16	64.0		
On discharge	Complete improvement	23	92.0	16	64.0	5.71	0.037*
	Partial improvement	2	8.0	9	36.0		

Table (3): Time for chest tube removal of the studied groups

Time for chest tube removal (day)	Medical thoracoscopy group (n=25)	Intrapleural fibrinolysis group (n=25)	t	P-value
Mean \pm SD Min – Max	5.68 \pm 1.44 4 – 9	6.56 \pm 1.26 5 – 9	2.30	0.026*

Table (4): Hospital stay of the studied groups

Hospital stay (day)	Medical thoracoscopy group (n=25)	Intrapleural fibrinolysis group (n=25)	t	P-value
Mean \pm SD Min – Max	5.68 \pm 1.46 4 – 9	6.64 \pm 1.32 5 – 9	2.44	0.019*

Table (5): Post procedure mortality of the studied groups

Post procedure mortality	Medical thoracoscopy group (n=25)		Intrapleural fibrinolysis group (n=25)		FET	P-value
	No	%	No	%		
No	25	100.0	25	100.0		-

Table (6): Post procedure complications of the studied groups

Post procedure complications	Medical thoracoscopy group (n=25)		Intrapleural fibrinolysis group (n=25)		X ²	P-value
	No	%	No	%		
Mild bleeding	1	4.0	3	12.0	8.34	0.040*
Surgical emphysema	1	4.0	0	0.0		
Persistent empyema	2	8.0	9	36.0		
No	21	84.0	13	52.0		

Table (7): US chest pre-procedure of the studied groups

US chest pre-procedure	Medical thoracoscopy group (n=25)		Intrapleural fibrinolysis group (n=25)		FET	P-value
	No	%	No	%		
Septated pleural effusion	16	64.0	15	60.0	0.09	1.000
Pleural effusion	9	36.0	10	40.0		

Table (8): US chest 1-week post procedure of the studied groups

US chest 1-week post	Medical thoracoscopy group (n=25)		Intrapleural fibrinolysis group (n=25)		FET	P-value
	No	%	No	%		
Total improvement	23	92.0	16	64.0	5.71	0.037*
Partial improvement	2	8.0	9	36.0		

Table (9): Lung expansion and referral for surgery of the studied groups

Lung expansion and referral for surgery	Medical thoracoscopy group (n=25)		Intrapleural fibrinolysis group (n=25)		FET	P-value
	No	%	No	%		
Total lung expansion	23	92.0	16	64.0	5.71	0.037*
Partial lung expansion and referred to surgery	2	8.0	9	36.0		

DISCUSSION

This current study included fifty patients with empyema, as regard age the group A (thoracoscopic group): contains twenty five patients with age range (33 -67) years, mean (52) on the other hand the group B (STK group): contains twenty five patients with age range (36-64) years, mean (50) and no significant statistical difference. Regarding sex in the group A (thoracoscopic group): contains 15 male patients and 10 female patients, on the other hand the group B (STK group): contains 16 male patients and 9 female patients with and without significant statistical differences (table 1) in agreement with **Hewidy and Elshafey**⁽⁸⁾ reported the same as age. This study included 40 patients (24 males and 16 females) with empyema. The patients were randomly divided into two groups, medical thoracoscopy (MT) group 1 and group 2 intercostal tube with streptokinase group and both groups were compared with regard to clinical,

laboratory, radiological and hospital stay duration endpoints.

As regard smoking habit the group A (thoracoscopic group): contains 15 patients smokers and 10 patients nonsmokers, on the other hand the group B (STK group): contains 16 patients smokers and 9 patients non smokers with no significant statistical difference. Regarding general comorbidity in group A (thoracoscopic group): 17 patients have chronic disease as hypertension and 8 patients have not a chronic disease in group B (STK group): 15 patients have a chronic disease and 10 patients have not a chronic disease with no significant statistical difference (table 1). Regarding CXR at time of presentations for patients in group A 25 patient with pleural effusion, on discharge 23 patients were completely improved (92%) and 2 patients (8%) partial improved and referred for further maneuver (table 2).

Group A in agreement with **Hewidy and Elshafey**⁽⁸⁾. In group 1 from 20 patients, 19 patients

(95%) were improved and 1 patient (5%) partially improved and referred for further maneuver. In **Marten et al.**⁽⁹⁾ reported 127 patients with empyema in comparable with group A (thoracoscopic group) in the present study, 115 patients (91%) CXR improved at time of discharge and 12 patients referred for further maneuver (**table 2**). **Tassi et al.**⁽¹⁰⁾ reported 69 patients with empyema managed by medical thoracoscope as group A (thoracoscopic group) in the present study, 64 (93%) patients CXR improved and 5 (7%) patients not improved CXR and referred for further maneuver. Group B in the present study, CXR at time of presentations for 25 patient with pleural effusion, on discharge 16 patients were completely improved (64%) and 9 patients (36%) partial improved and referred for further maneuver (**table 2**). Group B (STK group) in agreement with **Hewidy and Elshafey**⁽⁸⁾ in group 2 (STK group) from 20 patients 12 patients (60%) were improved and 8 patients (40%) partially improved and referred for further maneuver.

Andreas et al.⁽¹¹⁾ reported in comparable with group B (STK group) 44 patients with empyema divided them into 2 groups Group 1, 22 patients by instillation of streptokinase intra pleural through intercostal tube 250,000 iu with mean 4.5 and SD 2 days. Group 2, 22 patients used normal saline to wash intrapleural through intercostal tube to compare both groups' results. In group 1, 15 patients (68.1%) were improved totally in CXR and 7 patients (31.8%) not improved at general and in CXR in agreement with group B in the present study we used Streptokinase 250,000 U in 100 ml of normal saline solution was instilled through intercostal tube to the pleural cavity, tube was clamped for 8 hours then unclamped to continue drainage, this procedure was repeated daily for 4 days (**table 2**).

In **Andreas et al.**⁽¹¹⁾ group 2 (saline group) 9 patients were improved (40%) and 13 patients not improved (60%). **Andreas et al.**⁽¹¹⁾ study proved that streptokinase is working and successful facility for dealing with empyema in agreement with the present study. Also, **Masood et al.**⁽¹²⁾ study was conducted on 45 patients (40 males and 5 females) with a mean age of 40 years. Bedside intercostal tube drainage was done by conventional chest tube (24-30 F) in all patients. The median dose of STK used was three-times for 3 days. There was significant drainage $1,000 \pm 110$ ml (mean \pm SD) and radiological clearance in 30 (67%) cases.

The remaining 15 patients had insignificant drainage (300 ± 100 ml) and minimal radiological resolution. **Masood et al.**⁽¹²⁾ study in comparable with group B (STK group) in the present study in CXR 30 patients (67%) improved and 15 patients (33%) not improved in agreement with the present study. According to CXR results with significant statistical difference between group A and group B in the present

study. Regarding the time of chest tube removal of studied groups Group A (thoracoscopic group) mean 5.86 and SD 1.44 with range (4-7) days. In group B (STK group) mean 6.56 and SD 1.26 with range (5-9) days (**table 3**).

Ahmad et al.⁽¹³⁾ study on role of thoracoscope in empyema in comparison of group A (thoracoscopic group) in the present study the time for chest tube removal for 30 patients in this study were, mean 6.3 and SD 1.2 with range (4-9) days in agreement with group A in the present study results. In **Marten et al.**⁽⁹⁾ study the time for chest tube removal, mean is 7.5 days agreement with group A in the present study results. **Andreas et al.**⁽¹¹⁾ in comparable with group B (STK group) reported the time for chest tube removal, mean 8.2 days. The time for chest tube removal in the present study was with significant statistical difference. In the present study according to hospital stay of both studied groups in group A (thoracoscopic group), mean 5.68 and SD 1.46 with range (4-9) days. In group B (STK group), mean 6.64 and SD 1.32 with range (5-9) days.

Most studies^(Ref) not talking about hospital stay as most patients after chest tube removal were discharge from hospital, but in some patients in the present study we wait about 24 hours to follow up patients with symptoms as fever or chest pain for reassurance. **Hewidy and Elshafey**⁽⁸⁾ Study reported hospital stay in group 1 (thoracoscopic procedures), mean 4.70 and SD 1.45 and in group 2 (STK instillation), mean 6.95 and SD 2.04 in agreement with the present study (**table 4**). According to hospital stay in both groups in the present study there is a significant statistical difference. According to post procedure mortality rate in the present study among 50 patients were zero in agreement with **Hewidy and Elshafey**⁽⁸⁾ study (**table 5**).

Ahmad et al.⁽¹³⁾ in comparison of group A in the present study in 30 patients (thoracoscopic procedure) were zero. **Tassi et al.**⁽¹⁰⁾ reported 69 patients with empyema managed by medical thoracoscope as group A in the present study with no mortality rate among the patients. In disagree with the present study in group B (STK group) **Andreas et al.**⁽¹¹⁾ in comparable with group B, one patient in each group died during hospitalization because of overwhelming sepsis (saline group) and newly diagnosed small-cell lung cancer but the cause of death in 2 patients were away of the use of streptokinase or normal saline. Regarding post procedure complication of studied groups in group A (thoracoscopic group) one patients with surgical emphysema, one patient with mild bleeding and 2 patients with persistent empyema, the persistent empyema not truly a complication but normal failure rate, in group B (STK group) 3 patients with mild bleeding and 9 patient with persistent empyema with significant statistical difference (**table 6**).

In disagree with the present study in comparable with group A (thoracoscopic group). **Marten et al.**⁽⁹⁾ study reported 127 patients with empyema in comparable with group A in the present study, 115 patients (91%), 115 patients from 127 patients included in this study were improved at time of discharge with no post procedure complications, in the present study group A, were two patients with complications, one patient developed mild bleeding controlled by injections of adrenaline as a vasoconstrictor drug during procedure and stopped rapidly and the other patient developed mild surgical emphysema around the site of incision and improved without any medical interference just we follow up it for 5 days after procedure. But, **Marten et al.**⁽⁹⁾ in agreement with present study in persistent empyema and referral for further maneuver. In comparable with group B in the present study (STK group), **Masood et al.**⁽¹²⁾ study was conducted on 45 patients Bedside intercostal tube drainage was done by conventional chest tube in all patients STK used was three-times for 3 days with one patient developed mild fever and one another patient developed chest pain controlled by analgesic, this result proved the safety and efficacy of streptokinase as management of empyema in agreement with the present study. Regarding the use of chest ultrasound in the present study in group A (thoracoscopic group), 16 septated pleural effusion and 9 patients with free pleural effusion, in group B (STK group), 15 septated pleural effusion and 10 patients with free pleural effusion with no significant statistical difference (table 7). According to US follow up after one week in group A 25 patient with pleural effusion, on discharge 23 patients were completely improved (92%) and 2 patients (8%) partial improved and referred for further maneuver. Group B in the present study, US follow up in 25 patient with pleural effusion, on discharge 16 patients were completely improved (64%) and 9 patients (36%) partial improved and referred for further maneuver with significant statistical difference (table 8).

As regard lung expansion and referral for surgery for 50 patients were in the present study, lung expansion was assessed by CXR, CT chest and chest US with the result as radiological assessment in group A 25 patient with, on discharge 23 patients were completely improved and lung expanded (92%) and 2 patients (8%) partial improved and referred for further maneuver. Group B in the present study, 25 patient on discharge 16 patients were completely improved and lung expanded (64%) and 9 patients (36%) partial improved and referred for further maneuver with significant statistical difference (table 9).

These results in the present study are in agreement with **Reynard et al.**⁽¹⁴⁾ who reported five cases of pleural empyema successfully treated with medical thoracoscope as 100% cure rate the small

deference in percentage is due to a little number of patients in this study. In agreement of the present study **Ravaglia et al.**⁽¹⁵⁾ reported that medical thoracoscope was successful management without any additional interventional procedures in 35 of 41 (85.4%) patients with empyema in agreement with group A managed by thoracoscope in the present study. In another study in comparable with the present study **Soler et al.**⁽¹⁶⁾ also reported on 16 patients with empyema, in whom after a failure of tube drainage attempt, MT was performed for debridement and insertion of a chest tube. MT was successful in the treatment of 12 of 16 (75.0%) patients included in the study.

Solar study is deferent of the present study as they deals with patients after failure of intercostal chest tube drainage to remove and deadhesion of septa and open locules to good drainage In the present study we interfered with patients with empyema by medical thoracoscope from the start as one procedure is best for patient and less in complication and for patient tolerance and more compliance. **Ohuchi et al.**⁽¹⁷⁾ in another study of 29 patients, the majority (79%) were successfully managed with medical thoracoscopy (MT) in agreement with group A managed by thoracoscope in the present study.

CONCLUSION AND RECOMMENDATION

We conclude that medical thoracoscope is very effective, successful and safe in management of patients with parapneumonic effusion and empyema. Also, we conclude that the use of streptokinase as fibrinolytic is safe and effective but not with the same degree of medical thoracoscope. The patients with parapneumonic effusion and empyema must be managed probably to avoid the risk of surgery and other complications.

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