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Original Article

Short Term Outcome of Plasma Pleurodesis in Post Pulmonary Resections Persistent Air Leak

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Abstract

Background: Air leak is the most common morbidity after pulmonary resection surgery. It may result in prolonged duration with chest tubes with their annoying chest pain, prolonged hospital stay time with increased financial costs, pneumonia, empyema, and patient dissatisfaction. Our objective was to evaluate the efficacy of plasma pleurodesis for stoppage of air leak after lung resection, in comparison to conservative measures.

Methods: This prospective single-blinded randomized study included 60 patients randomly divided into two groups. Group A: included 30 patients who received intrapleural fresh frozen plasma. One bag of FFP, contains 250 ml of plasma, matched for the ABO group was installed through the apical chest tube into the pleural cavity. Group B: a control group of 30 patients who did not receive any sclerosing agent. They were managed with under-water seal and observation.

Results: This study showed that the stoppage of air leak in group A was faster "which stopped in 9-10 days" in comparison to control group B "24-25 days", (P-value <0.001). There was a significant difference between groups A and B regarding the hospital stay, which was in 9-10 days in group A in comparison to group B "26-28 days (P-value <0.001).

Conclusion: Intrapleural fresh frozen plasma appears to be a valuable option to stop persistent air leaks post pulmonary resections. It's a cheap, available, and safe agent. It reduced hospital stay, costs and morbidities.

KEYWORDS

Persistent air leak; Intrapleural fresh frozen plasma injection; Pulmonary resection

Article History

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Introduction

Persistent Air leak (PAL) remains a challenging complication for thoracic surgeon. It is one of the most common complications after pulmonary resection. It is of variable degrees as it may be due to alveolar-pleural fistula (APF) or bronchopleural fistula (BPF). PAL is common after lung surgery, especially lung volume reduction surgery (LVRS) and resection. Its incidence was reported up to 26% [1].

It was difficult to define persistent air leak (PAL). However, many authors considered air leaks lasting longer than 5–7 days post-operative as persistent. However, no true consensus exists to define the PAL Most air leaks stop spontaneously

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within 5 days of surgery and are managed by observation in the presence of the chest tube [2].

Many risk factors contribute for PAL. Some of these are the low forced expiratory volume in the first second (FEV1), patients with underlying lung disease, pleural adhesions, patients on steroids or with low immunity, previous chemotherapy or radiation, and diabetes [3].

Different modalities were described to treat PAL starting by observation and then pleurodesis using different chemicals or sealants, Heimlich valve, one-way endobronchial valve, and reoperation. One of these was the fibrin sealants that act by simulating the final step in the clotting cascade to seal the site of air leakage. However, they carry the risk of bloodborne diseases if human plasma or animal proteins are used as they are potentially antigenic. In addition to potential growth for microbes that can increase postoperative infection rates [4].

Chemical sealants have some side effects besides their cost including fever, severe pain, allergic reaction, acute lung injury, breathlessness, dense adhesions with lung restriction, and pleural loculations with empyema [5].

The intrapleural administration of fresh frozen plasma (FFP) is a new modality aimed at stopping air leaks after pulmonary resections with the advantage of avoiding the adverse effects of other chemical agents used in pleurodesis [6].

Our objective was to evaluate the efficacy of plasma pleurodesis for stoppage of air leak after lung resection, in comparison to conservative measures.

Patients and Methods

Research design

Our study was a prospective single-blinded randomized study conducted on (60) patients with persistent postoperative air leaks between February 2020 to December 2021 in Cardiothoracic Surgery Department at Kafr El-Sheikh and Benha University Hospitals.

Patients in the study were divided into 2 groups: 1) Group A: included 30 patients who received intrapleural fresh frozen plasma and 2) Group B: a control group of 30 patients who did not receive any sclerosing agent. They were managed with under-water seal and observation.

Inclusion and Exclusion criteria

The study included patients at any age of both genders, patients with air-leaks unchanged at the 7th day post-Operatively, patients with above moderate and expiratory only air-leaks. Standardized surgical procedure and post-operative management, spirometry, and physiotherapy were followed in all patients. We excluded patients sensitive to blood products, patients with bronchopleural fistula, patients with Pneumothorax in chest x-rays.

We have used sealed envelopes as a method for randomization. The sample size was calculated on the basis of previously published data by Konstantinou et al. who reported a minimum success rate of 92% and a maximum success rate of 98% after intrapleural infusion of FFP. Thus, assuming mean efficacy to be 95%, and a non-inferiority margin (delta) of 5.51%, a sample size of 60 patients was accepted to demonstrate non-inferiority at 80% power.

The procedure

It was done under complete aseptic conditions. A side-way was connected between the apical chest tube and the line of the underwater seal. Through this side-way, an infusion line attached to the plasma bag could be infused into the apical chest tube.

FFP is infused into the pleural space via the apical tube by elevating the infusion line high above the bed. This should take only few minutes. One bag of FFP “contains 250 ml of plasma”, matched for the ABO group, is used. During infusion, the basal chest tube is clamped to prevent the plasma from leaking into the underwater bottle while the air will be allowed to escape through the apical one.

After that, the patient will be then asked to roll over in the bed and to change his posture every 20

Table 1: Distribution of the studied groups regarding their age and sex

	Cohort (n=30)	Control (n=30)	P value
Age			
Mean ± SD	40.4 ± 9.59	41.2 ± 9.78	0.745
Min – Max	24 - 55	24 - 55	
Median (IQR)	41 (33.5 – 48.25)	43.5 (32.75 – 48.25)	
Sex			
Male	21 (70.0%)	20 (66.7%)	0.781
Female	9 (30.0%)	10 (33.3%)	

minutes for about 2 hours to ensure uniform distribution of the FFP within the pleural cavity. After six-eight hours, the side-way is taken out, and chest tubes will be both connected again their underwater seal. When the air leak stops, the basal chest tube will be removed and on the next day, the apical chest tube could be removed.

Data collection

Data regarding end-points of outcome was collected as continuous values by an individual blinded to the patient's group allocation. We have considered the stoppage of air leak as the primary outcome and hospital stay as the secondary outcome.

Ethical consideration

The study was conducted after an approval from our institutional ethical committee.

Statistical analysis:

Data management and statistical analysis were performed using SPSS version 21 (IBM, Armonk, New York, United States). Non-parametric quantitative data were presented by mean, SD, range, median, Interquartile range (IQR) and it was evaluated by Mann Whitney U test. Categorical data were presented by number and percent and evaluated by chi square test and when it was inappropriate, it was replaced by Monte Carlo Exact test. P value was considered significant at the level of < 0.05 and highly significant at the level of < 0.001.

Results

Age and sex distribution among the studied patients were shown in Table 1. We have not found a significant difference between both groups when we had compared age and sex distribution (p > 0.05). Furthermore, we have not reported a significant statistical difference between the two groups regarding the risk factors as shown in Table 2.

Table 2: Distribution of the studied groups regarding risk factors

Risk factors	Cohort (n=30)	Control (n=30)	p
Diabetes			
No	21 (70.0%)	22 (73.3%)	0.774
Yes	9 (30.0%)	8 (26.7%)	
Emphysema			
No	24 (80.0%)	23 (76.7%)	0.745
Yes	6 (20.0%)	7 (23.3%)	
PLI			
No	25 (83.3%)	25 (83.3%)	1.00
Yes	5 (16.7%)	5 (16.7%)	
Smok.his.			
No	20 (66.7%)	20 (66.7%)	1.00
Yes	10 (33.3%)	10 (33.3%)	

PLI: Previous lung infection; Smok.his.: smoking history

We have reported the different surgical procedures used in all patients and regarding the procedures, the statistical difference was not significant. Table 3 shows these details.

This study showed that the difference in the stoppage of air leak was highly significant between groups where in group A it was faster "which stopped in a mean of 9.3 ± 0.48 days" in comparison to control group B "16.5 ± 8.34 days", (P-value <0.001) as shown in Table 4.

Furthermore, the total success rate of air leak stoppage in group A was 70% (21 patients) and

90% (27 patients) after 24 and 48 hours of intrapleural plasma instillation respectively. In three patients (10%) air leak stopped within 3-5 days after plasma instillation. In control group, the success rate was 40% (12 patients) within 10 days postoperative, 70% (21 patients) within 14 days. In 30% (9 patients) the air leak stopped between 15 and 30 days.

Table 3: Surgical procedures used in all patients

Operations	Cohort (n=30)	Control (n=30)	p
Lobectomy	12 (40.0%)	11 (36.7%)	1.00
Decortication	8 (26.7%)	9 (30.0%)	
Segmentectomy	6 (20.0%)	6 (20.0%)	
VATS Bullectomy	3 (10.0%)	3 (10.0%)	
Pericardiectomy	1 (3.3%)	1 (3.3%)	

When comparing the length of hospital stay, the p-value was highly significant (<0.001) between both groups. The mean stay duration was in 10.3 ± 1.52 days in group A in comparison to group B "18.5 ± 7.78 days". These values are presented in Table 4.

Discussion

In our study, the total success rate of air leak stoppage in group A where it was 70% (21 patients) and 90% (27 patients) after 24 and 48 hours of intrapleural plasma instillation respectively. In three patients (10%) air leak stopped within 3-5 days after plasma instillation. Konstantinou F et al reported nearly similar results where the success of FFP in stopping air-leak post lobectomies for lung cancer was in 90 patients (92%) and in 96 patients (98%) within 24 and 48 hours respectively. Though we differ with Konstantinou F. et al in that they focused on PAL post lobectomies for cancer patients, while we included a variety of resections, not only lobectomies [6].

The work done by Stamenovic et al. on plasma pleurodesis showed high success 76.5-80% in two cohorts which were similar to ours. They used a different approach including three treatments "250 ml of plasma once daily for three consecutive days which we disagree with and so we used a single treatment of the same amount of plasma "250ml". They also focused on miscellaneous lung surgeries as we reported. They started plasma pleurodesis treatment after 3 days of sustained air leak which was earlier than what we have done. We started treatment of sustained air leak on the 7th day post-operative [7].

A review by Moon Y on plasma pleurodesis focused on the scarcity of literature on the usage of intrapleural plasma instillation for the treatment of air leak. He mentioned both studies by Konstantinou F. et al and Stamenovic et al. and discussed their success, their limitations, and his remarks on them. We tried to avoid many of these limitations when feasible. Our study was designed to be prospective, which Moon Y agreed on as he criticized the retrospective design of Stamenovic et al. Our groups were homogenous as much as possible "same surgeries, same age range, same standard surgical procedure" which again what Moon Y noticed to be lacking in Stamenovic et al study as their data were heterogeneous [8].

Table 4: Distribution of the studied groups regarding stoppage of air leak and hospital stay

Variables	Control (n=30)	Cohort (n=30)	p
Stoppage of air leak (in days)			
Mean ± SD	16.5 ± 8.34	9.3 ± 0.48	<0.001
Median (IQR)	14 (14 – 15)	9 (9 – 10)	
Hospital Stay (days)			
Mean ± SD	10.3 ± 1.52	18.5 ± 7.78	
Min – Max	9 – 14	10 – 31	<0.001
Median (IQR)	10 (10 – 11)	15 (15 – 16)	

Postoperative management for PAL includes pleurodesis by irritating the pleura using sclerosant agents such as (talc powder, Doxycycline, or Bleomycin), or the trial of enhancing clot sealing by autologous blood infused into the pleural space. However, reoperation is sometimes required to repair of the air-leaking site [9].

Effectiveness and complications of sclerosing agents and the use of autologous blood have been evaluated. Gözübüyük A et al reported side effects of both Talc and tetracycline. Despite the fairly effectiveness of tetracycline, fewer but serious complications were reported such as alveolar collapse with hemorrhage, inflammation, and pulmonary edema. In addition to systematic adverse effects. Such side effects were not encountered with plasma pleurodesis which makes it a safer and more viable option [10].

Sleijfer S studied Bleomycin as an alternative sclerosing agent. They have reported modest efficacy with using bleomycin. However, it is expensive. They have reported rare, but fatal pulmonary toxicity and anaphylaxis. It is worth noting that up to 45% of the intrapleurally instillated bleomycin enters the circulation. Plasma on the other hand is cheap, available and have a far safer profile with no such extreme side effects and it doesn't enter the bloodstream [11].

As regard to Autologous blood, although non-toxic, and carry less hazardous side effects and could stop air leak within 72 hours as reported by Andreetti et al achieving best results in his study population "25 patients received treatment VS 15 patients in a control group" by injecting 50-100 mL of autologous blood intrapleural after day 6 post-operative [12].

Williams P et al reported that using autologous blood injection has the risk of causing tension pneumothorax by clotting the chest drain. Furthermore, blood is a good media for bacterial growth [13]. It was also reported by Ploenes et al to have inferior results when used for pleurodesis [14].

We have found many benefits regarding the use of FFP for treating air leaks. First, it is safe with near-zero risk of local or systemic complications. In addition, the presence of anti-bodies in the fresh plasma helps to protect against infection. Second, it is easy to apply and tolerable by patients. Third, it is not expensive and cost-effective because 70% of the plasma-treated patients were discharged after the 8th postoperative day, 90% after the 9th day, and 100% within the 14th postoperative day, which was a meritorious achievement considering our past experience in patients with post-resection PAL. Such promising results can then be applied afterwards and alleviate the burden of significant hospital costs. The follow up of the cohort group at two-week period showed neither recurrence nor pneumothorax in chest radiographs.

Study limitations

Limitations included the bias of enrolling patients with variable degrees of air leakage, and we have studied only the early outcome till the time of home discharge.

Conclusion

This study showed that using fresh frozen plasma as an agent for pleurodesis is an ideal option in terms of efficacy, safety and reducing hospital stay and costs.

Conflict of interest: Authors declare no conflict of interest.

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