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Original Article / Özgün Makale

The effectiveness of blood amount used in pleurodesis to prevent prolonged air leakage

Plöredezde kullanılan kan miktarının uzamış hava kaçağını önlemedeki etkinliği

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ABSTRACT

Background: This study aims to investigate the effects of different amounts of blood used in autologous blood patch pleurodesis on clinical outcomes in patients with secondary spontaneous pneumothorax.

Methods: Between January 2015 and April 2019, a total of 42 patients (36 males, 6 females; mean age 52.1±16.0 years; range, 25 to 83 years) with SSP treated in our clinic with persistent air leakage for more than seven days were retrospectively analyzed. The patients were divided into two groups as receiving 60 mL autologous blood patch pleurodesis (Group 1, n=20) and 120 mL autologous blood patch pleurodesis (Group 2, n=22). Data including age, gender, operation side, complications, recurrence rates, time to tube withdrawal, and length of hospital stay were recorded and compared between the groups.

Results: The mean duration of air leakage was 3.3±2.4 (range, 1 to 11) days, the mean number of pleurodesis was 1.6±0.7 (range, 1 to 3), the mean time to tube withdrawal was 5.2±3.3 (range, 1 to 16) days, the mean length of hospitalization was 7.1±3.6 (range, 3 to 18) days. There were statistically significant differences in all variables analyzed between Group 1 and Group 2 (p<0.001).

Conclusion: Autologous blood patch pleurodesis is an effective and safe method in the treatment of prolonged air leakage in secondary spontaneous pneumothorax. In addition, 120 mL of blood seems to be more effective option for pleurodesis.

Keywords: Air leakage, blood, pleurodesis, pneumothorax.

ÖZ

Amaç: Bu çalışmada sekonder spontan pnömotorakslı hastalarda otolog kan yama plörodezinde kullanılan farklı kan miktarlarının klinik sonuçlar üzerindeki etkileri araştırıldı.

Çalışma planı: Ocak 2015 - Nisan 2019 tarihleri arasında kliniğimizde tedavi edilen ve yedi günü geçmiş inatçı hava kaçağı olan sekonder spontan pnömotorakslı toplam 42 hasta (36 erkek, 6 kadın; ort. yaş 52.1±16.0 yıl; dağılım, 25-83 yıl) retrospektif olarak değerlendirildi. Hastalar 60 mL otolog kan yama plörodezi yapılanlar (Grup 1, n=20) ve 120 mL otolog kan yama plörodezi yapılanlar (Grup 2, n=22) olmak üzere iki gruba ayrıldı. Yaş, cinsiyet, işlem tarafı, komplikasyonlar, nüks oranları, tüpün çekilme süresi ve hastanede kalış süresi dahil olmak üzere veriler kaydedildi ve gruplar arasında karşılaştırıldı.

Bulgular: Ortalama hava kaçağı kesilme süresi 3.3±2.4 (dağılım, 1-11) gün, ortalama plörodez sayısı 1.6±0.7 (dağılım 1-3), ortalama tüp çekilme süresi 5.2±3.3 (dağılım, 1-16) gün ve ortalama hastanede kalış süresi 7.1±3.6 (dağılım, 3-18) gün idi. İncelenen tüm değişkenlerde Grup 1 ve Grup 2 arasında istatistiksel olarak anlamlı farklar bulundu (p<0.001).

Sonuç: Otolog kan yama plörodezi, sekonder spontan pnömotoraksta uzamış hava kaçağının tedavisinde etkili ve güvenli bir yöntemdir. Ayrıca, 120 mL kan ile yapılan plörodez daha etkili bir seçenek olarak görünmektedir.

Anahtar sözcükler: Hava kaçağı, kan, plörodezis, pnömotoraks.

Since there is an underlying lung disease in secondary spontaneous pneumothorax (SSP), its complications and mortality rates are higher, compared to primary spontaneous pneumothorax. Although the initial treatment of SSP is tube thoracostomy, lung collapse and prolonged air leakage for more than seven days are seen in approximately one-fourth of these patients.[1]

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Prolonged air leakage is one of the most challenging issues in thoracic surgery. Although different treatment modalities vary from patient to patient, there is still controversy regarding the optimal treatment of this devastating complication. Pleurodesis is an excellent method for treating prolonged air leakage.[2] In addition to surgery, different types of sclerosing agents such as talcum powder, antibiotics, antineoplastic agents, and autologous blood may be used in this method.[2] Although there are different opinions regarding the timing of the administration and amount of blood to be transfused in autologous blood pleurodesis, there is a general agreement that it can be used as an effective method in the treatment of SSP.[3-8]

In the present study, we aimed to investigate the effectiveness of different blood amounts on time to stop air leak, the occurrence of complications, duration of chest tube removal, and duration of hospitalization in patients with SSP.

PATIENTS AND METHODS

In this retrospective study, medical records of a total of 102 patients who were complicated by SSP and treated in our clinic between January 2015 and April 2019 were reviewed. Twenty patients who received only tube thoracostomy, thoracentesis, or nasal oxygen and 40 patients who underwent surgery were excluded from the study. Forty-two patients (36 males, 6 females; mean age 52.1±16.0 years; range, 25 to 83 years) with persistent air leakage of more than seven days due to a first-episode spontaneous pneumothorax and who had a radiologically proven bullous lung pathology were included in the study. Autologous blood pleurodesis was applied to these patients after a seven-day time limit. The patients were divided into two groups as receiving 60 mL and 120 mL autologous blood patch pleurodesis in Group 1 (n=20) and Group 2 (n=22), respectively. The prevalence of bullous emphysema and lung parenchyma status were not considered in the randomization. Data including age, gender, operation side, complications, recurrence rates, tube withdrawal, and length of hospital stay were recorded and compared between the groups.

A written informed consent was obtained from each patient. The study protocol was approved by the University of Health Sciences, Bursa Yüksek İhtisas Training and Research Hospital Ethics Committee. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Pleurodesis technique

Blood samples of 60 and 120 mL were taken from the femoral vein of the patients with SSP and immediately given to the pleural cavity with the help of apical chest tube (28F), without the use of anticoagulants. No sedation or analgesia was applied. Twenty milliliter of standard saline was administered immediately after the blood to prevent coagulation in the drain and to allow all blood to enter the thoracic cavity. The procedure was performed under aseptic conditions at the bedside. The chest tube was, then, raised 40 to 50-cm above the patient to prevent blood return to the tube (Figure 1). To avoid the increase or recurrence of pneumothorax, clamping of the chest tube was withheld during and after delivery of blood to the pleural space. To ensure optimal distribution of blood in the thoracic cavity, the patients were instructed to change positions in the bed for three hours (left decubitus, right decubitus, Trendelenburg, and Fowler) every 15 min. A posteroanterior chest X-ray was taken the next day. The chest tube was terminated on the same day, if the air leakage was stopped and the lung was expanded. In patients with ongoing air leakage, these procedures were repeated two days later. None of the patients had respiratory failure, cough, or other side effects, and had no significant decrease in the hematocrit values.

Statistical analysis

Statistical analysis was performed using the IBM SPSS version 25.0 software (IBM Corp., Armonk, NY, USA). Data were presented in mean ± standard deviation (SD), median (min-max), or number and frequency. The chi-square test, Fisher's exact test, independent samples t-test, and Mann-Whitney U test

Figure 1. Chest drain is hooked up over a drip-stand allowing air to escape, while blood pleurodesis remains within the chest.

Table 1. Demographic characteristics of study population

	Group 1			Group 2				
	n	%	Mean±SD	n	%	Mean±SD	t/Chi-square	*p*
Age (year)			51.9±16.6			52.4±15.8	0.093	0.927
Gender							0.016	1.000*
Male	17	85.0		19	86.4			
Female	3	15.0		3	13.6			

SD=Standard deviation; * Fisher's exact test.

were used for the comparison of the groups. A *p* value of <0.05 was considered statistically significant.

RESULTS

Of the patients, 24 had chronic obstructive pulmonary disease (COPD), 10 had tuberculosis, six had interstitial lung disease, and two had histiocytosis. There was no statistically significant difference in the age and gender between the groups (Table 1).

The mean duration of air leakage was 3.3±2.4 (range, 1 to 11) days. In Group 1, the number of patients whose air leakage was stopped within the first 48 hours was 10 (50%), while this number was 20 (90.9%) in Group 2. The mean number of pleurodesis application was 1.6±0.7 (range, 1 to 3). In Group 1, pleurodesis was repeated once in 12 patients, twice in four patients, and thrice in four patients, while in Group 2, it was repeated once in 20 patients and twice in two patients. The mean duration to tube withdrawal was 5.2±3.3 (range, 1 to 16) days and the length of hospitalization was 7.1±3.6 (range, 3 to 18) days. The mean values of all variables analyzed were significantly lower in Group 2 (p<0.001) (Table 2, Figure 2).

Most of the cases (73.8%; n=31) had no complications, while eight (19.0%) had pain, and three (7.1%) had a fever. Although pain and fever were more frequent in Group 2, it did not reach statistical significance (Fisher exact test=5,204; p=0.051) (Table 3). However, when we evaluated the presence of complications (n=2 in Group 1 vs. n=9 in Group 2), the difference was found to be significant (chi-square=5,177; p=0.023). There was no significant difference between the male and female patients in terms of the numerical variables examined, and there was also no significant difference in complication rates (chi-square=0.158; p=667). The follow-up duration was 12 and 24 weeks in Group 1 and Group 2. During this period, two patients died due to comorbidities; none had recurrent pneumothorax or complications.

DISCUSSION

Spontaneous pneumothorax is classified as primary and secondary entities. Contrary to primary spontaneous pneumothorax, patients with SSP have an underlying lung pathology. To date, numerous diseases

Table 2. Variables analyzed between patient groups

	mL	n	Mean±SD	t/Z	*p*
Cessation of air leakage (days)				-3.624	<0.001*
Group 1	60	20	4.5±2.8		
Group 2	120	22	2.1±1.2		
Number of pleurodesis				3.726	0.001†
Group 1	60	20	1.9±0.7		
Group 2	120	22	1.2±0.4		
Duration of tube removal (days)				-5.116	<0.001*
Group 1	60	20	7.5±3.3		
Group 2	120	22	3.1±1.3		
Duration of hospitalization (days)				-5.184	<0.001*
Group 1	60	20	9.6±3.6		
Group 2	120	22	4.7±1.2		

SD: Standard deviation; * Mann-Whitney U test; † Independent samples t-test.

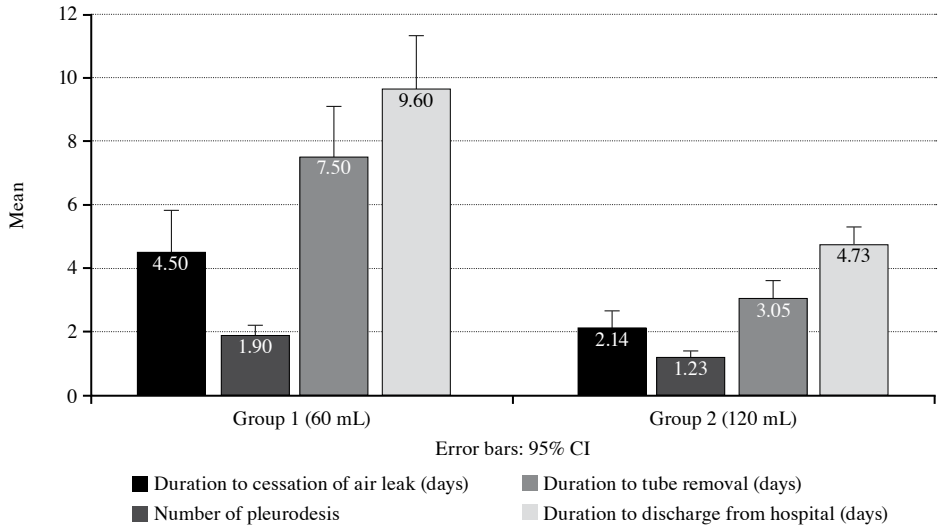

Figure 2. Comparison of variables analyzed between groups.
CI: Confidence interval.

have been accused in the etiology of SSP. However, the most common factor is COPD, which is responsible for about 70% of all cases.[1,9] In our study, 57% of the patients had COPD, consistent with the literature.

The suggested first-line treatment for SSP is tube thoracostomy. However, it is linked to a persistent air leakage or collapsed lung for more than seven days in almost 20% of patients.[1] The usual treatment for these patients is thoracotomy or video-thoracoscopy under general anesthesia.[10-12] Nevertheless, some patients are not suitable for surgery or general anesthesia due to old age, underlying lung pathologies, or compromised pulmonary functions, and an alternative approach is required for these patients.

Conservative management of persistent air leakage such as prolonged drainage, physiotherapy, pleurodesis with talc, bacterial components, antibiotics, anticancer agents, and the use of a Heimlich valve is no longer preferred.[2] Although these methods may yield encouraging results in selected settings, they do not promise a definite solution to the problem. Robinson[5] reported pleurodesis with an autologous blood patch to treat a persistent air leakage after pneumothorax and found 85% success in a series of 25 patients. Also, some authors used the same technique for treating prolonged air leakage after pulmonary resections.[11-15] Many researchers have lately employed this method as a first-line treatment for air leakage after lung resection, in primary as well as secondary SSP patients.[3,5,6,8,10,12-15]

An essential application of autologous blood pleurodesis lies in several specific patient groups, in which chemical or surgical pleurodesis may be undesirable or contraindicated. The use of talc is frequently avoided in younger patients due to concerns regarding its long-term side effects. In addition, surgery may not be always possible in elderly or in those with multiple comorbidities. We believe that autologous blood has many advantages over all other agents (such as being safe, economic, effective, non-immunogenic, simple, inexpensive, widely available, and allowing lung expansion).

Table 3. Complications

	Group 1		Group 2		Total	
	n	%	n	%	n	%
Complication						
None	18	90.0	13	59.1	31	73.8
Pain	2	10.0	6	27.3	8	19.0
Fever	0	0.0	3	13.6	3	7.1
Total	20	100.0	22	100.0	42	100.0

Autologous blood pleurodesis may work by several mechanisms. There is an immediate mechanical action of the fibrin which causes a blood patch effect, leading to direct sealing of the leak with hematoma or coagulated blood. The inflammation of the pleural surfaces caused by blood in the cavity induces adhesions between the pleural layers.[3,6-8,13-16] Early termination of air leakage in most of our cases supports this mechanism. We also believe that the localization of the chest tube plays a role in the success of blood pleurodesis. Blisters and blebs which cause spontaneous pneumothorax are usually located in the lung apex. Autologous blood given from an apical chest tube descends downward, stroking the lung, and causing the fibrin to clog the parenchymal leaks. Moreover, for the homogeneous distribution of blood in the pleural cavity, patients must be rotated to certain positions in the bed. In our study, the patients who benefited the most from this method were COPD patients.

In a small series of six patients, 100% success 24 hours after the procedure was reported using autologous blood.[17] However, another study administering the same method to 25 patients with relapsed pneumothorax reported only 84% success rate.[5] Also, Cagirici et al.[8] treated 32 patients with autologous blood and found 84% success rate. Even lower success rates were reported by Blanco Blanco et al.[18] They followed 17 patients for more than a year and had an immediate success rate of 71% using autologous blood. In our study, the success rate was 50% in Group 1, compared to 90.9% in Group 2, within the first 48 hours.

There is still no consensus on the timing of pleurodesis.[15] Some authors have suggested the use of autologous blood pleurodesis on Day 9 of continuing air leak, while others have recommended starting treatment on Day 5.[6,15] In our series, patients with continuing air leakage for more than seven days were selected for autologous blood patch pleurodesis, as in some other studies.[6,13] We believe that an earlier application of pleurodesis may prevent long-persistent air leakage, thus, contributing to eliminate the risk for empyema and decreasing the length of hospital stay.

Despite the agreement in the effectiveness of this technique, there is still an ongoing debate concerning the amount of blood required.[6,19,20] Andreetti et al.[16] randomized patients to receive either 50 or 100 mL of blood at each instance. They reported a tendency of higher effectiveness with larger volumes. Additionally, Droghetti et al.[14] reported that higher blood volumes of 100 to 150 mL could lead to earlier cessation of the leak. However, Lang-Lazdunski et al.[13] argued that a greater volume of blood could lead to a greater risk for pleural sepsis and recommended using a maximum of 50 mL. Nevertheless, there is no solid evidence behind any of these suggestions. In the light of these discussions, Droghetti et al.[14] claimed that if the first dose of blood was not capable to stop air leakage within 48 hours, a further treatment was, then, indicated. In our study, 60 mL of autologous blood was used in Group 1 and 120 mL in Group 2. In 30 patients, we obtained successful sealing within 48 hours. Pleurodesis was repeated in the patients with continuing air leakage at the end of this period.

Complications may arise after blood pleurodesis, such as tension pneumothorax, and empyema.[6,8,21] Tension pneumothorax was observed in a patient where small pleural catheters were used for pleurodesis. In our series, blood injection was performed through a 28-F drainage tube. As also used in our study, 20 mL of saline was flushed by other clinicians into the drain right after the blood instillation to prevent lumen obstruction during the procedure. Hanging the line of drain 40 to 50 centimeters above the patient and leaving it unclamped during the intervention to ensure the evacuation of air from the thoracic cavity may keep the lung expanded. In our study, a total of 11 patients developed complications. Eight of these patients (19.0%) had pain, and three (7.1%) had a fever. These complications were more common in Group 2, probably due to the excessive amount of blood administered. Duration of complications did not exceed 24 hours in our study. Complete blood count, erythrocyte sedimentation rate, and C-reactive protein values did not improve in patients with fever, and there was no growth in the blood cultures. These complications occurred only once and did not recur. No additional treatment was performed for these complications, and the complaints improved within 24 hours. The patients with multiple blood pleurodesis did not develop respiratory failure, tension pneumothorax, empyema, or cough and hematocrit values did not decrease significantly. The most common complaint was pain.

The main limitations to the present study include its retrospective design and small sample size in each group. Further large-scale, prospective studies would provide contribution to the body of knowledge on this topic.

In conclusion, based on our study results, we highly recommend the application of autologous blood patch pleurodesis in the treatment of prolonged air leakage in patients with secondary spontaneous pneumothorax.

Besides, the dose of blood used for pleurodesis should be proportional to the surface area of the pleura, and 120 mL of blood seems to yield successful results.

Declaration of conflicting interests

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