Feasibility of Chemical Pleurodesis with Small Bore Catheter in Patients with Symptomatic Malignant Pleural Effusions

Semptomatik Malign Plevral Efüzyon Hastalarında Küçük-Çaplı Kateter ile Kimyasal Plörodezisin Uygulanabilirliği

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ABSTRACT

Objective: To investigate the feasibility of small-bore catheters in sclerotherapy of malignant pleural effusions. Conventionally, malignant pleural effusions are treated with tube pleurodesis. Recently, small-bore catheters were placed with no notable difference in results.

Material and Method: Two groups of 20 patients underwent drainage of malignant pleural effusions with small and large bore catheters. In the absence of limiting complications, pleurodesis with bleomycin was performed in all patients The 30 day postpleurodesis chest radiographs were compared with primary radiographs. Complications were recorded.

Results: The global success rates in the case vs. control groups, were 80% vs. 81%, with 7 (46.7%) vs. 9 (56%) complete responses, 5 (33.3%) vs. 4 (25%) partial responses, and 3 (20%) vs. 3 (19%) no response among 15 vs. 16 successful pleurodesis procedures in the two groups. Mean hospitalization days (p=0.006) and mean pleurodesis duration (p=0.005) were significantly lower in the case group. Complications in the case vs. control groups included chest pain (20% vs. 40), fever (15% vs. 25%), pneumothorax (10% vs. 5%), nausea (5% vs. 5%), and cellulitis (0% vs. 5%).

Conclusion: This study continues to support a role for malignant pleural effusion pleurodesis via small-bore catheter with acceptable success rate, low discomfort, low pleurodesis and hospitalization days. *(Tur Toraks Der 2012; 13: 18-22)*

Key words: Pleurodesis, bleomycin, malignant pleural effusion

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ÖZET

Amaç: Malign plevral efüzyonlar konvansiyonel olarak tüp plörodezisi ile tedavi edilir. Son dönemde, küçük-çaplı kateterler sonuçlarda belirgin bir fark olmadan kullanılmıştır. Çalışmanın amacı, malign plevral efüzyonların skleroterapisinde küçük-çaplı kateterlerin uygulanabilirliklerinin araştırılmasıdır.

Gereç ve Yöntem: Yirmi hastadan oluşan 2 gruba küçük ve geniş çaplı kateterlerle malign plevral efüzyon drenajı uygulandı. Hastalara, sınırlayıcı komplikasyonlar olmadan, bleomisin ile plörodezis uygulandı. Plörodezis sonrası 30 günlük göğüs radyografileri önceki radyografilerle karşılaştırıldı. Komplikasyonlar kaydedildi.

Bulgular: Vaka grubuna karşılık kontrol grubunda global başarı oranı %80'e karşılık %81 idi. İki gruptaki başarılı plörodezis prosedürü 15'e karşılık 16 olup bunlardan tam cevap alınan 7'ye (%46.7) karşılık 9 (%56), kısmi cevap alınan 5'e (%33.3) karşılık 4 (%25), hiç cevap alınamayan ise 3'e (%20) karşılık 3 (%19) idi. Ortalama hastanede yatış günü (p=0.006) ve ortalama plörodezis süresi (p=0.005) vaka grubunda anlamlı olarak daha düşüktü. Vaka ve kontrol grubundaki komplikasyonların karşılaştırmaları şu şekildeydi: göğüs ağrısı (%20'ye karşılık %40), ateş (%15'e karşılık %25), pnömotoraks (%10'a karşılık %5), bulantı (%5'e karşılık %5), selülit (%0'a karşılık %5).

Sonuç: Bu çalışma, küçük-çaplı kateterin malign plevral efüzyon plörodezisindeki rolünü uygun görülebilir bir başarı oranı, az rahatsızlık vermesi, kısa plörodezis ve hastanede yatış süreleri ile desteklemeye devam etmektedir. *(Tur Toraks Der 2012; 13: 18-22)*

Anahtar sözcükler: Plörodezis, bleomisin, malign plevral efüzyon

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INTRODUCTION

Malignant pleural effusions are common in patients with primary pleuropulmonary or metastatic cancers [1]. Patients with pleural effusions experience dyspnea, cough or pleuretic chest pain which can negatively affect their quality of life [2].

Currently, lung cancer and breast cancer are the most common metastatic tumors of the pleura in men and women respectively [3]. Together, both malignancies account for approximately 50-65% of all malignant effusions. Lymphomas, tumors of the genitourinary tract, and gastrointestinal tract as a group are account for a further 25% of primary malignancies. Pleural effusions from an unknown primary are responsible for 7-15% of all malignant pleural effusions [4].

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Several palliative treatment options include repeated needle thoracocentesis, tube thoracostomy with chemical or biologic sclerotherapy, pleurectomy, and pleuroperitoneal shunt [2]. Among these options, chemical pleurodesis is the most common and useful method. Traditionally, conventional large-bore chest tubes have been used for thoracostomy and chemical pleurodesis [5]. Other invasive methods such as video assisted thoracoscopic surgery (VATS) have also been used successfully for pleurodesis. More recently, small-bore catheters were placed with no notable difference in results of pleurodesis via large-bore catheters [2,5-7]. Small bore catheters were well tolerated by the patients, and were decreased the hospitalization days. They also have been used in ambulatory settings in some studies [8].

Several biologic and chemical sclerosing agents have been tried for pleurodesis including talc, tetracycline, doxycycline, bleomycin and etc.

This prospective clinical trial study was therefore undertaken to determine the feasibility of small-bore catheter pleurodesis in patients with known malignant pleural effusions and to making a comparison between the results, hospitalization charge, pleurodesis duration and complications of pleurodesis with a small bore catheter versus conventional large bore catheters.

MATERIAL and METHOD

In a two years period, consecutive patients with known malignant pleural effusions who were referred by the medical oncology department to the thoracic surgery and pulmonary medicine services for palliative management of a symptomatic pleural effusion, were entered into the study.

Predrainage chest radiography was performed in all patients. Our inclusion criteria were adult cooperative patients with symptomatic malignant pleural effusions whose symptoms were relieved by drainage but the effusion had relapsed rapidly. Patients with coagulopathy were excluded from our study.

After obtaining informed consent, patients who met the study inclusion criteria underwent drainage of malignant pleural effusions by a small-bore catheter (10F). After drainage, in the absence of limiting complications such as incomplete expansion of the lungs and pneumothorax, pleurodesis with bleomycin was performed in the patients.

Six hours after catheter placement, a control chest radiography was obtained for evaluating the likelihood of pneumothorax. As much as 1-1.5 L fluid was aspirated at the time of catheter placement, depending on the patient's comfort and symptoms. The catheter was then placed in continuous wall suction to -20 cmH_20 with a water-seal device, drainage was performed at a rate of 100-150 cc/hr, then up to complete expansion of lungs. Bleomycin pleurodesis was performed when chest radiography showed complete expansion of lungs and little or no residual fluid. Before bleomycin instillation, 15 cc lidocain 1% in 50 cc saline solution was administrated through the catheter, then 4 vials (60U) of bleomycin in 50 cc saline solution was instilled through the catheter into the pleural space. The intercostal tube was clamped for 1-2 hours following sclerosant administration. The catheter was then opened and reconnected to suction and catheter output was recorded. Pleurodesis with instillation of 60U bleomycin were repeated if catheter output was more than 150 cc in the first 24 hrs. After obtaining control chest radiography, in the absence of excessive fluid drainage (>150 ml/day) after sclerosant administration, the intercostal tube was removed. The 30 day postpleurodesis chest radiographs were obtained and compared with primary prepleurodesis and immediate postpleurodesis chest radiographs.

According to the American Thoracic Society and European Respiratory Society consensus [9], complete response was defined as:

1. Long-term relief of symptoms related to the effusion with absence of fluid reaccumulation on chest radiographs until death;

2. Partial response, as diminution of dyspnea related to the effusion with only partial reaccumulation of fluid (less than 50% of the initial radiographic evidence of fluid) and no further therapeutic thoracocenteses required for the remainder of the patient's life;

3. No response or failed pleurodesis as lack of success as defined above.

Global response was defined as complete response plus partial response.

Complications such as fever (temperature >37.6°C), pain, dyspnea, empyema or pneumothorax were recorded.

Twenty patients (matched for age and sex) were also entered into the study as a control group. Drainage via large bore conventional chest tubes was performed for them. In the absence of limiting complications such as incomplete expansion of the lungs and pneumothorax, pleurodesis was performed in the patients.

The local ethical committee approved the study and written informed consent was obtained from all patients.

SPSS 17 for Windows program was used to perform statistical analysis. Results are expressed as mean±SD. Unpaired t- test was used to assess the significance of result parameters in the case and control groups. The statistical significance was set at $p<0.05$.

RESULTS

Between 58 referred patients with malignant pleural effusions, 20 patients (10, 50% men, 10, 50% women) included in the study underwent drainage of malignant pleural effusions by small-bore catheter and pleurodesis with bleomycin was then performed in 15 patients. Mean±SD ages of the patients were 59.40±25.36 years.

The underlying primary tumors were pulmonary adenocarcinoma (5, 25%), pulmonary squamus cell carcinoma (4, 20%), breast cancer (4, 20%), pulmonary small cell carcinoma (2, 10%), gastrohepatic (2, 10%),

sarcoma (2, 10%), and ovarian cancer (1, 5%). Of a total of 20 patients with malignant pleural effusion, 11 (55%) patients had a pulmonary origin cancer.

Among 20 candidate patients for small bore catheter pleurodesis, catheters were removed in 5 patients (3 women, 2 men) because of pneumothorax in 2 patients (10%), and incomplete expansion of lungs in 3 (15%) patients. The global response rate of pleurodesis was 80%, with 7 (46.7%) complete responses, 5 (33.3%) partial responses, and 3 (20%) no responses, among 15 procedures from patients whose drainage and bleomycin instillation via small bore catheter was performed successfully. Pleurodesis with 60U bleomycin was repeated in only one patient.

Among 20 candidate patients for large bore catheter pleurodesis, catheters were removed in 4 patients (2 women, 2 men) because of pneumothorax in 1 patient (5%), and incomplete expansion of lungs in 3 (15%) patients.

The global response rate of pleurodesis was 81% with 9 (56%) complete responses, 4 (25%) partial responses, and 3 (19%) no responses, among 16 procedures from patients who drainage and bleomycin instillation via small bore catheter were performed successfully.

Mean hospitalization days in the case and control groups were 6.75±2.22 and 10.35±5.02 respectively which was a statistically significant difference (p=0.006).

Mean pleurodesis duration in the case and control groups were 4.55±2.28 days and 8.20±5.15 days respectively, with a statistically significant difference (p=0.005).

Comparison between mean hospitalization charge of the case and control group showed no statistically significant difference (p=0.46).

Complications in the case group included fever after bleomycin instillation in 3 (15%) patients that lasted 24 hours in 2 patients. One of three patients had a high grade fever (40 degrees C) which lasted in 2 days. One (5%) patient experienced nausea and vomiting after bleomycin instillation which continued for 3-4 days. Pneumothorax, but not tension pneumothorax was reported in 2 (10%) patients, chest tube was placed for them.

Four patients (20%) experienced mild to moderate chest pain, 2 were patients with unsuccessful pleurodesis due to pneumothorax. No cellulitis or empyema was reported in the patients.

Complications in the control group included: fever (25%), nausea and vomiting (5%), pneumothorax (5%), chest pain (40%), and cellulitis (5%).

DISCUSSION

Conventional large bore catheters (24-32 F) have traditionally been used for malignant pleural effusion drainage and sclerotherapy in patients with malignant pleural effusions. They have traditionally been used because they are thought to be less prone to obstruction by clots, but there is little published evidence to confirm this theory (4). Large bore chest tubes, however, limit patient mobility and are uncomfortable.

More recently, small bore catheters (10-14 F) have been placed with or without radiologic guidance with no noticeable difference in the response rates [2,5-7]. Additionally, small bore catheters are well tolerated and suitable for ambulatory, outpatient treatment [8].

The pleurodesing agent selection still remains debatable.

Talc is the most effective sclerosant available for pleurodesis, but it is allied with unfavorable effects. Talc pleurodesis is followed by pulmonary and systemic inflammation [3]. A small number of patients (<1%) may develop acute respiratory failure following talc administration, especially when 10gr of talc have been used for sclerotherapy [5]. However, there are many studies which suggest talc as the first choce sclerosant agent [5,10-12].

Tetracycline was safe and effective with a 77% response rate, but the intravenous form of this drug for sclerotherapy is no longer manufactured, so alternative analogues such as Doxycycline have been used with a response rate of 72%-95% [5,13].

Bleomycin an antineoplastic agent is another alternative sclerosant with a 54%-80% response rate [5,14]. Although reported adverse effects such as nausea, vomiting, rash, diarrhea, bone marrow suppression, and high cost have limited its utility, bleomycin was the preferred sclerosing agent in some studies [14].

Comparison between small bore and large bore intercostal tubes has been considered in many studies. Effectiveness of pleurodesis can be studied with a 30-day postpleurodesis interval because most pleural effusions reaccumulate within this time, and it is the accepted standard when modes of therapy for pleural effusions are compared [15].

In our study, the global response rate of pleurodesis was 80% with 7 (46.7%) complete responses, 5 (33.3%) partial responses, and 3 (20%) no responses among 15 procedures in patients who drainage and bleomycin instillation via small bore catheter performed successfully for them.

In a similar study on 28 patients in Taiwan, the global response rate of pleurodesis was 77% (41% complete response, 36% partial response), which is similar to our results [16]. In other studies, similar success rates have been reported. Yildirim et al. [2] in Turkey reported a global success rate of 64% for pleurodesis with bleomycin via a small bore catheter. Sartori et al. have been reported a global success rate of 84% in their study on 50 patients with known malignant pleural effusions [4]. Parulekar et al. in another study in Canada have reported a success rate of 50% for small bore catheter pleurodesis, which was equal to the results of conventional pleurodesis via large bore catheter in their control group [7].

The majority of studies have reported a decrease in pleurodesis duration and hospitalization period [1,2,9].

In our study, the mean pleurodesis duration was 4.55±2.28 in the case group versus 8.20±5.15 in the control group, which was a statistically significant difference (p=0.005). Comparison between hospitalization days of the case and the control groups revealed a statistically significant difference (6.75±2.22 days in the case group versus 8.20±5.15 days in the control group) (p=0.005).

Comparison between mean hospitalization charge of the case and control group showed no statistically significant difference (p=0.46).

Some other studies have reported a lower hospitalization charge for small bore catheter pleurodesis [2,17]. More recently, small bore catheters for pleurodesis have been used in ambulatory settings in some studies [8,18].

The results of our study may be influenced by the difference of catheter prices (40 US Dollars for small bore catheters versus 3US Dollars for large bore catheters) in our country.

Pleuritic chest pain and fever are the most common side effects of sclerosant administration [2,4,16]. In our study, complications included fever after bleomycin instillation in 3 (15%) patients, nausea and vomiting in one (6.6%) patient, and pneumothorax, but not tension pneumothorax, in 2 (10%) patients. Four patients (20%) experienced mild to moderate chest pain. No cellulitis or empyema has been reported in the patients.

Comparison of the complications in the case and control groups showed that the controls had more complaints of chest pain (40% vs. 20%). Fever occurrence was slightly higher in the control group (25% vs. 15%). There was no significant difference in the other complications of the two groups.

There are variable reports of complications in other studies. Fever after pleurodesis has been reported in 77% of patients in Taiwan, and another study in Turkey reported a 31.8% rate for fever in their patients. On the other hand, 5%-41% of American patients have experienced fever after sclerosant instillation [5,11,13,16]. Porcel et al. [9] reported fever after pleurodesis in only 8% of their patients in Spain.

Twenty percent of our patients have complained of chest pain. Chest pain is a subjective parameter, thus it is easily predictable that different subjects of different cultures may have variants of pain-tolerance, as has been reported in several studies.

Nausea and vomiting after instillation of bleomycin was reported in only one patient in our study (6.6%). Chen et al. from Taiwan reported nausea and vomiting in 14% of their patients.

Pneumothorax occurred in 2 (10%) patients in our study. In a study in the US, pneumothorax was reported in 31% of their patients, thus they concluded that pneumothorax is a common complication of small bore catheter thoracostomy; In contrast, there was no report of pneumothorax in another study in 9 patients in Denmark [19,20]. It seems that pneumothorax occurrence depends on the experience of physicians and safety of devices and connectors.

Although adverse effects such as diarrhea, bone marrow suppression, and rash have been reported in the patients after bleomycin instillation for pleurodesis, none of the above complications have been detected in our patients.

There was no report of empyema or cellulitis in our patients. According to other similar studies there were rare reports of cellulitis or empyema, except for Mousani et al. who reported cases of empyema in their outpatient managed cases and Mourad et al. in their study in Egypt [18,21].

A conclusive comparison of the results between the case and control groups showed that, despite the similar success rates of both methods, small bore catheters are more comfortable, and could decrease hospitalization and pleurodesis days.

Comparison between complications and success rates in our study and recent published studies is shown in Table 1 [5,9,22]. With respect to the results of our study, small-bore catheter thoracostomy followed by bleomycin sclerotherapy successfully resolves symptomatic pleural effusion in patients with known malignancies.

Table 1. Comparison between complications and success rates in our study and recently published studies

Variable	Firouzbakhsh et al.	Marom et al.	Porcel et al.	Sahin et al.
Fever	15%	41%	8%	31.8%
Nausea and vomiting	5%	N.R.*	N.R.	N.R.
Chest pain	20%	19%	36%	18%
Pneumothorax	10%	6%	N.R.	N.R.
Cellulitis	0%	N.R.	N.R.	N.R.
Empyema	0%	N.R.	N.R.	N.R.
Global success rate**	80%***	84%	81%	84.2%

*N.R. Not reported, **Global Success Rate Defined as complete response rate plus partial response rate, ***Global Success Rate among patients in whom small bore catheter pleurodesis procedure has been completed (catheters were removed in 5 patients, because of pneumothorax in 2 patients, and incomplete expansion of the lungs in 3 patients) (n=15)

In conclusion, results of this study continue to support a role for malignant pleural effusion drainage and pleurodesis via small-bore catheter with lower pleurodesis duration, shorter hospitalization period, less discomfort for the patient and with response rates equivalent to those obtained with large bore conventional chest tubes.

Conflict of Interest

No conflict of interest was declared by the authors.

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