Rapid Pleurodesis for Malignant Pleural Effusions*

Peter A. Spiegler, MD, FCCP; Adam N. Hurewitz, MD, FCCP; and Maritza L. Groth, MD, FCCP

Study objective: To determine the feasibility of rapid pleurodesis in patients with malignant pleural effusions in order to reduce hospital length of stay in patients with a limited life expectancy.

Design: Prospective case series.

Setting: Two university hospital programs.

Patients: Thirty-eight patients with symptomatic pleural effusions associated with malignancy.

Interventions: A 14F catheter was inserted percutaneously into the pleural space after radiographic confirmation of free fluid by lateral decubitus views. Following radiographic confirmation of complete fluid evacuation, a sclerosing agent (ie, talc slurry or bleomycin) was instilled into the pleural space. This was accomplished within 2 h of chest tube insertion, unless the tube was inserted in the evening or if the lung was trapped. After clamping the tube for 90 min, the pleural space was drained for 2 h, after which the chest tube was removed. The intervention was scored as “successful” if no radiographic evidence of fluid reaccumulation was noted at 4 weeks. A “partial successful” score indicated reaccumulation of fluid that did not produce symptoms and did not require repeat pleural drainage of any sort. All other outcomes were scored as “unsuccessful.”

Measurements and results: Forty chest tubes were inserted into 38 patients. Four procedures revealed the presence of a trapped lung and did not result in any attempt at pleurodesis. Five patients who received pleurodesis died in less than 1 month and therefore were not evaluable. Two patients had technical problems with the chest tube and were not evaluable. Of the remaining 29 procedures, drainage procedures with pleurodesis were performed in 27 patients, a complete response was seen in 14 patients (48%), a partial response was seen in 9 patients (31%), and 6 patients (21%) did not respond to pleurodesis. Chemical pleurodesis was completed as an outpatient procedure in only two patients. In one of these, the outcome was unsuccessful. In the remainder, insertion of the chest tube in the evening or additional medical problems necessitated hospital admission, but the entire procedure was completed within 24 h.

Conclusions: Chemical pleurodesis can be accomplished with good results in < 24 h in the majority of patients with malignant pleural effusions.

Key words: bleomycin; malignant; pleural effusion; pleurodesis; talc slurry

The accumulation of pleural fluid in patients with cancer signals advanced disease. The vast majority of these effusions are caused either by direct pleural seeding or by tumor invasion into mediastinal lymph nodes. These malignant pleural effusions preclude surgical resection in patients with primary lung cancer and are associated with dismal long-term survival rates. Many of these patients die within 1 month of detecting the effusion.1,2

Chemical pleurodesis can be palliative for recurrent, symptomatic malignant pleural effusions. The extent to which pleurodesis is successful is a function of tumor bulk, pleural fluid pH, and the choice of sclerosing agent. The size of the catheter used to drain the effusion is no longer regarded as a critical factor.3,4 The typical duration of hospitalization for chemical pleurodesis is 5 to 7 days.5 Much of this time is a consequence of prolonged chest tube drainage both prior to and immediately following pleurodesis. The justification for these periods of prolonged drainage is not substantiated in the literature.6

We hypothesized that effective pleurodesis could
be accomplished within 24 h by shortening the following: (1) the time of initial drainage of the pleural effusion, (2) the time that the sclerosing agent resides within the pleural cavity, and (3) the duration of pleural space drainage after pleurodesis. Furthermore, we proposed that in selected patients, effective chemical pleurodesis could be performed as a single-day ambulatory procedure. We studied the feasibility of rapid pleurodesis using a small-bore catheter drainage system and either bleomycin or talc slurry as the sclerosing agent.

**Materials and Methods**

Thirty-eight patients with histologic or cytologic evidence of malignancy and pleural effusion were studied. These patients were referred to the pulmonary service for pleurodesis.

We investigated the extent of pleural fluid loculation by lateral decubitus radiographs prior to tube thoracostomy. Using local anesthesia and IM analgesia, we inserted a small-bore (14F) chest tube catheter (Arrow International; Reading, PA) into the pleural space in the posterior axillary line. We attempted to guide the catheter toward the mediastinal portion of the posterior pleural gutter. Immediately after chest tube insertion, we drained the pleural space using a water-seal system (Pleur-evac; Deknatel Inc; Fall River, MA) without added suction. After 15 min, we added suction at 20 cm H2O unless drainage exceeded an arbitrary volume of 1 L. No special instructions were given to the patient regarding position to facilitate drainage. Pleural space drainage was subsequently evaluated using a portable chest radiograph obtained 2 h after tube insertion.

Pleurodesis was initiated only after obtaining radiographic evidence of the complete evacuation of the fluid. Incomplete evacuation required continued suction drainage and a repeat chest radiograph 2 h later. If the chest radiograph demonstrated changes that were consistent with a trapped lung, pleurodesis was not attempted. A radiologic diagnosis of trapped lung was based on incomplete parenchymal expansion, absent markings peripheral to the visceral pleura, and a pleural space lucency of similar shape and size as that of the initial effusion. Patients with a trapped lung that did not expand with increased intrapleural suction and who had a reasonable long-term prognosis were referred either for thoracoscopy or pleuropertitoneal shunt drainage.

**Chemical Pleurodesis**

We initially selected bleomycin as our sclerosing agent in order to avoid the pain previously noted with doxycycline. Although bleomycin is expensive, talc slurry was not initially available at our institution. The last 11 patients who were reported received talc slurry pleurodesis. All patients received intrapleural lidocaine (10 mL 2% solution) prior to instillation of the sclerosing agent. Systemic analgesia was administered as needed. Sixty units bleomycin or 4 g talc slurry were diluted in 50 mL saline solution and were injected through the side port of the chest tube. The chest tube was clamped for 90 min with the patient lying in bed, but having not been requested to assume any special positions. The tube was unclamped. When possible, the tube was removed after 2 h of suction. In many patients, drainage proceeded overnight in order to avoid the removal of the tube during the evening. A chest radiograph was obtained to document the degree of lung expansion.

**Outcome Scoring**

The outcome was considered to be successful if the patient either had no recurrence of pleural fluid (ie, a complete response) or had a sufficiently small effusion that did not require thoracentesis within 4 weeks after pleurodesis (ie, a partial response). All other outcomes were considered to be failures. A similar scoring system has been used in previous studies. Data from patients who died within 30 days of undergoing pleurodesis were not analyzed.

**Results**

Of the 38 patients who had been referred for pleurodesis, 5 died in <1 month and were considered to be nonevaluable. In none of these five patients did the insertion of the chest tube or the instillation of the sclerosing agent appear to contribute to the early mortality. Of these five patients, three had received bleomycin and two had received the talc slurry. Four patients had radiographic evidence of a trapped lung after chest tube insertion. They did not receive pleurodesis and were also considered to be nonevaluable. One patient had a kinked chest tube with inadequate drainage, and in another patient the tube inadvertently fell out shortly after the talc slurry had been inserted. Of the remaining 27 evaluable patients, 2 had sequential pleurodesis of a malignant effusion in each hemithorax. These occurred on separate occasions. This resulted in the 29 pleurodesis procedures for which data were presented. Of these patients, the primary site of malignancy was the lung in nine patients (33%), the breast in eight patients (30%), lymphoma in three patients (11%), and various other sites in the remaining patients, including the kidney, pancreas, and uterus.

Despite the use of a relatively small-bore (14F) catheter system, the malignant effusions were rapidly and completely drained in all patients. Other than the four patients with trapped lung, complete evacuation of the pleural fluid was radiographically confirmed within 2 h of chest tube insertion, even in those patients with large effusions. The mean volume drained was 1.5 L (range, 0.8 to 2.5 L). The time from chest tube insertion to pleurodesis varied from 2 to 18 h depending largely on what time of the day the tube was inserted. If the chest tube was inserted in the evening or at night, pleurodesis was delayed until the following morning. In 11 procedures (10 patients), the entire procedure was completed on the same day. In these patients, a chest tube was inserted in the morning, and pleurodesis and removal of the tube were completed by mid-afternoon. Two of these patients had pleurodesis performed as an ambulatory procedure. The other patients in this subpopulation had been admitted for
reasons other than pleurodesis. Of the remaining patients (nine procedures) completed on the same day but not discharged to home, a complete response was seen in five and a partial response was seen in one. Three patients died within 1 month and were therefore nonevaluable.

At week 4 of follow-up, chemical pleurodesis resulted in a complete response in 14 of 29 patients (48%), and in evaluable procedures and a partial response in another 9 of 29 (31%), thus combining to give a successful outcome in 79% of procedures. There was no apparent relationship between tumor type and outcome. The two patients receiving completely ambulatory procedures had reaccumulation within a 1 month at follow-up, although only one patient required an intervention (one failure, one partial success).

The complications resulting from this procedure were minimal. Three patients had moderate pain immediately following the placement of the chest tube. We attributed the pain to irritation of the diaphragmatic pleura. We administered narcotic analgesia to these patients with good response. Two patients developed transient fever after bleomycin injection and required no further therapy. Three patients complained of pain during pleurodesis, which was readily controlled with analgesic agents. One patient developed a pneumothorax when air was inadvertently allowed to enter the pleural space during the administration of the bleomycin.

The fluid in several patients drained so rapidly that the tube was clamped for 10 to 15 min at the discretion of the clinician to reduce the possibility of the occurrence of reexpansion pulmonary edema.

**DISCUSSION**

These data demonstrate the feasibility of rapid chemical pleurodesis in most patients with symptomatic malignant pleural effusions. Combining the complete response and partial response groups, 79% of our pleurodesis procedures (23 of 29) did not require further intervention in the subsequent month of monitoring. Completing pleurodesis within 24 h is appealing not only from the point of view of cost containment but also as a means of reducing hospital length of stay for patients with a short life expectancy.

Reducing the initial drainage time after catheter insertion substantially shortens the time of pleurodesis. We observed complete evacuation of the effusion within 2 h in all patients other than those with trapped lung. In many patients, we briefly clamped the chest tube after insertion because >1.5 L drained within the initial 15 min. This finding suggests that small-bore (14F) catheters are sufficient to drain most malignant pleural effusions. The primary goal of drainage prior to pleurodesis is to remove sufficient pleural fluid to appose the pleural surfaces. Some clinicians delay pleurodesis until the rate of chest tube drainage is <100 to 150 mL per 24 h, based on the hypothesis that abundant fluid production reduces the efficacy of pleurodesis. Based on previous animal and human data, we propose that this is not necessary. However, we do not know from these data whether drainage for 24 h in some or all patients would improve the outcome.

The duration of time that the sclerosing agent should remain in contact with the pleural surfaces (ie, dwell time) also has not been studied rigorously. We reduced this time to 90 min with the chest tube clamped but did not compare outcomes with either a shorter or longer duration of dwell time.

Another factor leading to prolonged hospital lengths of stay is delayed removal of the chest tube after pleurodesis. The common recommendations are to remove the chest tube only after the pleural fluid drainage rate falls to <150 mL per day. We obtained results similar to those published for doxycycline and bleomycin despite a reduction of pleural drainage to 2 h after unclamping the chest tube. Although some pleural fluid did accumulate after chest tube removal, the amount was small and did not result in increased dyspnea. The efficacy of limiting drainage to a few hours after pleurodesis is consistent with data from animal models. In several studies of pleurodesis in rabbits, good outcomes were obtained by the injection of a sclerosing agent without tube thoracostomy drainage. In these animal models, extensive pleural fibrosis and adhesions were found despite an initial accumulation of large quantities of pleural fluid after the procedure.

The two major causes of failed drainage are trapped lung and loculated effusions. Trapped lung occurred in 10% of our patients with malignant pleural effusions, and there were no instances of failed drainage due to loculations. Occasionally, the trapped lung radiograph is interpreted as a pneumothorax since the radiologist cannot discern intrapleural air from a gas-free intrapleural space. The shape of the "space," the absence of an air leak, and the failure to expand the lung despite a functional chest tube all point toward a trapped lung. It has been suggested that measurement of the elastance of the pleural space can be predictive of the presence of a trapped lung and the likelihood of the success of chemical pleurodesis. Although not observed in our patient sample, rapid pleural drainage in patients with trapped lung can be associated with dyspnea and hypoxemia. It is believed that this is due to reexpansion lung edema that is associated with markedly negative intrapleural pressures.
Although talc is recognized as the most effective sclerosing agent, many other chemical products are still widely used because of availability, reduced toxicity, or simply greater familiarity. Doxycycline is inexpensive and readily obtained, but in several studies it has had efficacy in only 61 to 81% of patients. Bleomycin also has been used for pleurodesis with similar response rates. We found that bleomycin induced substantially less pain than doxycycline, however, it is significantly more expensive. Talc slurry is effective in >90% of patients but was not initially selected in this study because of limited availability and reported complications, including acute respiratory failure, empyema, and arrhythmias, and because of extensive systemic absorption in a rat model. We did not detect a difference between the outcomes with talc and those with bleomycin in this pilot study, but, due to the small population size, a statistically significant difference cannot be excluded.

These data support our hypothesis that the mechanics of chemical pleurodesis for the treatment of malignant pleural effusions can be accomplished more rapidly than previously has been reported. Although our data on two patients in whom pleurodesis was completed as an ambulatory procedure were not uniformly successful, the overall outcomes in procedures completed within 24 h were comparable to those reported in other studies of rapid pleurodesis. This could result in a substantial reduction in cost and in improved quality of life for these patients.

The issue of rapid pleurodesis previously has been investigated. Villanueva and associates were able to shorten the duration of chest tube drainage to an average of 2 days with no effect on response rates. In a similar study, Hsu and associates also showed that rapid pleurodesis can be performed once the pleural fluid is drained and the lung expanded. In their study, this was accomplished within 2 days. To our knowledge, ours is the first study that has shown that pleurodesis can be accomplished within 24 h, and in many cases, on the same day. We think that the critical factor in obtaining successful pleurodesis is the ability to fully drain the pleural space and to expand the lung. Furthermore, this can be accomplished effectively and rapidly with a small-bore catheter in the absence of pleural loculations.

REFERENCES
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