

CHEMICAL PLEURODESIS, AN EFFECTIVE SYMPTOMATIC TREATMENT OF MALIGNANT PLEURAL EFFUSION

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ABSTRACT

Objective: To assess the efficacy of chemical Pleurodesis in patients with malignant pleural effusion.

Material and Methods: The prospective, Open labeled interventional study was conducted in the department of medicine, Postgraduate Medical Institute, Lady Reading Hospital, Peshawar in collaboration with the Chest unit and the patients were enrolled for six months. The study lasted for 18 months from January 1995 to June 1996. After observing the excluding criteria 20 patients with malignant pleural effusion (metastatic or mesothelioma), were enrolled in the study. Tube thoracostomy was performed in all selected patients and after draining the effusion to the maximum; either tetracycline or bleomycine was instilled in the intrapleural space as pleurodesing agent. The selection for either agent was made at random.

Results: Twenty patients with almost equal male to female ratio and an age range of 35 to 85 (mean age 62) received either tetracycline or bleomycine with equal frequency (10 patients receiving tetracycline and 9 bleomycine). One patient was lost to follow up. Response was seen in all patients [complete response in fifteen patients (78.5%) and partial response in four patients (21.5%)]. There was no failure in either group. All patients tolerated the procedure quite well without any major complaints.

Conclusion: Chemical Pleurodesis is an effective and safe palliative procedure in patients with recurrent malignant pleural effusion who are not fit for surgery and that both Tetracycline and bleomycine are equally effective.

Key words: Chemical pleurodesis, Malignant pleural effusion.

INTRODUCTION

Approximately 50% of the patients with metastatic cancer develop malignant pleural effusion with an average life expectancy of about six months¹. Pleural effusion may be the only manifestation of malignancy, acting as a diagnostic source² and providing prognostic information as it shows incurability³. Diagnosis is established by pleural biopsy or finding malignant cells on pleural fluid cytology⁴. During their final months, dyspnea is the most common symptom and requires palliation. A decision relating to palliation and the modality of therapy should be based on total assessment of the patient and not a single variable. Local treatment remains the most common and effective palliation. Assessing the response to therapeutic thoracentesis determines the degree of relief of dyspnea and the time-course of recurrence. Lack of a beneficial effect suggests the patient may have a trapped lung, atelectasis, lymphangitic carcinomatosis, or tumor embolism. Many therapeutic options are available for the management of patients with malignant pleural effusion, which includes repeated pleuro-centesis, tube thoracostomy alone, chemical pleurodesis and pleurectomy. Chest tube drainage alone has variable results and is not recommended. Chemical pleurodesis through a standard chest tube or small-bore catheter is a commonly used and effective treatment, which has been shown to be effective and less invasive than other options available for stopping or slowing the reaccumulation of the fluid⁵. Talc slurry consistently produces the highest success rates, followed by the tetracyclines and bleomycin⁶. The latter two are the mainstay of current treatment and are about 85% effective¹ and therefore were chosen for our study.

MATERIAL AND METHODS

All patients who had documented malignant pleural effusion were included in

the study. Those who were unfit to undergo the procedure or whose lungs did not expand after tube thoracostomy were not included in the study. After taking informed consent twenty patients were enrolled in this study and were given either Tetracycline or Bleomycine at random through intercostal tube as pleurodesing agent.

Using aseptic technique and meticulous care, tube thoracostomy was performed on the affected hemithorax under local anesthesia and the fluid was drained until it reduced to less than 100 ml/day. Chest tube was then clamped and either one gram Tetracycline in 50 ml or 60 mg Bleomycine in 20 ml of normal saline were given through the intercostal tube into pleural space followed by 20 ml of normal saline to flush the tube. Chest tube was then clamped for twenty-four hrs after which the clamp was removed and fluid allowed to drain till it drained less than 50 ml/day. A chest X-ray was then done to ensure expansion of the lung following which the chest drain was removed. The patients were followed up by serial chest X-rays to detect recurrence of pleural effusion.

The response to therapy was classified as complete, partial or failure. Complete response is defined as lake of reaccumulation of fluid on chest X-ray for at least two months. Partial response was defined as

Histology	No	Agent in number	Response
Metastatic Carcinoma	15	Tetracycline in 8	7 CR 1 PR
		Bleomycine in 7	4 CR 3 PR
Mesothelioma	4	Tetracycline in 2	2 CR
		Bleomycine in 2	2CR

Table showing the detail of the studied patients and their response to the treatment.

Key: CR = Complete response. PR = Partial response.

recurrence of a small effusion not requiring any further treatment for at least two months. All other cases were considered as failure.

RESULTS

Twenty patients were included in the study. One patient was lost to follow up after one month, leaving 19 patients available for final analysis. Out of them 9 were females and 10 were males ranging from 35 to 85 years in age (mean 62 years). Four patients were lost to follow up after two months and two patients after three months. Ten patients received tetracycline while Bleomycine was instilled in nine patients. Complete response was obtained in fifteen patients (nine in tetracycline and six in Bleomycine group) and partial response was obtained in four patients (three in Bleomycine and one in tetracycline group) and all had metastatic carcinoma while all four patients with Mesothelioma had complete response. There was no failure with either Tetracycline or Bleomycine.

DISCUSSION

Management of patients with malignant pleural effusion is challenging and problematic. Malignant effusions recur, and therefore repeated thoracentesis, especially if the fluid rapidly reaccumulates, is usually not a good long-term solution unless the patient's overall prognosis and current condition prohibits a more invasive option. The standard option for recurrent effusions is insertion of a chest tube. If the lung re-expands, chemical pleurodesis is attempted to achieve adherence of the visceral to the parietal pleura⁷

Many therapeutic options are available and all have shortcomings. Repeated thoracentesis has only short-term effect⁸ and pleurectomy is very risky, as patients are

usually not fit to undergo major surgery⁹. Therefore chemical pleurodesis has attracted the attention of most of the physicians dealing with malignant pleural effusions. Many drugs and physical agents have been tried as pleurodesing agents which include tetracycline¹⁰, Radioactive gold¹¹, Talc¹², Doxorubicin^{13,14}, Quinacrine^{15,16}, Mechlorethamine^{17,18}, tube drainage alone¹⁹, Bleomycine²⁰, *Corynebacterium parvum*²¹⁻²⁵, mitoxantrone²⁶, cytarabine and cisplatin²⁷. In our study both Tetracycline and Bleomycine have been shown to be effective pleurodesing agents. Our combined complete and partial response rate is 100%. There are several studies, either in favor or against the superiority of either of these two agents. Ruckdeschel et al²⁸ showed a clear advantage with Bleomycine at both 30 and 90 days endpoints, with 30 days recurrence of 36% vs 67% ($p=0.023$) and 90 days recurrence of 30% vs. 53% ($p=0.047$). However others^{29,30} hold the opinion that both the agents are of equal efficacy and that the economic cost, drug availability and local experience should be kept in mind while choosing between these two agents. Considering these factors, tetracycline seems to be the agent of choice in our setup. Apart from the agent chosen the success rate also depends upon proper selection and meticulous technique³¹. The mechanism of pleurodesis appears to be chemical pleural irritation and fibrosis of pleural surfaces while in case of tetracycline it is probably the result of low pH initiating an inflammatory reaction in the pleura causing fibrosis³². Pleuro-peritoneal shunt insertion is an option for patients with an intractable, symptomatic malignant effusion who cannot undergo or who have failed pleurodesis.^{33,34} We conclude that with good selection criteria and meticulous technique, pleurodesis with either tetracycline or bleomycine are equally effective in relieving symptoms due to large malignant pleural effusions and can improve the quality of life.

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