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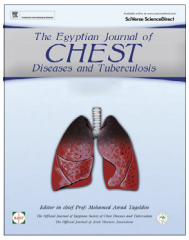

ORIGINAL ARTICLE

Chemical pleurodesis for malignant pleural effusion

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KEYWORDS

Malignant pleural effusion;
Pleurodesis;
Tetracycline;
Talcslurry;
Iodopovidone;
Bleomycin

Abstract *Background and Objectives:* Malignant pleural effusion is a common complication of primary and metastatic pleural malignancies. It is usually managed by drainage and pleurodesis, but there is no consensus as to the best method of pleurodesis, this study was designed to compare the effectiveness, side effects, and cost of different chemical pleurodesis agents used in patients with malignant pleural effusion.

Methods: Seventy-five patients with malignant pleural effusion were assigned into five groups each of 15 patients, Talc slurry 5 gm, Tetracycline500 mg, Bleomycin1 IU/kg, Iodopovidone (2%) and patients underwent tube drainage only. Tube thoracotomy was performed in all patients and agents were administered through the chest tubes.

Results: Tetracycline, talc slurry, iodopovidone andbleomycin, resulted inan insignificantly different success rates of 80%, 80%, 66.6%.73.3%, at 30 days and, 66.6%, 73.3%, 60%, 66.6%, at 60 days respectively while tube alone was much lower, 40% and 26.7% respectively. Chest tubes were removed after an average of 7.2 ± 1.4 days for tetracycline, 7 ± 0.8 days for talc slurry, 7.6 ± 0.9 days for iodopovidone and 6.4 ± 1.5 days for bleomycin which did not differ significantly. Chest pain was more common in the tetracycline group, dyspnea was more common in the talc group, and fever was more common in the iodopovidone group.

Conclusion: Since tetracycline, talc slurry, iodopovidone, andbleomycin achieved comparable success rates in this study, we suggest that the drug availability and cost are important factors in choosing a sclerosing agent in developing countries.

Introduction

Although the real incidence of malignant pleural effusion is not established, it is one of the most common problems that pulmonologists and oncologists face in their daily practice [1]. In one autopsy series metastatic pleural involvement was found in 29% of 191 cases of malignancy, but pleural effusion was present in only slightly more than half of these cases. Therefore, the

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incidence of malignant pleural effusion in patients dying of malignancy in this particular series was 15% [2]. About 75% of malignant pleural effusions are secondary to malignancies of the lungs, breast or lymphoma [1]. In the United States more than 150,000 new cases of malignant pleural effusion are estimated to occur each year, with 75% being due to lung or breast cancers [3].The presence of a malignant pleural effusion indicates that the patient has advanced disease with an ominous prognosis, and with a very small chance of long-term survival. Many patients with malignant pleural effusion have dyspnea which limits the quality of their life. Tube thoracostomy with bedside pleurodesis has become the most common approach to palliate symptoms related to the effusion [1]. Pleurodesis is the obliteration of the pleural space by fusion of the visceral and parietal pleurae with fibrous tissue. Recurrent symptomatic pleural effusions and pneumothoraces are indications for pleurodesis. Most of the agents used for pleurodesis injure the pleura and cause an inflammatory reaction together with a pleural effusion. Subsequently, the local activation of the coagulation system and the production of fibrogenic cytokines such as transforming growth factor ß lead to the production of collagen that can result in a pleurodesis.[4].

Tetracycline, doxycycline, bleomycin, and talc have been the agents most commonly used to produce pleurodesis [5] .Tetracycline has been replaced by doxycycline because the former is no longer available for parenteral use in most countries. Talc can be administered as either poudrage during thoracoscopy or as slurry via tube thoracostomy, with similar success rates [6]. Talc slurry is less expensive when the cost of the thoracoscopic procedure is considered [7].

The aim of this study was to compare the efficacy of tetracycline, talc slurry, Iodopovidone, bleomycin, and chest tube alone in producing pleurodesis in patients with malignant pleural effusions.

Patients and methods

The study protocol was approved by chest department, faculty and university councils including the Institutional Review Board at Zagazig University Hospitals. The study was performed in the chest, cardiothoracic surgery, oncology and radiotherapy departments between June2003 and September 2005. Initially, 125 patients were enrolled in the study. However, we encountered great difficulty in getting follow-up for all patients because many patients did not return for their visits, did not have telephones and lived a long way from the hospital. Accordingly, we continued the study until we had 60 day follow-up in 15 patients in each group. The patients with malignant pleural effusion met the following inclusion criteria.

1. Malignancy as proven by positive pleural fluid cytology, needle biopsy of the pleura or thoracoscopic biopsy.
2. A pleural effusion which was massive (occupying more than three quarters of the hemithorax or extending beyond the second rib anteriorly in the PA chest radiograph) or rapidly reaccumulating (dyspnea necessitating thoracenteses every 3 days or less).
3. Subjective improvement of patient's dyspnea following thoracocentesis.
4. Total re expansion of the lung after fluid drainage.
5. Pleural fluid pH > 7.2.

The following were exclusion criteria:

1. Atelectasis due to endobronchial obstruction.
2. Pleural fluid pH < 7.2
3. Prior intrapleural therapy
4. Any radiotherapy to the affected hemithorax.

All patients included in the study signed an informed consent which was approved by the Institutional Review Board, after which a new chest Xray was obtained and a diagnostic thoracentesis was performed to confirm that the patient still met the inclusion criteria.

The following investigations were done for pleural fluids:

- Pleural fluid glucose, protein concentration, LDH (the upper limit of normal for serum was 480 IU/L, using the Dimension RXL Machine:

DADE Behring.DIAMOND DIAGNOSTICS Holliston, MA, USA.

- Pleural fluid total and differential WBCs (CELL-DYN. ABBOTT, TEXAS, USA.)
- Pleural fluid pH using arterial blood gas machine ;(OMNI-C, ROCH, DIAMOND DIAGNOSTICS Holliston, MA, USA.)

All patients underwent tube thoracotomy using large bore chest tubes (30 French). The patients were assigned to one of the following five groups. Every fifth patient received the same treatment. The intrapleural injections were done once the pleural fluid output through the chest tube was less than 150 ml/day. Lidocaine 20 cc of 2% (AstraZeneca, London, UK) was installed intrapleurally 30 minutes before any chemical agent was injected.

Group1: Intrapleural injection of 500 mg of tetracycline (*Pfizer*, *MiddleEast*, *Cairo*, *Egypt*) mixed with 100 ml of sterile saline. [8].this low dose of tetracycline was intended to lessen the pain; it was used before by Wallach [9].

Group2: Intrapleural injection of 5 g of talc (*mixed particles, sized from10–45μm in maximum diameter*) (*Algomhorya .co. Ltd, Zagazig, Egypt*), in 100 ml of normal saline. The slurry was made by mixing 5 gm of talc with normal saline and agitated gently [10].

Group3: Intrapleural injection of 20 ml 10% iodopovidone (*NilePharmaceutical Co, 10th Ramadan City, Egypt*) mixed with 80 ml normalsaline [11].

Group4: Intrapleural injection of 1 IU/kg bleomycin (*Nippon Kayaku Co., Ltd. Tokyo, Japan*), in 100 ml normal saline [3].

Group5: Chest tube only with no intrapleural injections.

In the first four groups whom received chemical agents, the tube was clamped immediately after injection of the pleurodesing solution and remained clamped for 2.5 h. During this time the patient was turned to the supine, prone, right and left lateral decubitus and sitting positions so that the chemical substance could come in contact with all pleural surfaces. The patient was kept in each position for 30 min.

- After 2.5 h, the chest tube was unclamped.
- Follow up chest radiographs were done every 24 h until the tube was removed.