Egyptian Journal of Chest Diseases and Tuberculosis (2012) **61**, 399–404

The Egyptian Society of Chest Diseases and Tuberculosis

Egyptian Journal of Chest Diseases and Tuberculosis

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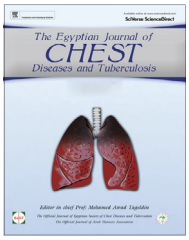

ORIGINAL ARTICLE

Pleurodesis using different agents in malignant pleural effusion

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Received 14 July 2012; accepted 25 July 2012
Available online 24 January 2013

KEYWORDS

Pleurodesis;
Malignant pleural effusion (MPE);
Bleomycin;
Doxycycline;
Povidone iodine;
5-Fluorouracil

Abstract *Objective:* Malignant pleural effusions (MPE) are characterized by rapid reaccumulation, after tapping, and many symptoms related. Pleurodesis, for the management of MPE, is intended to achieve symphysis between parietal and visceral pleura, and to prevent relapse of pleural effusion. Many chemical agents are tried to induce abrasion and damage of the pleural mesothelial layer to achieve this symphysis.

Aim: The aim of this study is to compare the results of medical pleurodesis, using 4 different chemical agents in these cases, to reach an efficient one with minimal complications.

Methods: Between July 2010 and July 2012, 40 patients with MPE, divided into 4 groups, underwent medical pleurodesis using 4 chemical agents in comparison: bleomycin, doxycycline, povidone iodine and 5-fluorouracil.

Results: Immediately and for 3 months after the procedure, the results of pleurodesis were assessed and the final reported success rates were 70% for bleomycin, 80% for doxycycline and 80% for povidone iodine, while 5 fluorouracil had the lowest success rate (50%) (P-value < 0.05).

Conclusion: Bleomycin, doxycycline and povidone iodine are nearly equally effective and safe pleurodetic agents when used in the optimal dose, while 5-fluorouracil had a much higher failure rate. Although povidone iodine and doxycycline are as effective and safe as bleomycin, they are cheaper alternatives and more available chemical agents for pleurodesis in cases with MPE.

Introduction

Malignant pleural effusions (MPE), which comprise a heterogeneous group of conditions, represent an important source of morbidity for patients with underlying cancer [1].

The standard management approach begins with a diagnostic and/or therapeutic thoracentesis. If the effusion recurs, other options include repeated thoracentesis, tube thoracos-

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Peer review under responsibility of The Egyptian Society of Chest Diseases and Tuberculosis.

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tomy with chemical pleurodesis, placement of an indwelling cuffed, tunneled pleural catheter with or without pleurodesis, medical thoracoscopy or video-assisted thoracoscopic surgery with pleurodesis [2].

Pleurodesis is the obliteration of the pleural space by fusion of the visceral and parietal pleurae with fibrous tissue in recurrent and symptomatic pleural effusions and pneumothoraces. 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 β lead to the production of collagen that can result in a pleurodesis [3].

It has been supposed that the ideal pleural sclerosing agent should be easily administered, safe, inexpensive, and widely available [4]. None of the agents presently used meet all of these criteria, and the search is still on. Huge varieties of sclerotic agents have been tested, with various success rates and drawbacks. They include talc, antibiotics (tetracyclines, minocycline, doxycycline), antimalarials (quinacrine, mepacrine), antineoplastic drugs (bleomycin, 5-fluorouracil, mitomicin, thiotepa, nitrogen mustard), 50% glucose and water, immunomodulating agents [interferon (IFN)-α, IFN-γ], iodopovidone, radioactive colloidal gold, autologous blood, fibrin glue, biological agents (suspension of killed *Corynebacterium parvum*, or bacille Calmette–Guérin), and finally nitrates [3,4].

Aim

The aim of this study is to compare the results of medical pleurodesis, using 4 different chemical agents; bleomycin ampoules, doxycycline capsules, povidone iodine solution and 5-fluorouracil ampoules, in cases of MPE, as regards; efficacy, safety, availability and cost.

Patients and methods

This study was carried out on 40 patients with MPE (23 patients had right and 17 patients had left pleural effusions), consisted of 4 females and 36 males, with age ranging from 45 to 76 years, admitted in, and referred to, the Chest Department, Menoufiya University during the period from July 2010 to July 2012. Regarding the aetiology of MPE, 14 cases were due to mesothelioma, 10 cases were due to metastasic adenocarcinoma of unknown origin and 16 cases were due to metastasis from different known origins: [lymphoma (3 cases), squamous cell lung carcinoma (3 cases), small cell lung carcinoma (2 cases), breast carcinoma (3 cases), hepatocelluler carcinoma (2 cases), abdominal sarcoma (one case), cancer-cervix (one case), and transitional cell carcinoma of bladder (one case)].

They were evaluated by detailed medical history, clinical examination, laboratory and radiological investigations (including CT chest), thoracentesis and pleural fluid analysis and closed pleural biopsy, using Abrams needle. All patients included in this were having free MPE, clinically and on CT examination, and those with probable adhesions were excluded. They were subjected to pleurodesis through an intercostal tube 28–36 French gauge, inserted under local anesthesia in the 5th intercostal space in the mid-axillary line.

They were randomized into four equal groups, each group consisted of 10 patients. The patients of the first group (***Group-I***) were subjected to pleurodesis with 60 mg *bleomycin sulfate* (bleocine® Nippon-kayaky Company, 4 vials 15 mg/vial, cost 125 EP/vial with total cost of 500 EP), were used for each patient, diluted in 50 ml of saline 0.9% and 10 ml of 2% xylocaine solution [5]. Seven milligram per kilogram of *doxycycline* (vibramycin, Pfizer Company, 100 mg capsules, costing 20 EP for the pack and the total cost for the patient), diluted in 50 ml of saline 0.9% and 10 ml of 2% xylocaine solution were used for pleurodesis in each patient in the second group (***Group-II***) [6].

Twenty milliliter of 10% *povidone iodine* (betadine, Mundipharma AG Company, 200 ml bottle of 10.5 EP cost for each patient), diluted in 50 ml of saline 0.9% and 10 ml of 2% xylocaine were used for pleurodesis in the third group (***Group-III***) [7]. Patients in the fourth group (***Group-IV***) were subjected to pleurodesis with *5 fluorouracil*(floracil®, Cipla Company, vials 500 mg/5 ml, 10 EP for the vial with a total cost of 40 EP for the patient), administered intra-pleurally in doses of 2 g diluted in 50 ml of saline 0.9% plus 10 ml of 2% xylocaine [8]. After intrapleural injection of the pleurodetic agent, the tube was clamped and the patient was rotated for 1 h, to guarantee adequate pleural distribution. After 1 h, the tube was opened for up to 72 h drainage, without negative suction application, and when the fluid drained was less than 250 ml/24 h, the tube was removed. All patients were followed up through the days of hospital stay, till discharge and for 3 months after pleurodesis, with clinical and radiological chest assessment.

The response to pleurodesis was considered to be;

* *Complete response (CR)*: if there was no reaccumulation of pleural fluid in the same hemithorax, after tube removal, during the 1st week of the procedure and all through the follow up period.
* *Partial response (PR)*: if there was accumulation of some fluid, early after tube removal (1–7 days), not causing symptoms and not requiring repeated thoracocentesis or tube drainage.
* *Failure of pleurodesis*: was considered if there was difficulty to remove the tube, because the pleural fluid drained through it is more than 250 ml/24 h (***primary failure***) or there was fluid reaccumulation after tube removal, that caused symptoms to the patient or necessitated repeated thoracocentesis or intercostal tube drainage, during the follow up period (*secondary failure*).

Results

Tables 1 and 2 show that the age of the patients in the first group ranged from 45 to 73 years, with a mean value of 60.7 ± 8.7 years; 9 males and one female. In the second group; the age ranged from 49 to 76 years with a mean 62.5 ± 8.6 years; 8 males and 2 females. In the third group; the age ranged from 46 to 71 years with a mean 64.3 ± 7.6 years; all the 10 patients in this group were males. Lastly, in the fourth group; the age ranged from 50 to 74 years with a mean value of 64.5 ± 7.7 years; 9 males and one female. There were insignificant differences between