EDITORIAL

PLEURODESIS: THE AGENT OF CHOICE

Muhammad Irfan

A malignant pleural effusion usually signifies advanced metastatic disease and is associated with a poor prognosis with median survival between 3 and 12 months, depending on the primary site [1]. Optimal management of these effusions has been debated over the years. Management choices include repeated therapeutic aspiration alone, for patients at the very end of life, chest tube drainage with chemical pleurodesis, thoracoscopic drainage and talc poudrage, or placement of an indwelling pleural catheter (IPC) [2]. Most of us would agree that the ideal method should be effective, safe, inexpensive, readily available and should require a short or no hospital stay.

Chemical pleurodesis, that is, the induction of pleural inflammation to cause fibrosis and obliteration of the pleural space, is mainly used to prevent reaccumulation of malignant pleural effusions. Over the past 70 years many agents have been tried including radioisotopes, quinacrine, antineoplastics (nitrogen mustard, bleomycin, mitoxantrone), tetracycline derivatives (tetracycline, doxycycline, minocycline), talc, erythromycin, sodium hydroxide, silver nitrate, iodopovidone, killed Corynebacterium parvum and OK-432 which is an immunostimulant obtained from Streptococcus pyogenes [2].

In the 1980's tetracycline was the most commonly used agent. However, in the late 1980's the company that produced parenteral tetracycline terminated its production in West. Subsequently it was shown that doxycycline and minocycline were comparable in efficacy to tetracycline [2, 3]. In our country tetracycline is still used, with powder obtained from oral capsules dissolved and used for pleurodesis.

When tetracycline became unavailable, the use of talc as a pleurodesis agent increased rapidly throughout the world. Indeed, it is the agent most commonly used for pleurodesis at the present time. Talc is probably the most effective sclerosing agent, with a success rate of greater than 80% [4].

The primary problem with talc, especially when small particle size talc is used, is its association with acute respiratory distress syndrome (ARDS) which is fatal in approximately one percent of patients who receive it intrapleurally [5]. Recent multi-center trials showed that large particle talc does not provoke ARDS, which is a fatal complication of pleurodesis with small particle talc [6]. There is evidence however that even large particle talc causes local and systemic inflammation, manifested by chest pain, fever and impairment of oxygen exchange [7]. Moreover, limited availability and the cost of medical talc have led several physicians in Pakistan to use cosmetic talc and other sclerosing agents. However, safety concerns relating to the unpredictable physical and chemical features of various preparations, together with the need for sterilization before use, are serious shortcomings associated with the use of cosmetic talc.

Talc can be administered either as an aerosol (insufflation) or a suspension (slurry). A large multicenter trial comparing talc poudrage vs. talc slurry showed no clear benefit of one technique over the other, with a success rate of 70% [8].

Section of Pulmonary and Critical Care Medicine, Department of Medicine, Aga Khan University, Karachi, Pakistan.

In this issue of *PJCM*, Humayon and colleagues report the results of their short term comparative study of talc poudrage through pleuroscope vs pleurodeisis with tetracycline through chest tube in malignant pleural effusion [9]. They assessed success rate at the end of 4 weeks on the basis of chest radiographs. Their results show success in 87% patients in the talc group as compared to 65.2% in tetracycline group. The sample size of the study was rather small to make an effective conclusion and their results are in line with the available data present in literature. It would have been better had they compared talc poudrage with pleuroscope and talc pleurodeisis through chest tube. Secondly they have not mentioned the difference in length of stay in hospital, quality of life and the reason of failure in both groups.

A systematic review of pleurodesis for malignant pleural effusion included 46 randomized controlled trials (RCTs) with a total of 2053 patients[10]. Talc was identified as the most efficacious agent and is currently recommended as the pleurodesis agent of choice by international guidelines [1, 10]. The success rate with talc is further increased when talc insufflation is used with pleuroscope as compared to chest tubes.

The other management option for the management of malignant pleural effusion is the placement of indwelling pleural catheters (IPC). In a systematic review of 19 studies evaluating the efficacy and safety of IPC for treatment of malignant pleural effusion in a total of 1370 patients, symptomatic improvement was reported in 95% of patients [11]. There were shorter lengths of hospital stay with IPC. Currently international guidelines advocate IPC for cases of known trapped lung or as second-line therapy after an initial unsuccessful talc pleurodesis[1].

In recent years there has been a shift from radiographic end points in clinical trials to more patient-centered outcomes. Successful management of malignant pleural effusion should therefore be measured in terms of the need for repeat pleural interventions in the patient's lifetime and prolonged improvements in dyspnea, rather than radiographic improvement alone [12].

Research over the past decade has provided a considerable body of knowledge regarding currently available sclerosing agents, and has attempted to address the role of alternative agents. Now there is a need of adequately powered randomized trials that use clinically relevant end-points for efficacy like level of dyspnea, quality of life and safety in order to generate robust evidence concerning the clinical utility of these agents. There is also a need of basic research as well in parallel, to further elucidate and experimentally target the steps in the pathogenesis of malignant pleural effusion for future development of effective, safe and convenient therapeutic interventions.

References:

1. Roberts ME, Neville E, Berrisford RG, Antunes G, Ali NJ. BTS Pleural Disease Guideline Group. Management of a malignant pleural effusion: British Thoracic Society Pleural Disease Guideline 2010. Thorax. 2010;65(suppl 2) ii32-ii40
2. Light RW: Pleural Diseases. 5th Edition. Lippincott, Williams and Wilkins, Baltimore, MD 2007.
3. Wu W, Teixeira LR, Light RW: Doxycycline pleurodesis in rabbits. Comparison of results with and without chest tube. Chest 1998; 114:563-8.
4. Haas AR, Sterman DH, Musani AI. Malignant pleural effusions. Chest. 2007;132:1036-1041.

5. Light RW: Talc should not be used for pleurodesis. Am J Respir Crit Care Med 2000; 162:2023-6.
6. Janssen JP, Collier G, Astoul P *et al*. Safety of pleurodesis with talc poudrage in malignant pleural effusion: a prospective cohort study. *Lancet* 2007; 369: 1535–9.
7. Maskell NA, Lee YC, Gleeson FV et al. Randomized trials describing lung inflammation after pleurodesis with talc of varying particle size. Am. J. Respir. Crit. Care Med. 2004; 170: 377–82.
8. Dresler CM, Olak J, Herndon JE II, et al; Cooperative Groups Cancer and Leukemia Group B; Eastern Cooperative Oncology Group; North Central Cooperative Oncology Group; Radiation Therapy Oncology Group. Phase III intergroup study of talc poudrage vs talc slurry sclerosis for malignant pleural effusion. Chest 2005;127(3):909-915
9. Humayon GM, Mushtaq MA, Ayyaz S, Shahzad MI, Kamran MH, Hafeez A,et al. Short term comparison of talc poudrage with tetracycline for medical pleurodesis in malignant pleural effusion. PAK J Chest Med. 2012; 18(4):**-**
10. Tan C, Sedrakyan A, Browne J, Swift S, Treasure T. The evidence on the effectiveness of management for malignant pleural effusion: a systematic review. Eur J Cardiothorac Surg. 2006;29(5):829-838
11. Van Meter ME, McKee KY, Kohlwes RJ. Efficacy and safety of tunneled pleural catheters in adults with malignant pleural effusions: a systematic review. *J Gen Intern Med*. 2011;26(1):70-76
12. Maskell NA. Treatment options for malignant pleural effusions: patient preference does matter. JAMA 2012; 307(22):2432-3.