

Chemical Pleurodesis for Malignant Pleural Effusion: How Far Have We Come in 80 Years?

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Malignant pleural effusion (MPE) is one of the most common causes of pleural exudates worldwide. Approximately 30–50% of all patients with metastatic malignancies will have pleural involvement at autopsy, and half of these will have pleural effusions, ranging from insignificant to massive [1].

Patients with a symptomatic MPE and an expected median survival of more than 3 months should be offered definitive palliative intervention, which may include chemical pleurodesis and/or the insertion of an indwelling pleural catheter (IPC). Globally, there is major heterogeneity in the therapeutic approach to MPE, mostly because of the paucity of high-quality evidence [2].

Chemical pleurodesis is achieved by the instillation of a sclerosant via a small-bore chest tube, IPC or during thoracoscopy. Amazingly, the most commonly used agent, talc, was first introduced as far back as 1935 [3]. In the largest randomised study on MPE of over 450 patients, the success rate of talc pleurodesis was approximately 75% at 1 month, but it was progressively reduced to approximately 50% at 6 months [4]. The same study found that talc poudrage was not superior to talk slurry, except in cases with lung and breast cancer [4].

Respiratory failure and acute respiratory distress syndrome (ARDS) have been associated with talc pleurode-

sis, most likely because of the systemic absorption of small-size talc particles [2]. In a multicentre, open-label, prospective cohort study of 558 patients with MPE who underwent thoracoscopy and talc poudrage with 4 g of calibrated French large-particle talc, no patients developed ARDS, although oxygenation deteriorated in the first few days after talc pleurodesis [5].

Other agents that have been used for chemical pleurodesis over the years include bleomycin, tetracycline and doxycycline. A meta-analysis of 10 randomised studies found that non-recurrence of effusion was more likely with talc than other sclerosants, suggesting that there is little advantage of using other agents over large-particle talc [6]. Only doxycycline has success and complication rates comparable to talc [7].

The search for the most effective and safe agent for chemical pleurodesis is ongoing. Many reports have suggested that iodopovidone (povidone-iodine) may be as effective as talc, with a comparable complication rate, although others have suggested that its use may be associated with serious complications including renal failure, confusion, visual loss and even neonatal hyperthyroidism [8]. Neto et al. [9] previously reported a retrospective analysis of 61 pleurodesis procedures with iodopovidone performed in 54 patients. They observed a very high suc-

cess rate of 98.4%, with a paucity of complications, and suggested that the agent may be a good option for chemical pleurodesis [9].

In this issue of *Respiration*, Andrade Neto et al. [10] describe the safety profile of iodopovidone when used as a sclerosant to achieve pleurodesis in MPE. A total of 60 patients with MPE, who were not allergic to iodine, had a good performance status and had total or near total lung expansion after pleural drainage were enrolled in their prospective study. Patients were randomised to pleurodesis with either 1 or 2% iodopovidone. The overall failure rate was very low, which was also not unexpected given the inclusion criteria and the fact that the majority of patients had metastatic breast cancer. A total number of 47 serious events were reported in 34 of the 60 patients, implying that more than half of all patients experienced at least one serious adverse event. Pleuritic pain was common, as expected, but of concern was the frequency of metabolic disturbances, including hyponatremia and deranged liver enzymes. Subclinical hypothyroidism was observed in 5 patients. No differences were observed between the groups randomised to either 1 or 2% iodopovidone with regard to adverse events, efficacy and quality of life.

The same group recently reported the safety profile of three different doses of silver nitrate used for pleurodesis

in MPE [11]. Once again, adverse events raised concerns. Serious events included acute kidney injury, ARDS and confusion. Four patients died during this study, with one death possibly related to the agent [11].

The Brazilian team of investigators should be commended for seeking effective and safe alternatives to talc pleurodesis, albeit that their recent studies suggest that neither iodopovidone nor silver nitrate will soon replace large-particle talc as the agent of choice for chemical pleurodesis.

Clearly, little progress has been made over the past eight decades in finding the ideal sclerosant for chemical pleurodesis, and in an era of high-quality evidence-based medicine, the management of MPE is still largely based on expert opinion rather than high-quality data.

Studies comparing chemical pleurodesis with IPC have yielded conflicting evidence with regard to efficacy, quality of life and cost-effectiveness [2]. Current interest focuses around combining IPC with pleurodesis, either spontaneous or chemical [2]. Ultimately, the answer probably lies in an individualised approach rather than any one specific modality, as many factors, including patient preferences, tumour type, prognosis, performance status, recurrence rate of the effusion and involvement of the underlying lung, impact on the success of any intervention offered.

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