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EDITORIAL

Management of malignant pleural effusion at the beginning of 2014

Prise en charge de l'épanchement pleural malin au début de l'année 2014

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A recent study from Viet Nam has reopened the decades-long discussion regarding the best palliative treatment for chronic malignant pleural effusion, by re-introducing the use of pleural bleomycin injections via small bore catheter to provoke pleurodesis [1].

Although talc pleurodesis has achieved widespread popularity for treatment of malignant pleural effusions, other modalities of care have found niches around the world, including placement of indwelling small bore catheters [2], and pleural sclerosis created with other chemical agents, including doxycycline [3], bleomycin [1], and iodopovidone, the largest study of which was performed in Ho Chi Minh City [4] Talc, which has often been unavailable in Asia, may be the least expensive and currently USP talc is sold in the United States in bulk at a price that amounts to sixty American cents per patient*.

Iodopovidone is also inexpensive and in large controlled studies appears to be only slightly less effective than talc slurry and thoracoscopic talc poudrage (unpublished data). Conversely, bleomycin is rather expensive (cost in Viet Nam was not stated [1]) but many oncologists feel comfortable with it since they use it often for chemotherapy and they hope that intrapleural bleomycin may add some as yet unproven benefit.

Tetracycline (TCN) pleurodesis has been largely abandoned since the preparation is unavailable in many countries. In addition, it is very painful and a multicenter study of pneumothorax showed it to be less effective for pleurodesis in man (75%) than expected from rabbit studies [4]. Furthermore, Boutin prospectively demonstrated that although tetracycline success in pleurodesis at one month could be similar to thoracoscopic talc poudrage (80%), at six months of follow-up 80% of the talc patients remained free of pleural effusion, while the TCN patients' success rate had dropped to 50% [5]. For this reason, we have since focused our attention at long term success, at 3, 6, and 12 months, rather than one month.

Recent studies have focused on the use of indwelling catheters for palliation of dyspnea due to pleural fluid, instead of using a sclerosing agent to induce pleurodesis. However, a large prospective randomized study supported by a catheter manufacturer recently showed that talc slurry pleurodesis (talcum powder suspended in saline and injected via a chest tube into the pleural space) was "NOT inferior" to the indwelling catheter technic [6].

Furthermore, several studies have favored thoracoscopic talc poudrage over talc slurry - especially in lung cancer and breast cancer - though not all have been statistically significant [7-9]. This suggests thoracoscopic talc pleurodesis may be more effective than the catheter technic, but we need controlled prospective studies comparing indwelling catheters to thoracoscopic talc poudrage. Current practices in the West often choose the technic most in favor locally or they choose the patient's preference. Further studies might also settle the question of why Tremblay's study of 250 catheter insertions showed

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better survival when the indwelling catheter induced pleurodesis (254 days survival) than when pleurodesis never occurred (71 days survival) [2]. If patients live 3.6 times longer when pleurodesis occurs, perhaps it is better to use a sclerosant than an indwelling catheter in those patients expected to live for at least several months. Many experts agree that the catheter is preferred in patients with limited life expectancy or with trapped lung.

The data on talc reaching as high as 90% long-term success was itemized in a thoracoscopy textbook in 1991 [10] and in a paper the same year showing 92% success after one year [11]. Subsequently questions were raised whether talc might induce the Acute (Adult) Respiratory Distress Syndrome (ARDS), but there were no cases of ARDS among 360 cases published by Boutin and collaborators [12], using calibrated talc prepared in France (Luzenac). European pulmonologists then published a prospective study of 555 patients pleurodesed with Luzenac talc, finding zero cases of ARDS [13]. Rare ARDS cases do arise in the USA, where Luzenac talc is not available, but it is not clear if this is due to use of small particle talcs or to other factors.

Although doxycycline has its defenders, it is probably more painful than talc and as a congener of tetracycline the question remains if doxycycline, too, has declining effectiveness over time. Furthermore, tetracycline was shown to be ineffective in low pleural pH effusions [14], which would include 50% of mesotheliomas. In a recent retrospective study comparing 138 cases of doxycline pleurodesis with 450 talc pleurodeses in malignant pleural effusion, the ratio of success in various tumor types was 49 - 70%, favoring talc [3].

The absence of publications on doxycline or bleomycin pleurodesis in mesotheliomas - a most difficult tumor to control - and with other low pH malignant effusions suggests that they are as ineffective as tetracycline. Lam Quoc's comment on non-significance of low pH and low pleural glucose in his bleomycin study is important enough to warrant publication of the exact data [1]. What were the numbers and the p values between groups ?

With this background,what can be said about bleomycin today. First of all, the data presented by Lam Quoc et al may not be generalizable to other treatment centers in Viet Nam, for several reasons: Over half the tumors were lung cancer and 2/3 were males. In some studies women may predominate with primary disease of the breast & ovary. In other centers, mesothelioma may be predominant, a tumor where only studies of pleurodesis with thoracoscopic talc poudrage have been published in large numbers [12]. Although mesothelioma has been infrequently diagnosed in Viet Nam for lack of pathological expertise and the expensive reagents needed to make the diagnosis with certainty, capability for diagnosis appears to be improving (unpublished data). With large-scale importation of asbestos continuing in Viet Nam, the percentage of effusions due to mesothelioma is likely to increase.

Small bore catheters - which we have used for drainage for 30 years - were advocated in the 1990s in conjunction with bleomycin [15]. Although the authors were enthusiastic about the technic, only 56% of the patients were either alive or evaluable at 30 days. So their report of 72% short-term successes amounts to one month success in only 39% of all patients. This must be compared, for instance, with 100% success in 26 consecutive mesothelioma patients treated with talc poudrage and living a median of 19 months [16].

In comparison with earlier studies [15] the current authors have wisely chosen patients with a high performance status and a life expectancy more than 3 months. Their report of 88% 'success' with bleomycin pleurodesis after one month sounds impressive, but with four qualifiers: they combine "partial" and "complete" success, to achieve 88% success. We therefore need to know their definition of "partial" and "complete" success and the numbers in each group before we can begin to compare their results with other reported data.

Furthermore, we are more interested in the results at 3 and 6 months, for the reasons mentioned above. Hopefully, this related information will be forthcoming, permitting more relevant statistical analyses. We need also to learn what was the total number of malignant pleural effusions seen in the Cho Ray hospital during the period of the study, in order calculate what portion of all patients met the qualifications for the study. And ideally, prospective randomized, controlled studies will appear comparing cost, success, side effects of this technic with (a) thoracoscopic talc poudrage and (b) small bore catheters without the addition of bleomycin.

The authors' data does not support the concluding remarks that bleomycin may help augment the quality of life in cancer patients whose cancers are resistent to chemotherapy, any more than the other sclerosants. In addition, pleurodesis by any sclerosant provides palliation to both chemotherapy sensitive and resistent patients, many of whom will live for over a year before succumbing to their disease.

In summary, Lam Quoc's study re-presents bleomycin as an option for palliation in malignant effusions,

but the data so far is less impressive than studies of talc and iodopovidone and bleomycin is more expensive. Randomized prospective studies will help us sort out which modalities of care are the least costly and the most effective.

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CONFLIT D'INTERETS

Aucun.

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