Development of a Disposable Spray Canister for Talc Pleurodesis*

A Preliminary Report

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Talc pleurodesis has been used for more than 50 years in both the United States and in Europe, and it has proven to be safe and effective in patients with malignant pleural effusions as well as recurrent pneumothorax. In this preliminary report, we describe a disposable, single-use spray canister that allows intrapleural administration of sterile, asbestos-free Luzenac talc, thus facilitating thoracoscopic talc insufflation for pleurodesis, particularly in patients with recurrent malignant effusions. The talc is delivered ready to use, administered via a hollow plastic delivery catheter that can be inserted through the pleural trocars used during thoracoscopy. Use of this spray canister allows practitioners to avoid complex handling and sterilization procedures required for bulk talc powder.

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Pleurodesis is usually recommended when patients with persistent or recurrent pleural effusions have failed multiple drainage procedures. The vast majority of these patients have malignant pleural effusions (MPE), often with pleural metastases, and are no longer responsive to systemic therapy. Others have paramalignant effusions or effusions related to massive ascites or peritoneal carcinomatosis.1 During the last 100 years, surgeons and chest physicians have searched for an effective means of pleurodesis, and many chemical, as well as other agents have been employed with varying degrees of success.2 Although never approved for intrapleural use by the Food and Drug Administration, tetracycline has been most frequently used in the recent past, but is no longer available.3 Bleomycin, a cytotoxic agent reportedly successful in up to 70% of instances, is costly and has systemic adverse effects.4 With the recent resurgence of thoracoscopy, talc pleurodesis, once quite popular, is increasingly used, and several investigators have shown that talc is superior to other agents in both clinical and experimental settings.5-7

Description of Spray Canister

The purpose of this report is to describe a spray canister that allows intrapleural administration of sterile, asbestos-free talc powder (developed in collaboration with Luzenac Europe [Toulouse, France] and Axion [Aubagne, France] and distributed by Bryan Corp. [Woburn, Mass.] as aerosolized talc). The talc is from Luzenac, a small town located in the area of Ariege, France, the site of one of the largest open-air talc mines in the world. Luzenac talc is known for its relative purity: the canister contains 4 g of Luzenac PR 7841 white talc powder (talc and chloride concentration greater than or equal to 95%) with a pH of 9, a real density of 2.58 to 2.83, and a solubility in water less than 0.1%. Associated minerals include dolomite (less than 3%), calcite (trace elements only), and quartz (less than 3%). No amphiboles have ever been detected (x-ray diffraction as described in the Cosmetic, Toilettry, and Fragrance Association J4-1 norms of the American cosmetic industry). Products have been systematically controlled since 1978 (information supplied by the manufacturer). Additional elements include soluble calcium (0.17%), soluble magnesium (0.09%) soluble iron (60 ppm), chloride (> 140 ppm), and insoluble calcium (<200 ppm). This aerosolized talc fulfills requirements for material safety as per EEC directive 91-155, March 5, 1991, and fulfills criteria for European Pharmacopoeia. Indeed, Luzenac already provides much of the medical and cosmetic grade talc powder for Western Europe.

Instructions for Use

Each specially designed single-use, disposable canister provides delivery of at most 4 g of asbestos-free Luzenac talc at a maximum rate of 0.4 g/s. The talc is distributed as a fine mist of similarly sized particles. Talc is not delivered by metered dose, but depends on the extent and duration of manual compression of the nozzle (Fig 1). The talc-filled canister is sterilized...
by gamma radiation and marketed in a sterile peel pack in which are also enclosed 15- and 25-cm hollow plastic delivery catheters. The propellant is dichlorodifluoromethane.

Prior to pleurodesis, the sterile talc canister and nozzles should be removed from the sterile packaging, after which the protective cap on the canister may be removed and the canister shaken. The nozzle and delivery catheter are then securely attached to the canister. Usage of the shorter 15-cm catheter is recommended for application through pleural trocars or at the thoracotomy site. The distal extremity should not be in close proximity to lung parenchyma. It is somewhat sharp and may cause parenchymal damage. In addition, the talc is delivered under pressure. Although no pressure-related damage has yet been seen, it is a potential danger of pressurized talc spray administration. While firmly holding the nozzle and delivery catheter together in one hand, pressure is applied to the nozzle on the canister. The distal extremity of the delivery catheter should be pointed in several different directions to ensure equal and extensive delivery over all pleural surfaces. The talc canister is kept vertical to maximize distribution. In case of limited talc pleurodesis, talc is applied only to the area of interest. During talc delivery, the canister becomes cold, signaling near total talc evacuation. If talc is delivered through a pleural trocar during thoracoscopy, care should be taken to keep the distal extremity of the delivery catheter about 0.5 cm beyond the tip of the pleural cannula. Otherwise, talc will adhere to the sides of the cannula, and intrapleural distributions will be unsatisfactory. After application, the talc canister and delivery catheters should be discarded.

**Preliminary Clinical Experience**

We have used this device in 12 patients with MPE and in 9 patients with spontaneous pneumothoraces (in addition to bleb or bulla resection). Pleurodesis was successful at 90 d (defined as absence of symptoms attributable to effusions, clinically insignificant increase of pleural effusion evidenced on chest x-ray film compared with baseline films, and requiring no further thoracentesis) in 11 of 12 patients and in all patients with pneumothorax (the follow-up was 1 year). No complications of talc administration occurred, although about 30% of patients had low-grade temperatures after thoracoscopy. A prospective study comparing talc pleurodesis using this device and routine talc powder administration using a standard pneumatic atomizer (Richard Wolf Co.) is underway.

**Possible Benefits and Pitfalls**

Overall, this disposable canister is effective and practical. Complex in-hospital sterilization and handling procedures of bulk talc powder are avoided, and talc administration is simple, rapid, and clean. The canister is expensive, however, when compared with other talc preparations. For example, at University of California, San Diego, Medical Center, routine talc preparation, including purchase, sterilization, packaging, and handling, costs only $4.00. Another drawback of the canister is the inability to quantify talc administration. For example, we use the entire contents of a canister for patients with MPE and extensive neoplastic parietal pleura involvement, but we use only a few spray applications for limited pleurodesis in patients with benign disease or pneumothorax. Unfortunately, there is no way of quantifying the amount of talc delivered is less than the entire contents is used. This is quite different from the way standard talc powder is packaged in our institutions (in sterile plastic test tubes containing either 1.2 or 2.5 g of sterile talc powder).

Some minor pitfalls relate to the delivery catheters. Their tips are too sharp and could tear lung parenchyma. We have easily done this in experimental animal models. Also, talc tends to clump if the delivery catheter is held too close to the lung or to the chest wall parietal pleura. We believe that thorascopic administration of talc with the canister through a single point of entry is more difficult than through two points of entry, where the delivery catheter’s position can be easily verified thorascopically. The delivery catheter also may detach from the nozzle as pressure is applied. For this reason, the canister, nozzle, and catheter should be held firmly during application. In regard to previous suggestions of aerosolized talc delivery through an indwelling chest tube, we find this totally unsatisfactory. Talc clumps...
up inside the chest tube, even when the longer 25-cm delivery catheter is used. Therefore, we do not believe that aerosolized talc delivery through an indwelling chest tube can replace talc slurry administration.

**DISCUSSION**

Talc pleurodesis was first suggested in 1935 by Bethune, a Canadian surgeon who investigated methods of achieving adherence of lung parenchyma to the chest wall prior to performing lobectomy. In this study, Bethune actually credits a deceased Canadian physician, R. U. Harwood, for suggesting the use of commercial talc for this technique because of the known fibrogenic properties of silicate powders. Bethune also describes the first thoracoscopic administration of talc powder using a specially designed “return-air” blower made by the Filling Company. Subsequently, thoracoscopic talc poudrage (poudrage, which is French for powdering, consists of spraying sterile talc powder over the visceral and parietal pleura surfaces) was used for pleurodesis in patients with tuberculosi as well as in patients with spontaneous pneumothorax, although several surgeons later preferred talc administration via thoracotomy, even in patients with malignant pleural effusions. In 1958, Chambers, a thoracic surgeon from San Diego, revived the technique of talc slurry pleurodesis (by talc slurry, one usually means that sterile talc powder is diluted in 50 to 200 mL of normal saline solution and instilled via pleural trocar or chest tube), reporting an 85% success rate after instillation through an indwelling chest tube. Similar results were reported in 1967 by Jones using thoracoscopic application of talc slurry, and in 1976 by Adler and Sayek. This thoracic surgeon from New York also described a novel talc powder aerosol delivery system developed in cooperation with the Union Carbide Corporation in 1967. Microcel B, an amorphous calcium silicate used to fluidify talc and avoid clumping, was added in small amounts to US Pharmacopoeia-approved talc inside a metal container. A small Teflon delivery catheter was employed for administration into the body cavity during thoracotomy. Although successful, this product was not commercialized owing to lack of interest by the company (verbal communication, R. Adler, MD, December 1993).

Although talc was repeatedly used for pleurodesis in patients with MPE in both Europe and the United States throughout the 1960s, it was largely abandoned in the 1970s, especially in the United States. Indeed, there had been suggestions that proportional mortality from carcinoma of the lung and pleura among talc workers was four times that of a control population. In addition, tetracycline was becoming a most popular agent since the first report of its successful use for pleurodesis by Rubinson and Bolooki in 1972.

A potential problem of intrapleural talc administration, therefore, is the carcinogenicity of the talc. The issue surrounding talc use is particularly confusing because many mineral talcs, especially those previously mined from New York, were heavily contaminated with tremolite or anthophyllite. Talc asbestosis, produced by inhalation of talc with asbestos fibers, is a well recognized medical illness. Talc is, after all, a hydrous magnesium silicate (Mg6SiO20(OH)4), sometimes containing a small amount of aluminum silicate. Its formula is similar to that of asbestos. The formula for chrysotile asbestos, for example, is Mg6Si4O10(OH)8, and contamination of talc with asbestos, especially tremolite, has been reported. Other minerals such as dolomite (calcium magnesium carbonate) may also “contaminate” talc. The results of experimental studies of Wagner et al and Rubino et al as well as those of retrospective studies performed by the Research Committee of the British Thoracic Association in England and by Leophonte et al in France show that pure talc (containing no asbestos) is not carcinogenic. Both the European and American Pharmacopoeia, therefore, have instituted strict guidelines for medical-grade and cosmetic-grade talc composition, not only addressing requirements for asbestos-free talc, but also limiting its contamination with bacteria or other minerals. Although further research is required in this area, current evidence suggests that fears of asbesto-free, pure talc-induced neoplasms are unfounded. To our knowledge, no cases of neoplasm caused by intrapleural administration of sterile, asbestos-free talc have been reported.

Many studies have demonstrated that talc pleurodesis is a safe and effective means of achieving apposition of the pleural surfaces in patients with MPE. Success rates are reportedly greater than 85% . In animal experiments as early as 1941, Lelourd showed that pleurodesis was achieved by the 7th day after talc administration. In a recent canine study, Bresticker et al reported that pleural symphysis from talc was comparable to that obtained by mechanical abrasion. Mathlouti et al showed that talc caused an inflammatory reaction confined to the pleural surfaces, confirming previous work done by Frankel et al. Controversy subsists, however, regarding the ideal method of administration, and it is unclear whether poudrage has any advantages over slurry. Boutin et al, for example, have repeatedly advocated thoracoscopic talc poudrage. Additional support for this procedure, which may be safely performed with the patient under local or general anesthesia, is provided by several studies. Ohri et al reported 95.5%
success in 42 patients, and Aelony et al44 showed success in 23 of 28 (82%) patients. Hartman et al8 compared the use of insufflation of talc under thoracoscopic guidance with control populations who had received either tetracycline or bleomycin pleurodesis, reporting a 95% success rate of talc at 90 days compared with 70% for bleomycin and 47% for tetracycline. Poudrage may be more effective than simple administration of talc slurry through a previously placed chest tube because adhesions and loculated fluid collections seen during thoracoscopy can be removed prior to pleurodesis. Additional, prospective, multi-armed randomized protocols and animate laboratory research are necessary, however, to further define indications for the selected techniques of talc administration.

In contrast to many favorable clinical reports of talc pleurodesis, there are reports of immediate adverse effects of intrapleural talc administration and those suggesting potential restrictive ventilatory impairment years after talc pleurodesis for recurrent pneumothorax.52 Roujeau and Rose53 linked talc use to pulmonary talcoma. Talc pachypleuritis (pleural inflammation and thickening), although not constant radiographically, has been described.17,49 Acute pneumonitis54,55 and acute respiratory distress syndrome56 also have occurred shortly after intrapleural talc administration, although definite causal relationships between respiratory insufficiency and talc, however, have not been established. Whether adverse effects of talc are related to dose or mode of administration requires investigation. In regard to potential long-term restrictive lung disease after intrapleural talc administration in patients with pneumothorax, Lange et al57 performed pulmonary function tests on 114 patients during a 22- to 35-year follow-up study. Only mild, statistically insignificant differences in ventilatory function were discovered. In the experimental setting, McGahren et al58 showed that talc pleurodesis did not affect dynamic or static lung compliance in growing swine. It appears, therefore, that fears of decreased lung function due to talc pleurodesis probably are unfounded.

In summary, if talc is to be recognized by medical and surgical communities as an effective and safe method of pleurodesis, clinical and laboratory studies need to be performed to answer specific questions regarding mode of administration, talc composition, and effects of talc pleurodesis compared with other methods of pleural symphysis. Practical problems also must be addressed. Intrapleural talc administration has not been formally recognized by the US Food and Drug Administration, and lack of standardization regarding dose, mode of administration, packaging, and handling persists. Many practitioners, for example, use European or US Pharmacopoeia-approved talc in its “pure” form. It is unclear whether the composition of talc obtained from different sources can alter its fibrogenicity. Others combine talc with thymol iodide, as originally described by Bethune.8,46 Advantages of this mixture over pure asbestos-free talc are undefined. It is noteworthy that several different talc sterilization techniques are available. For example, talc may be gamma-radiated and placed into sterile peel packs,59 whereas, at the University of California, San Diego, Medical Center, medical-grade asbestos-free US Pharmacopoeia-approved talc powder is purchased in bulk form, packaged in unit doses, and sterilized using a combination of ethylene oxide and dry heat. While some hospitals willingly share their handling guidelines, others refuse to do so categorically. The availability of a sterile, asbestos-free talc spray canister could facilitate talc acquisition and provide an alternative to institutionally prepared talc for pleurodesis.

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