Talc Pleurodesis for the Management of Malignant Pleural Effusions in Japan

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Abstract

Objective  Malignant pleural effusions are commonly treated with tube drainage followed by chemical pleurodesis to maintain the patient’s quality of life. While talc is now accepted to be a worldwide gold-standard sclerosing agent for treating malignant pleural effusion, it is not yet approved in Japan. Instead, many patients are administered OK-432 for pleurodesis, which carries the risk of complications such as high-grade fever, chest pain, anaphylactic shock, interstitial pneumonia and acute renal failure. To assess the efficacy and safety of talc as a sclerosing agent in the management of malignant pleural effusions in Japanese patients.

Methods  Pleurodesis was performed using 4 g of sterile talc with thoracoscopic talc poudrage or the administration of talc slurry via a chest tube in patients with malignant pleural effusions.

Results  A total of 57 patients were included. The success rate of pleurodesis assessed on chest radiography at 30, 90 and 180 days was 90.6%, 80.9% and 76.1%, respectively. Complications occurring after talc pleurodesis included fever in 10.5% of the patients and chest pain in 14.0% of the patients. No major complications were reported.

Conclusion  Talc pleurodesis is an effective and safe treatment for the management of malignant pleural effusion in Japanese patients.

Key words: malignant pleural effusion, talc poudrage, talc slurry, pleurodesis


Introduction

Malignant pleural effusion is a disease that is frequently faced by pulmonologists in association with the increased number of patients with malignant diseases. When treating malignant pleural effusions, pleurodesis is commonly performed in order to maintain the patient’s general condition. In Japan, OK-432, a purified preparation derived from *Streptococcus pyogenes*, is primarily used as a sclerosing agent. In contrast, the worldwide standard therapy for controlling malignant pleural effusions is pleurodesis with talc, as talc has been reported to have a better success rate and a lower incidence of side effects than other agents (1, 2).

Talc is a powder that includes various types of minerals used for chalks and cosmetics. Concerns have been raised that intrapleural talc administration may cause acute respiratory distress syndrome; however, studies have revealed that using talc with a large particle size does not lead to systemic inflammation (3, 4). According to these reports, we performed talc pleurodesis to treat malignant pleural effusions in order to assess the efficacy and safety of talc in Japanese patients using large particle sterile talc as a sclerosing agent.

Materials and Methods

Patients

Between May 2007 and April 2012, a prospective study was performed in patients with uncontrolled and symptomatic malignant pleural effusions requiring pleurodesis at St.
Marianna University Hospital. The enrollment criteria included an age over 20 years, the presence of malignant cells in the pleural effusion proven on cytology or the presence of malignancy in a pleural biopsy and the ability to understand and sign the informed consent forms. Patients were excluded if the pleural effusion was recurrent after one or more attempts of pleurodesis or when insufficient expansion of the lung was achieved. Any pleural fluid, if present, was aspirated through a drainage tube placed in advance. The chest tube was subsequently flushed with 50 mL of sterile saline for at least two days when less than 200 mL of fluid was drained per day.

Methods

Sterile talc with a large particle size (Steritalc®; Novatech; La Ciotat, France) (Figure A, B) was used in this study. Talc was administered with thoracoscopic talc poudrage or the administration of talc slurry via a chest tube.

Thoracoscopic talc poudrage

Thoracoscopy was performed under local anesthesia at the chest wall using 10 mL of 1% lidocaine, with an additional 10 mL if needed. Then, a flexible trocar (MAJ-1058; Olympus; Tokyo, Japan) was placed, and a flexi-rigid thoracoscope (LTF-240; Olympus) was inserted into the pleural cavity. Thoracoscopy was used to detect any acute adverse events and to check the position of the chest tube. If no problematic findings were found, the tube was subsequently connected to -10 to -20 cm H₂O suction for at least two days then removed when less than 200 mL of fluid was drained per day.

Talc slurry administration via chest tube

Talc slurry was administered at the bedside via a chest drainage tube placed in advance. The chest tube was clamped, and 4 g of sterile talc mixed with 50 mL of sterile saline (Figure F) was injected into the pleural cavity through the chest tube. The tube was subsequently flushed with 50 mL of sterile saline. After being clamped for six hours, the chest tube was opened again and connected to -10 to -20 cm H₂O suction for at least two days. The chest tube was removed when less than 200 mL of fluid was drained per day.

Data collection and assessment

All data were collected prospectively. The primary endpoint was efficacy and the secondary endpoint was the safety of the talc. We evaluated efficacy at 30, 90 and 180 days after talc pleurodesis using chest radiography. Cases in which the chest tube was successfully removed when fluid drainage decreased to less than 200 mL per day and in which chest radiography showed a pleural effusion occupying less than one-third of the pleural space were considered to be effective. Cases in which the chest tube could not be removed because fluid drainage did not decrease to less than 200 mL per day or those with an increased pleural effusion occupying one-third or more of the pleural space on chest radiography were recorded as ineffective. Patients who died due to progression of the underlying disease before 30 days after pleurodesis or who did not show up for follow-up chest radiography were excluded from the evaluation. Regarding complications, chest pain requiring a prescription
for pain control, a temporary fever over 38.0°C and the occurrence of any complications requiring additional treatment or procedures within 30 days after talc pleurodesis were noted.

### Results

A total of 57 patients, including 39 women and 18 men with a mean age of 68.1±10.5 years (range, 43 to 92 years), participated in this study. There were 28 patients with lung cancer (26 cases of non-small cell lung cancer and two cases of small cell lung cancer), three patients with malignant pleural mesothelioma, 15 patients with breast cancer, four patients with ovarian cancer, three patients with renal cell carcinoma, one patient with endometrial cancer, one patient with pancreatic cancer, one patient with malignant melanoma and one patient with leiomyosarcoma. Eight patients underwent thoracoscopic talc poudrage and 49 patients received talc slurry. Removal of the chest tube was unsuccessful in three patients because the fluid drainage did not decrease to less than 200 mL per day. Among the remaining patients, the mean duration of chest tube drainage after talc pleurodesis was 4.4±2.2 days (range, 2 to 12). Thirty-seven patients (64.9%) received subsequent systemic therapy for underlying diseases after talc pleurodesis.

Table 1 shows the efficacy results for talc pleurodesis. Four patients died due to the progression of the underlying disease before 30 days after pleurodesis and were excluded from the evaluation for efficacy. The success rate (effective cases/evaluable cases) of talc pleurodesis among all patients at 30, 90 and 180 days was 90.6% (48/53), 80.9% (38/47) and 76.1% (35/46), respectively. Among the eight patients who underwent thoracoscopic talc poudrage, the success rate (effective cases/evaluable cases) remained 100% (8/8) until 180 days after the procedure. The success rate (effective cases/evaluable cases) at 30, 90 and 180 days among the patients who received talc slurry was 88.9% (40/45), 76.9% (30/39) and 71.1% (27/38), respectively.

Table 2 shows the complications observed after the procedures. Temporary fevers over 38.0°C were observed in six patients (10.5%). Eight patients (14.0%) complained of chest pain requiring a prescription for pain control and, of these, two patients (3.5%) had accompanying temporary dyspnea without desaturation. No major complications occurred as a result of the procedures.

### Discussion

For uncontrolled and symptomatic malignant pleural effusions, pleurodesis is commonly performed to maintain the patient’s quality of life. In Japan, OK-432 is primarily used as the sclerosing agent. While the efficacy of OK-432 is acceptable, with a reported success rate of 73%, the high incidence of high-grade fever and chest pain is problematic (5). In Western countries, on the other hand, talc pleurodesis has been the gold standard treatment for malignant pleural effusions for many years (6). In this study, we applied talc in 57 Japanese patients with malignant pleural effusions in order to assess the efficacy and safety of this compound. The success rate at 30 days after talc pleurodesis was 90.6%, which is similar to the findings of previous reports (7-9).

Regarding complications, our study showed that only a small number of patients complained of fever and/or chest pain after talc pleurodesis, while OK-432 is associated with high incidences of fever, chest pain and dyspnea. For example, we reported that only 10.5% of the patients complained of a fever over 38.0°C, which is considerably lower than a previous finding of 76.9% for OK-432 (5). Although the number of patients evaluated in this study was limited, the complications resulting from talc pleurodesis are considered to be acceptable. It is important for patients with malignant pleural effusions to maintain a reasonable quality of life, as many already suffer from a poor general condition.

In order to administer talc into the pleural space, we performed both thoracoscopic talc poudrage and talc slurry through a chest tube. In general, a rigid thoracoscope is commonly used for talc poudrage (10). We used a flexi-rigid thoracoscope in this study, which has the advantage of being able to reach narrow spaces more easily with its bidirectional flexible tip that allows for pleural fluid aspiration and biopsy under visualization from a single port of entry. Flexi-rigid thoracoscopy is primarily performed to diagnose pleural effusions of unknown cause (11-13). Previously, we described the use of thoracoscopic talc poudrage under flexi-rigid thoracoscopy with one port of entry and a dedicated catheter (14). In this report, we revealed that all nine procedures, including those performed in three patients over 75 years of age and two patients with a Karnofsky Performance Status Scale of 50, were performed safely and effectively and concluded that this technique is useful, even in elderly patients or those with a relatively low performance status. In the present study, the success rate at 180 days after pleurodesis was 100% for talc poudrage and 71.0% for talc

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**Table 1. Effective Pleurodesis and Success Rates after 30, 90, and 180 Days**

<table>
<thead>
<tr>
<th></th>
<th>30 days</th>
<th>90 days</th>
<th>180 days</th>
</tr>
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<tbody>
<tr>
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<td>53</td>
<td>47</td>
<td>46</td>
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<tr>
<td>Effective pleurodesis, n</td>
<td>48</td>
<td>38</td>
<td>35</td>
</tr>
<tr>
<td>Success rate, %</td>
<td>90.6</td>
<td>80.9</td>
<td>76.1</td>
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**Table 2. Complications**

<table>
<thead>
<tr>
<th>Grade*</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3 or severer</th>
</tr>
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<tbody>
<tr>
<td>Fever</td>
<td>6</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Chest pain</td>
<td>0</td>
<td>8</td>
<td>0</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

* Scored according to Common Terminology Criteria for Adverse Events (CTCAE) version 4.0
slurry. In fact, some previous reports have shown higher success rates for thoracoscopic talc poudrage (7, 8). This is most likely because thoracoscopic talc poudrage can confirm talc distribution throughout the entire pleural cavity under visualization, while the administration of talc slurry is performed blindly. Therefore, performing thoracoscopic talc poudrage is recommended, even though it requires special equipment and operator skill.

In conclusion, talc is acceptable in terms of both efficacy and safety as a sclerosing agent for pleurodesis in Japanese patients. As for the administration of talc, depending on the skill of the pulmonologist and whether the facility can perform thoracoscopic talc poudrage, it is better to administer talc under thoracoscopy, otherwise talc slurry should be selected.

The authors state that they have no Conflict of Interest (COI).

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References