ABSTRACT

Aim To determine the efficiency and safety of talc pleurodesis in treating the malignant pleural effusion and recurrent spontaneous pneumothorax.

Methods The study included 54 patients with malignant pleural effusion and recurrent spontaneous pneumothorax, who underwent talc pleurodesis using the “talc slurry” method of pleural talc obliteration.

Results Pleurodesis was successful in 52 (96%) patients. The average duration of thoracic drainage was 4.4 days. Procedure complications included higher body temperature, pneumonia and pleural effusion separation. All of the patients had satisfying radiological findings at the point of discharge and three months later. There was no death outcome related to the procedure of pleurodesis itself.

Conclusion Our study has proved the efficiency and simplicity of talc pleurodesis in treating symptomatic malignant pleural effusions and cases with recurrent spontaneous pneumothorax. Appropriate patient selection and compliance with surgical principles during the procedure make this method safe, efficient and successful in treating pleuropulmonary diseases. Large particle talc should be used for pleurodesis because of the minimum risk of complications.

Key words: surgery, malignant pleural effusion, pneumothorax
INTRODUCTION

Malignant pleural effusions (MPE) mostly appear as consequences of primary or metastatic cancer (1). Approximately half of those suffering from metastatic cancer will develop pleural effusion; lung cancer or breast cancer is present in 75% of the cases (2-4). The development of malignant pleural effusion often leads to the symptoms like dyspnea or cough, which considerably lowers the quality of life. Unfortunately, most malignant effusions do not react to systemic therapy and demand another different treatment approach (5,6).

Today, symptomatic malignant pleural effusion is considered an option in repeated thoracocentesis, the placement of permanent pleural chest tube and chemical pleurodesis (6). Repeated thoracocentesis and the placement of pleural catheters are good solutions for the patients who are expected to die soon (2). After a while, accumulated liquid causes repeated symptoms and repeated thoracocentesis becomes unpleasant and painful with possible complications (5). Also, repeated thoracocentesis results in the loss of proteins and electrolytes (5,6).

Spontaneous pneumothorax of secondary type occurs in patients with already existing lung disease. Those are mostly patients with chronic obstructive pulmonary disease and tuberculosis (7). The associated heart weakness makes the surgical treatment of such patients a very risky one, so the obliteration of pleural cavity is performed by using the “talc slurry” method (8,9).

Talc is a substance which is insoluble in water. Chemically, it is a hydrated magnesium silicate used for the first time in 1935 as a pleurodesis agent (9,10). The size of the particles plays a big role as talc preparations with mid-size particles smaller than 15µ result in much stronger systemic inflammatory response and the reaction of lung parenchyma on the mid-size 25µ particles talc (4,11). In some cases, talc can be found in other organs (kidneys, spleen, liver) after the application in pleural cavity (12,13). Hereby, we present our experience with the malignant pleural fluid chest drainage or recurrent spontaneous pneumothorax and subsequent instillation of talc. This study will attempt to point out the need for the right selection of patients for pleurodesis. Results of the study will be useful for general practitioners, pulmonologists as well as surgeons in understanding the surgical aspects of these diseases.

PATIENTS AND METHODS

This retrospective study including 54 patients who underwent talc pleurodesis due to malignant pleural effusion and secondary spontaneous pneumothorax had been performed in the Department of Thoracic Surgery of University Clinical Centre of Tuzla between January 2005 and January 2013 (Table 1). The Ethics Committee of the Clinical Center of Tuzla approved this investigation. Criteria for the treatment were Karnofsky Performance Scale (KPS): score ≥ 60 (the patient capable to take care of himself/herself, however, needs help occasionally) and lung re-expanding again after a thoracic drainage without any air or liquid collections left (13). Antibiotics, corticosteroids and non-steroidal anti-inflammatory drugs were not systemically given during the procedure (14).

The only contraindication was empyema pleurae. Patients were divided into two groups: the first group consisting of 50 patients with MPE and second group comprising four patients with recurrent pneumothorax. Mean age of our patients with MPE was 55±12,58 ranging from 21-84 years; mean age of our patients with pneumothorax was 70±7,07 ranging from 58-76 years. In the group with MPE, there were 22 male and 28 female patients: 25 patients with lung cancer, 13 patients with breast cancer, six patients with ovaries cancer, two with sarcomas, and one patient with either colon cancer, kidney cancer or lymphoma, as well as one patient with cancer of unknown primary origin.

Four patients were treated for recurrent pneumothorax. All of them had severe bullous changes in lung parenchyma with a consequent chronic obstructive pulmonary disease (COPD). The Forced expiratory volume in first second (FEV1) values were between 0.7 and 0.9 L. Surgery performed by VATS procedure or classic thoracotomy (8,9) requires total anaesthesia with a high risk of the occurrence of complications related to the surgery itself and the following diseases.

<table>
<thead>
<tr>
<th>Pathology</th>
<th>MPE Group (N=50)</th>
<th>PNTX Group (N=4)</th>
<th>lung emphysema</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung carcinoma</td>
<td>25 (50)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breast carcinoma</td>
<td>13 (26)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ovary carcinoma</td>
<td>6 (12)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sarcoma</td>
<td>2 (4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other malignoma</td>
<td>4 (8)</td>
<td></td>
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These patients had bad-quality lung parenchyma, weak parenchymal re-expansion and in this case surgery is often doomed to failure. Drainage pipe with smaller diameter, up to 20 F was used. Larger drainage pipe could slow down the process of ruptured bullae healing process. After the air loss on the thoracic drainage pipe stopped, the "talc slurry" method (12-14) was performed in order to prevent the disease relapse.

The following parameters were measured in the patients: occurrence of high temperature, pain intensity, respiratory complications, length of drainage, air loss on the drainage pipe longer than 5 days, and efficiency of the procedure. Pain was assessed on VAS (Visual Analogue Scale) and was rated with grade 1 to 5. The patient marked his pain severity ranging from mild pain (score 1) to the most severe pain (score 5). Pleurodesis was never simultaneously performed on both sides. The pleurodesis was considered successful if there was no recurrent effusion or pneumothorax. The thorax drainage tube had previously been placed and the diagnosis had been cytologically confirmed in all patients. Steritalc (Novatech, France) was used to make the suspension whilst being particularly calibrated with an average particle size of 25µ in order to avoid systemic dissemination.

The pleurodesis procedure was performed after radiological confirmation on effusion evacuation and recurrent lung expansion and in the presence of <150 mL of pleural drainage in 24 hours. After thorax drainage and complete re-expansion of lung parenchyme, 12 g of talc was dissolved in 50 mL 0.9% physiological solution in order to get a mush emulsion which was installed through thorax drainage with 5 mL of 1% xylocaine. The drainage tube was then closed and the patient is advised to change position more often in order to distribute the emulsion evenly inside the pleural cavity. After 12 hours, the drainage tube was affiliated to negative underwater suction. On the third day of pleurodesis, the drainage tube was removed in accordance with radiological confirmation. The follow-up x-ray shots were made three months after the procedure in order to evaluate the efficiency of pleurodesis.

**RESULTS**

Pleurodesis was successful in 52 (96%) patients with malignant pleural effusion, while the effusion loculated in one patient, and one patient had empyema pleurae. The procedure was performed on both sides in four patients. The drainage tube was systematically removed on the third day after pleurodesis, except in patients with complications. The average duration of thoracic drainage was 4.4 days.

The instillation of talc into the pleural cavity produced the increase of temperature in seven (14%) patients. Raised body temperature was not above 38.5 °C. The pain that required continuous analgesics was present in 12 patients (22.2%) and in one case it was severe. It was systematically treated with paracetamol analgesics and the analgesics with central effect. Amongst the 54 patients who underwent talc pleurodesis, 28 (52%) patients did not have any chronic chest pain (visual analogue scale (VAS) score 1), 14 (25.9%) had score 2, four had score 3 (7.4%), seven had score 4 (12.9%), and one (1.8%) patient had score 5.

One patient developed empyema, in which case, the drainage tube was removed after 21 days, and the treatment was successfully ended with the help of antibiotics. The patient with pneumonia was also successfully treated with antibiotic therapy.

Four cases of effusion separation were recorded. Effusion separation was treated with additional drainage or with the mobilization of the existing drainage tube. Only in one case the effusion separation lead to the localization of talc emulsion in the pleural cavity, and the whole procedure was unsuccessful. In the group of patients with pneumothorax, there was one patient with a longer drainage time caused by a prolonged air loss on the chest tube. The case was routinely solved by gradual removal of the drainage tube.

The success of pleurodesis did not depend on age, sex, histological type of tumor. We did not notice the difference in treatment efficiency, concerning the type of primary disease. The recovery time depended more on the general status of the patient and the earlier lung parenchyma status. The patients with prompt lung re-expansion after the effusion had the most favorable outcome. Such a prompt reaction to the procedure was recorded in 45 patients (83%).

The pleurodesis was performed on both sides in four patients. In two cases, there was a mehastatic osteo and hondrosarcoma from limbs; in one case, the patient had soft neck tissues sarcoma and in one case...
the patient suffered from metastatic ovary cancer. In these patients, the pleurodesis was performed successively with the interval of one month. Talc slurry is usually well tolerated. There were no serious complications such as adult respiratory distress syndrome (ARDS) or respiratory failure related to the procedure (Table 2). No deaths were attributed to the procedure.

Table 2. Complications in patients with malignant pleural effusion (MPE) and recurrent spontaneous pneumothorax (PNTX) during and after the procedure of pleurodesis

<table>
<thead>
<tr>
<th>Complications</th>
<th>MPE Group (N=27)</th>
<th>PNTX Group (N=3)</th>
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<tbody>
<tr>
<td>Pain</td>
<td>11 (22)</td>
<td>1 (25)</td>
</tr>
<tr>
<td>High temperature</td>
<td>7 (14)</td>
<td>1 (25)</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>1 (2)</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Empyema (1)</td>
<td>1 (2)</td>
<td></td>
</tr>
<tr>
<td>Separated effusion</td>
<td>4 (8)</td>
<td></td>
</tr>
<tr>
<td>Prolonged air leak (&gt;5 days)</td>
<td>1 (25)</td>
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</tbody>
</table>

DISCUSSION

According to our results, talc pleurodesis is a quick and efficient method of obliteration of pleural cavity. It can be performed in patient’s bed as a minor surgical procedure (15). Pleural pain and high temperature were the most common problems that occurred after the talc installation during our study. Pleurodesis is generally a painful procedure, and thus adequate analgesia during and immediately post-procedure is essential (16-18). The reported incidence of chest pain varies from 7-43% and fever 10-59% (6,8,9,15). In our research, amongst the 54 patients who underwent talc pleurodesis, chronic chest pain and the increase of temperature is in accordance with the published studies (6,8-10,13). In the treatment of pain induced by talc pleurodesis some authors suggest the use of 2-4 mg of morphine intravenously in combination with lidocaine (15). In our study, the pain was successfully managed by paracetamol analgesics and the analgesics with central effect. Good cooperation with the patients is needed during and after the procedure. It is necessary to explain to the patients the purpose of the procedure and the necessity of changing the body position in order to improve dispersion of talc suspension in the chest (9,15). Rotation of the patient following intrapleural administration of a sclerosing agent is described in most pleurodesis studies (4,6,9,12,13). Some authors, however, consider that the uniformed distribution of talc in pleural cavity happens spontaneously while others suggest the necessity of patient’s rotation in order to achieve this (9). Our experience goes in favor of rotation of the patient.

Since the moment when talc has been introduced into clinical practice, there have been many disagreements regarding its use and efficiency in the treatment of MPE and pneumothorax because of its toxicity (19,20). Light (20) thinks that doxycycline is an optimal agent, superior to talc, while Ghio (21) believes that it should not be used in the case of nonmalignant effusion due to the risk of respiratory complications. Glazer, on the other hand, reports on the success of talc treatment of nonmalignant diseases with an acceptable risk (14). In most studies, the recommended dosage of talc is up to 10 grams, while the dosage of 6-10 grams is considered optimal. Namely, some authors consider a greater dosage of talc responsible for difficult complications including ARDS, air embolism and arrhythmia, while others consider the size of particles responsible for complications (15,21). In our study, we used 12 grams of talc and we did not notice and notice respiratory complications.

According to our study, size of particles plays a key role in the toxicity of the product, not the quantity. This conclusion is supported by most available studies (4,10,13,15,19). Talc pleurodesis has also been proven to be a safe and effective sclerosant agent in patients suffering from secondary spontaneous pneumothorax (7,16,17). However, in older persons, especially those who are classed as high surgical risk and with additional diseases, especially at an advanced COPD (chronic obstructive pulmonary disease) the administration has its full justification, which is consistent with our study. In our study, talc was not used in younger patients in accordance with the recommendations of the British Thoracic Society guideline, as well as other studies where the cancerous effect of talc is not excluded (8). We do not recommend the use of non-steroidal anti-inflammatory drugs and corticosteroids in the postoperative period to avoid the possibility of interfering with hemostasis or the formation of adherences. Preprocedure antibiotics were not given routinely. The procedure is performed in sterile conditions just like any other surgical procedure (6). In our study, one patient developed empyema because of a prolonged time...
with the intercostal tube and contamination of the pleural space.
However, in most studies talc was confirmed as the best sclerosing agent (4, 5-7,11,13). The current British Thoracic Society guideline advocated talc pleurodesis as first-line therapy for MPE(8). Respiratory complications are the most serious and seem to have no connection with the quantity of installed talc (6,10). Success rates (complete and partial response) for talc slurry range from 88% to 100% with a mean of 90%(2,4,5,8,14). In our research, pleurodesis was successful in 96% patients. In conclusion talc was confirmed as the best sclerosing agent. Large-particle talc should be used if talc pleurodesis is elected.

FUNDING
No specific funding was received for this study.

TRANSPARENCY DECLARATIONS
Competing interests: none to declare.

REFERENCES
**SAŽETAK**

**Cilj** Utvrditi efikasnost i sigurnost pleurodeze talkom u tretmanu malignog pleuralnog izljeva i recidivirajućeg spontanog pneumotoraksa.

**Metode** U studiju su bila uključena 54 pacijenta s malignim pleuralnim izljevom (MPE) i recidivirajućim spontanim pneumotoraksom, kod kojih je načinjena pleurodeza talkom metodom *talc slurry* obliteratione pleuralnog prostora.

**Rezultati** Pleurodeza je bila uspješna kod 52 (96%) pacijenta. Prosječno trajanje torakalne drenaže iznosilo je 4,4 dana. Kao komplikacije postupka zabilježili smo povišenu tjelesnu temperaturu, pneumoniju i separaciju pleuralnog izljeva. Svi pacijenti na dan otpusta, te tri mjeseca kasnije, imali su zadovoljavajuće radiološke nalaze. Nije bilo smrtnog ishoda vezanog za sâm postupak pleurodeze.

**Zaključak** Pleurodeza talkom, prema rezultatima našeg istraživanja, potvrdila je svoju efikasnost i jednostavnost u tretmanu simptomatskih malignih pleuralnih izljeva, te kod pacijenata s recidivirajućim spontanim pneumotoraksom. Pravilan odabir pacijenata i poštivanje hirurških principa tokom procedure čine ovu metodu sigurnom, efikasnom i uspješnom u tretmanu pleuropulmonalnih oboljenja. Talk velikih čestica treba biti korišten za pleurodezu zbog minimalnog rizika od komplikacija.

**Ključne riječi:** hirurgija, maligni pleuralni izljev, pneumotoraks