Experience of Pleurodesis with a 50% Glucose Solution in Patients with Secondary Pneumothorax: A Case Series

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Abstract
Secondary pneumothorax commonly encountered and it often recurs or becomes a refractory to treatment. Pleurodesis is usually selected for initial treatment in community hospitals. Recently, endobronchial intervention using the endobronchial Watanabe spigot and endobronchial valve for refractory pneumothorax has become available, but these procedures can be performed only at a few institutions with sufficient staff and equipment.

The use of a glucose solution for pleurodesis has been reported as a novel approach to persistent air leakage. Pleurodesis with a 50% glucose solution was occasionally empirically performed in community hospitals. However, only limited literatures have published. Here, I report the experience of five patients (4 men and 1 woman; 71 years to 84 years old), seven times with inoperable secondary pneumothorax who received pleurodesis with a 50% glucose solution. In our cases, two of them had pneumoconiosis, one had chronic obstructive lung disease (COPD), one had interstitial pneumonia (IP) and one had lung cancer. The procedure successfully stopped air leakage and allowed chest tube removal (4 days to 10 days) in three patients without severe complications. Same as previous report, temporary hyperglycemia occurred in three patients. Therefore, pleurodesis with a 50% glucose solution suggested possibility that a feasible and safe. Despite future large-scale studies should aim to examine the efficacy and tolerance of this technique, it would be beneficial to obtain the alternative agent of pleurodesis for patients with inoperable secondary pneumothorax and rural hospitals.

Keywords: Glucose solution (50%); Pleurodesis; Secondary pneumothorax; Refractory

Abbreviations:
COPD: Chronic Obstructive Lung Disease; IP: Interstitial Pneumonia; EWS: Endobronchial Watanabe Spigot

Introduction
Secondary pneumothorax can result from chronic obstructive pulmonary disease (COPD), interstitial pneumonia (IP), lung cancer and silicosis [1,2]. Drainage using a thoracic tube is the standard treatment for secondary pneumothorax [3]. Surgery and chemical pleurodesis may be required for a pneumothorax with persistent air leakage. However, surgery may be difficult in patients with low lung function, cardiac disease, or other chronic diseases. Recently, endobronchial intervention using the endobronchial Watanabe spigot (EWS) and endobronchial valve has become available [4,5], but these procedures can be performed only at a few institutions with sufficient staff and equipment.

Pleurodesis for malignant pleurisy and pneumothorax with prolonged air leakage is simple, effective, and safe [6-10]. OK-432, autologous blood, and minocycline are often used in pleurodesis for refractory pneumothorax [6,7,9,11].

A few recent studies have reported the efficacy and safety of pleurodesis with a 50% glucose solution for chylothorax and postoperative pneumothorax [12-15]. It is also the treatment of choice for inoperable patients with pneumothorax. I report seven times of five cases in which patients received pleurodesis with a 50% glucose solution and present their treatment outcomes retrospectively (Table 1). This procedure was occasionally empirically performed in community hospitals same as using minocycline. The 50% glucose solution does not contain a medical agent, and it therefore has only few side effects. In our hospital, this method was selected for patients without diabetes mellitus whose vital signs were stable. So their oral informed consent was obtained, but the procedure did not submit to Institutional Review Board of our hospital.

Methods
I experienced seven times of five cases in which patients received pleurodesis with a 50% glucose solution and present their treatment outcomes by extracting data from the medical records retrospectively (Table 1).

The procedure followed at our hospital is based on previous studies [12,13]. First, 10 ml of 1% lidocaine (local anesthetic) was instilled into the thorax through the chest tube. Subsequently, 200 ml of a 50% glucose solution and 50 ml of saline was infused into the thorax in sequence. A bolus infusion of saline (50 ml) was used to prevent blockage of the chest tube due to the highly concentrated glucose. When possible, the patient's position was changed every 15 min for a total of 2 h. If air leakage stopped the next day, the tube was clamped. The tube was removed the following day, if plain chest radiography did not show lung collapse.

Case Reports
Case 1: A 78-year-old man with a history of lung cancer for which he had received chemotherapy and radiotherapy experienced chest discomfort. Until 11 days before, he had been admitted because of right malignant pleurisy and pneumothorax for which drainage and pleurodesis with OK-432 were performed. Plain chest radiography...
indicated recurrence of right pneumothorax. Lung expansion improved on chest tube replacement. Pleurodesis with OK-432 was reconsidered because of the short-term risk of relapse. However, the patient refused it because he had experienced side effects previously. He then received pleurodesis with a 50% glucose solution. He had no procedural complications other than mild pleural effusion discharge during chest tube insertion (Figure 1) and could be extubated after 7 days. Since then, no recurrence had occurred until his death because of lung cancer, 157 days after tube removal.

**Case 2:** A 71-year-old man experienced sudden chest pain 3 days after being discharged from our hospital after treatment of left pneumothorax by drainage only. He had hypoxia and his chest computed tomography revealed severe emphysema and left pneumothorax with pneumoedema. Air started to escape through the thick chest tube. Despite lung expansion, the air leakage continued. Pleurodesis with a 50% glucose solution was performed. During the procedure, he experienced mild dyspnea and his oxygen saturation decreased from 96% to 90% on room air (Table 2). His symptoms and saturation levels improved immediately after pleurodesis. A light yellow and clear effusion (1025 ml) was discharged from the thoracic cavity within 24 h (Figure 1). 5 days later, the chest tube could be removed. He has remained recurrence free for 6 months.

**Table 1:** Characteristic of 4 patients that pleurodesis with a 50% glucose solution was performed.

| Case | Age | Sex | Side | Tube size | Underlying disease | Category | Days of until recurrence | Number of times | Results | Days of tube removement after pleurodesis |
|------|-----|-----|------|-----------|-------------------|----------|-------------------------|----------------|---------|---------------------------------|
| 1    | 78  | M   | right| 20 Fr    | lung cancer       | recurrence| 30 days                 | one            | success | 7 days                          |
| 2    | 71  | M   | left | 18 Fr    | COPD              | recurrence+ refractory | 3 days       | one            | success | 5 days                          |
| 3    | 74  | M   | right| 20 Fr    | pneumoconiosis    | refractory | --                      | two            | one      | --                              |
| 4    | 74  | M   | left | 20 Fr    | pneumoconiosis    | refractory | --                      | one            | success | 4 days                          |
| 5    | 87  | F   | left | 18 Fr    | cIPF              | recurrence | 3 days       | one            | success | 5 days                          |
| 5-1  | 87  | F   | left | 18 Fr    | cIPF              | recurrence | 2 days       | one            | success | 10 days                         |

**Case 3:** A 74-year-old man was admitted after experiencing right-sided chest pain. He had a history of pneumoconiosis and chronic respiratory failure from 7 years ago after receiving repeated pleurodesis using auto-blood and minocycline for left pneumothorax. Plain chest radiography indicated right pneumothorax, which started draining continuously. Air leakage persisted and lung expansion was insufficient. He underwent pleurodesis with a 50% glucose solution twice, but the pneumothorax did not improve. Mild dyspnea associated with infusion of solution and large volume of effusion occurred both times (Table 2, Figure 1). At another institution, he received EWS therapy, which reduced the air leakage. After an auto-blood patch, the chest tube could be removed. His pneumothorax improved, but right-sided pneumonia occurred after 1 month. His condition deteriorated and he died of severe pneumonia 4 days later.

**Case 4:** A 74-years-old man was referred for the management of left pneumothorax. He had a history of pneumoconiosis and experienced right and left pneumothoraces of 20 years and 3 months ago, respectively. Because of his low lung function, he could not undergo to surgery. His pneumothorax could be improved by pleurodesis using several agents at that time. However, despite adequate drainage, the air leakage did not stop. We performed pleurodesis with a 50% glucose solution. He had no dyspnea, chest pain, fever, or desaturation (Table 2). Volume of pleural effusion was 1545 ml in the initial 24-h period, with a small amount of
fluid drained over the following (Figure 1). After 4 days, his chest tube could be removed and he was discharged. Pneumothorax did not recur in the 4 months after discharge, and he is currently being followed up.

**Case 5:** An 87-years-old woman who had IP presented sudden chest pain and was carried to our emergency department. She was followed up IP without administrations. Initial plain chest radiography indicated left pneumothorax and started draining with thin tube. Chest tube could be removed soon, but pneumothorax reoccurred after 3 days. Thick tube was replaced and she underwent pleurodesis with a 50% glucose solution. Table 1, 2 and Figure 1 indicated her characteristics. She experienced chest pain that it is not necessary analgesics and it vanished immediately. After 5 days, her chest tube could be removed. More 2 days after, her pneumothorax occurred again, and it re-started draining with thick tube. Pleurodesis with a 50% glucose solution was performed again. Only a little effusion of day 1 discharged cause of being to drop tube out. After resolving the trouble, effusion forceful discharged on day 2, 3 (Figure 1). 10 days later, the chest tube could be removed. Her pneumothorax did not recur in the 2 month after discharge.

**Discussion**

Secondary pneumothorax is commonly encountered and it often recurs or becomes a refractory to treatment. Some patients with secondary pneumothorax cannot undergo surgery because of their condition and underlying disease. EWS and endobronchial valve therapy are effective in treating such patients [4,5]. However, it is difficult to perform these procedures at rural hospitals that have insufficient equipment and staff shortage. Instillation of chemical agents, doxycycline, and talc has been recommended in cases of prolonged air leakage. [3] Pleurodesis is an easy, safe, effective, and well-tolerated treatment for secondary pneumothorax [6,7,9,11]

Some studies have reported the effectiveness of pleurodesis using a 50% glucose solution in treating pneumothorax with prolonged air leakage after a surgical procedure or chylothorax [12,14,15]. To my knowledge, only a few studies have investigated patients with secondary pneumothorax in whom surgery is contraindicated [13]. After the publication of studies reporting the use of pleurodesis with a 50% glucose solution, this procedure was occasionally empirically performed in community hospitals. The 50% glucose solution does not contain a medical agent, and it therefore has only few side effects. In our hospital, this method was selected for patients without diabetes mellitus whose vital signs were stable. So their oral informed consent was obtained, but the procedure did not submit to Institutional Review Board of our hospital.

Here, I reported four cases in which pleurodesis with a 50% glucose solution was performed in inoperable patients with secondary pneumothorax. Pleurodesis using a 50% glucose solution proved to be safe and effective. In our cases, two of them had pneumonia, and one had COPD, one had IP and one had lung cancer. In four of these five cases, air leakage stopped immediately after treatment. But first treatment of Case 5 was observed recurrence before the patient discharge from hospital. In the remaining case (Case 3), the chest tube could not be removed even after performing pleurodesis using a 50% glucose solution twice. This patient required not only bronchial occlusion but also an auto-blood patch. Enough lung expansion could not be obtained in this case. Although Takuma et al. reported that lung expansion was not an important criterion for pleurodesis [13], sufficient lung expansion seems necessary for successful pleurodesis [16].

Some reports have indicated a large volume of pleural effusion after pleurodesis with a 50% glucose solution. One study even suggested that pleural effusion volume was significantly greater in the successfully treated group than in the unsuccessfully treated group [12]. In five of the seven treatments in the present report, the effusion volume in the initial 24 h period was over 1000 ml. However, the effusion volume reduced to less than 10 ml from the second day. In Case 1, only a mild effusion was observed, but air leakage stopped and plain chest radiography revealed no fluid accumulation. Effusion volume of second treatment of Case 5 was little in the initial 24-h period, cause of tube trouble. Finally, total volume was over 1000 ml for three days. The mechanism underlying the increase in pleural effusion after pleurodesis with a 50% glucose solution remains unclear. Pleural adhesion might be the cause of exposure to hyperosmotic stress, which results in the secretion of several growth factors from pleural macrophages and mesothelial cells [12-14]. Cytokines may also stimulate the inflammatory cells and induce pleural adhesion, resulting in systemic inflammations [17,18].

The main complications of conventional pleurodesis, such as pain and fever, [8,9] Present cases were obtained once with the use of a glucose solution, but it was unnecessary analgesics. In fact, the patient in Case 1 rejected to use OK-432 because of prior its side effects, despite it was effective. Although the patients experienced chest discomfort and mild desaturation during glucose instillation, these symptoms improved immediately after drainage of a large effusion.

None of my patients had diabetes mellitus. Three patients had five episodes of temporary hyperglycemia; their blood sugar levels increased within a few hours of treatment but decreased to normal after 6-8 h [12,13]. Therefore, pleurodesis with a 50% glucose solution may be contraindicated in patients with abnormal glucose tolerance.

In conclusion, same as previous study indicated, pleurodesis with a 50% glucose solution suggested acceptable outcomes and was well tolerated without complications like recurrence or refractory secondary pneumothorax. It would be mutual benefit to obtain the alternative agent of pleurodesis for these patients and rural hospitals. Otherwise,
clinical courses and outcomes were varied and their relationship is unclear. Future large-scale studies should aim to examine the efficacy and tolerance of this technique in inoperable patients with secondary pneumothorax.

References

1. Noppen M (2010) Spontaneous pneumothorax: epidemiology, pathophysiology and cause. Eur Respir 19: 217-219.
2. Kawano M, Miura H, Anan H, Shimizu M (2002) Treatment of secondary spontaneous pneumothorax complicating silicosis and progressive massive fibrosis. Kurume Med J 49: 35-40.
3. Baumann MH, Strange C, Heffner JE, Light R, Kirby TJ, et al. (2001) Management of spontaneous pneumothorax: An American Collage of Chest Physicians Delphi Consensus Statement. Chest 119: 590-602.
4. Sasada S, Tamura K, Chang YS, Okamoto N, Matsuura Y, et al. (2011) Clinical evaluation of endoscopic bronchial occlusion with silicone spigots for the management of persistent pulmonary air leaks. Intern Med 50: 1169-1173.
5. Travaline JM1, McKenna RJ Jr, De Giacomo T, Venuta F, Hazelrigg SR, et al. (2009) Treatment of persistent pulmonary air leaks using endobronchial valves. Chest 136: 355-360.
6. Aihara K, Handa T, Nagai S, Tanizawa K, Watanabe K, et al. (2011) Efficacy of blood-patch pleurodesis for secondary spontaneous pneumothorax in interstitial lung disease. Intern Med 50: 1157-1162.
7. Evman S, Alpay L, Melin S, Käräjä H, Demir M, et al. (2016) The efficacy and economical benefits of blood patch pleurodesis in secondary spontaneous pneumothorax patients. Kardiochir Thorakochirurgia Pol 13: 21-25.
8. Shaw P, Agarwal R (2004) Pleurodesis for malignant pleural effusions. Cochrane Database Syst Rev 1: CD002916.
9. How CH, Hsu HH, Chen JS (2013) Chemical pleurodesis for spontaneous pneumothorax. J Formos Med Assoc 112: 749-755.
10. Burgers JA, Kunst PW, Koolen MG, Willems LN, Burgers JS, et al. (2008) Pleural drainage and pleurodesis: implementation of guidelines in four hospitals. Eur Respir J 32: 1321-1327.
11. Chen JS, Tsai KT, Hsu HH, Yuan A, Chen WJ, et al. (2008) Intrapleural minocycline following simple aspiration for initial treatment of primary spontaneous pneumothorax. Respir Med 102: 1004-1010.
12. Fujino K, Motooka Y, Koga T, Osumi H, Matsubara E, et al. (2016) Novel approach to pleurodesis with 50% glucose for air leakage after lung resection or pneumothorax. Surg Today 46: 599-602.
13. Tsukioka T, Inoue K, Oka H, Mizuguchi S, Morita R, et al. (2013) Pleurodesis with a 50% glucose solution in patients with spontaneous pneumothorax in whom an operation is contraindicated. Ann Thorac Cardiovasc Surg 19: 358-363.
14. Tsukioka T, Inoue K, Oka H, Mizuguchi S, Morita R, et al. (2013) Intraoperative mechanical and chemical pleurodesis with 50% glucose solution for secondary spontaneous pneumothorax in patients with pulmonary emphysema. Surg Today 43: 889-893.
15. Chen Y, Li C, Xu L, Lin H, Cui Y, et al. (2010) Novel treatment for chylothorax after esophagectomy with 50% glucose pleurodesis. Ann Vasc Surg 24: e9-e13.
16. Rodriguez-Panadero F, Montes-Worboys A (2012) Mechanisms of pleurodesis. Commons below Respiration 83: 91-98.
17. Hojski A, Leitgeb M, Crnjac A (2015) Release of growth factors after mechanical and chemical pleurodesis for treatment of malignant pleural effusion: a randomized control study. Radiol Oncol 49: 386-394.
18. Brocker C, Thompson DC, Vasiloiu V (2012) The role of hyperosmotic stress in inflammation and disease. Biomol Concepts 3: 345-364.