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ORIGINAL ARTICLE



## Chemical pleurodesis for prolonged postoperative air leak in primary spontaneous pneumothorax

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KEYWORDS air leak; minocycline; OK-432 (picibanil); pleurodesis; pneumothorax; thoracoscopy	Background/Purpose: Prolonged air leak is the most common complication after thoracoscopic operation for primary spontaneous pneumothorax (PSP), and the role of chemical pleurodesis in treating air leaks remains unclear. This study evaluated the safety and efficacy of chemical pleurodesis with a comparison between minocycline and OK-432. <i>Methods:</i> Between 1994 and 2011, 1083 PSP patients were treated by thoracoscopic operation. After the operation, patients with persistent air leak for 3 days or more were managed by minocycline or OK-432 pleurodesis. The demographic and outcome data for these patients were collected by retrospective chart review. <i>Results:</i> Seventy-nine patients (7.3%) with prolonged air leak after thoracoscopy underwent minocycline pleurodesis (60 patients) or OK-432 pleurodesis (19 patients) as the primary treatment. The primary success rate was 63% (38/60) for minocycline pleurodesis and 95% (18/19) for OK-432 pleurodesis ( $p = 0.009$ ). Postpleurodesis pain was common and comparable between the two groups. No major complications were noted after a total of 121 treatments. Patients undergoing primary OK-432 pleurodesis had shorter durations of postpleurodesis chest drainage (mean 8.5 vs. 2.3 days; $p < 0.001$ ) and postoperative hospital stay (mean 11.9 vs. 6.8 days; $p < 0.001$ ) than those undergoing primary minocycline pleurodesis. After a median follow-up of 16 months, recurrence was noted in one patient in the OK-432 group and none in the minocycline group. Long-term pulmonary function in the two groups was comparable.

Conflicts of interest: The authors have no conflicts of interest relevant to this article.

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*Conclusion:* Chemical pleurodesis using OK-432 or minocycline is safe and convenient for prolonged air leak after thoracoscopic treatment for PSP. Our experience suggested that OK-432 may be more effective than minocycline in reducing air leak.

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## Introduction

Primary spontaneous pneumothorax (PSP) most commonly occurs in young, tall, lean males.<sup>1</sup> Advances in videoassisted thoracoscopic surgery (VATS) that combine bullectomy with some kind of pleurodesis, either abrasion or pleurectomy, have provided a preferred intervention for treating complicated or recurrent PSP.<sup>2–6</sup> Unfortunately, 2–10% of PSP patients experience prolonged or refractory air leak after surgical intervention, resulting in prolonged tube thoracostomy and hospital stay, or even reoperation.<sup>3–8</sup>

The optimal management for prolonged air leaks after VATS in PSP patients is unclear because only a few of these cases have been reported.<sup>3–8</sup> Recently, chemical pleurodesis has been employed in an attempt to stop air leaks and decrease the length of hospital stay after pulmonary resection.<sup>7–9</sup> Minocycline, a derivative of tetracycline, is effective in inducing pleural fibrosis and adhesions in rabbits.<sup>10,11</sup> In previous studies, we found that minocycline pleurodesis is a safe and convenient procedure that is associated with a lower rate of recurrence after thoracoscopic treatment of PSP.<sup>7,8</sup> OK-432 (picibanil) is another chemical irritant that has been used in sclerotherapy for malignant pleural effusions and intractable pneumothorax.<sup>12–14</sup> Comparison of the safety and efficacy of the two agents in treating prolonged air leak after VATS for PSP has not previously been reported.

In the present study, we report our experience of using minocycline and OK-432 pleurodesis for treating prolonged air leak after thoracoscopic treatment of PSP. The safety and efficacy of the two agents were also compared.

## Materials and methods

#### Study design and patients

The aim of this retrospective study was to evaluate the safety and efficacy of minocycline and OK-432 as sclerosing agents in patients with prolonged air leak after VATS for PSP. To identify patients with prolonged air leak after VATS for PSP, the medical records of all patients with spontaneous pneumothorax undergoing VATS in the Thoracic Surgical Division between April 1994 and February 2011 were screened. Patients aged >50 years or with pre-existing pulmonary diseases were excluded from this study to avoid patients with secondary pneumothorax. Prolonged air leak was defined as air leak that persist for 3 or more days requiring management after the operation. This study was reviewed and approved by the Research Ethics Committee of National Taiwan University Hospital (approval number 201202011RIC).

#### VATS procedures

Either conventional or needlescopic VATS was performed with the patient under general anesthesia and one-lung ventilation. The anesthesia, preparation, and operative procedures of the needlescopic VATS were almost identical to conventional VATS. Previous studies have shown that the short-term results and pneumothorax recurrence rates in both techniques are comparable, even though needlescopic VATS provides better cosmetic results and induces less residual chest pain.<sup>4,15</sup>

Under thoracoscopy, pleural adhesions were freed using electrocautery. When blebs were identified, they were excised with an endoscopic stapler. Blind apical stapling was done at the most suspicious area if no bleb could be identified. Mechanical pleurodesis was performed using pleural abrasion or apical pleurectomy, depending on the treatment policies of different surgeons or clinical trial protocols during different time periods.<sup>3</sup> For thoracoscopic apical pleurectomy, the parietal pleura above the fifth rib were excised. For thoracoscopic pleural abrasion, the parietal surface above the sixth rib was abraded by inserting the curved dissector with a diathermy scratch pad.<sup>3</sup> After postoperative lung reinflation, normal saline solution was instilled to check for air leaks. A chest tube (28F) was placed in the apex through one of the insertion wounds.

The patients were extubated in the operating room and observed for 1–2 hours in the recovery room. Chest radiography (CXR) was performed immediately after surgery or the next morning. The chest tube was connected to a low-pressure suction system (–10 cmH<sub>2</sub>O) if the lung was not fully expanded.

#### Chemical pleurodesis with minocycline and OK-432

When prolonged air leak occurred, chemical pleurodesis using minocycline or OK-432 was selected as the primary treatment. The attending surgeon made the choice between the two agents. The cost of OK-432 pleurodesis is higher in Taiwan because the national health insurance does not reimburse this treatment. In patients with persistent air leak, pleurodesis was repeated using the same or the other agent.

For minocycline pleurodesis, 20 mL of 2% lidocaine hydrochloride (400 mg) was instilled into the pleural cavity through the thoracostomy tube, followed by a solution of 300 mg or 400 mg (7 mg/kg) minocycline (Mirosin; Taiwan Panbiotic Laboratories, Kaohsiung, Taiwan) in 20 mL of normal saline. For OK-432 pleurodesis, 20 mL of 2% lidocaine hydrochloride (400 mg) was instilled, followed by a solution of 20 mL of normal saline containing 5–10 KE of OK-432 (KE = Klinische Einbeit; 1 KE contains 0.1 mg of

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