JCS Journal of Chest Surgery
https://doi.org/10.5090/jcs.23.006
pISSN: 2765-1606 eISSN: 2765-1614
J Chest Surg. 2023;56(4):240-243

Clinical Research

Chemical Pleurodesis Using Tetracycline for the Management of Postoperative Pneumothorax Recurrence

Jun Tae Yang, M.D.[1], Sahri Kim, M.D.[1], Hyoung Soo Kim, M.D., Ph.D.[1], Hee Sung Lee, M.D., Ph.D.[2], Yong Joon Ra, M.D.[1], Hong Kyu Lee, M.D.[1]

[1]Department of Thoracic and Cardiovascular Surgery, Hallym University Sacred Heart Hospital, Anyang; [2]Department of Thoracic and Cardiovascular Surgery, Hallym University Dongtan Sacred Heart Hospital, Hwaseong, Korea

ARTICLE INFO
Received January 4, 2023
Revised January 22, 2023
Accepted February 28, 2023

Corresponding author
Hong Kyu Lee
Tel 82-31-380-3815
Fax 82-31-380-3815
E-mail hklee0228@hallym.or.kr
ORCID
https://orcid.org/0000-0002-9087-7783

Background: Although there is no obvious recommendation for the management of pneumothorax recurrence after surgery, chemical pleurodesis with tetracycline has been applied as a significant treatment approach. The objective of this study was to evaluate the effectiveness of chemical pleurodesis with tetracycline for the management of postoperative recurrence of primary spontaneous pneumothorax (PSP).
Methods: We retrospectively analyzed patients who underwent video-assisted thoracic surgery (VATS) as therapy for PSP at Hallym University Sacred Heart Hospital from January 2010 to December 2016. Patients who had ipsilateral recurrence after surgery were included in this study. Patients who underwent pleural drainage with chemical pleurodesis were compared with patients who only underwent pleural drainage.
Results: In total, 932 patients who underwent VATS for PSP were analyzed, and ipsilateral recurrence after surgery occurred in 67 patients (7.1%). The treatment modalities for recurrence after surgery were observation (n=12), pleural drainage alone (n=16), pleural drainage with chemical pleurodesis (n=34), and repeated VATS (n=5). Eight of the 16 patients (50 %) treated with pleural drainage alone had recurrence again, while 15 of the 34 patients (44.1%) treated with pleural drainage and chemical pleurodesis experienced further recurrence. Chemical pleurodesis with tetracycline did not show a meaningful difference in the re-recurrence rate in comparison with pleural drainage alone (p=0.332).
Conclusion: Chemical pleurodesis with tetracycline for the management of postoperative recurrence of PSP was not effective. Further research is required to identify alternative drugs that can significantly decrease the re-recurrence rate.

Keywords: Lung, Pneumothorax, Recurrence, Pleurodesis, Tetracycline

Introduction

Primary spontaneous pneumothorax (PSP) mainly occurs due to the rupture of an apical subpleural bulla in patients with no other lung diseases conferring vulnerability to the condition or history of trauma [1]. In addition, we have previously studied the characteristics of PSP in adolescents [2]. For the first episode of PSP, some guidelines suggest conservative treatment, such as oxygen therapy with observation, simple aspiration, pleural drainage, and pleurodesis [3]. After treatment of the first PSP episode with these therapies, the recurrence rate has been reported to be 23%–50%, and it increases to 60% after further events [4]. Some reports have recommended video-assisted thoracic surgery (VATS) as the preferred treatment for PSP because it enables the safe and high-quality resection of bullae, pleurodesis, and pleural ablation and reduces the recurrence rate [5]. The use of surgical access has increased over the last 2 decades. Although the probability of postoperative recurrence has decreased, it still occurs, and various methods have been used to reduce the recurrence rate. Chemical pleurodesis has been primarily used to assist in resolving persistent air leaks and to reduce the recurrence rate in the nonsurgical treatment of spontaneous pneumothorax. Cardillo et al. [6] demonstrated a low rate of pneumothorax recurrence (1.9%) in patients undergoing VATS

with talc poudrage pleurodesis. However, there are no clear recommendations for the treatment of recurrent pneumothorax after VATS, and few studies have been published on this issue. We have used chemical pleurodesis clinically; however, the function of chemical pleurodesis in the management of recurrence after VATS remains uncertain. The objective of this study was to evaluate the effectiveness of chemical pleurodesis with tetracycline for the management of recurrence after surgery for PSP.

Methods

This study was reviewed and approved by the Institutional Review Board of Hallym University Sacred Heart Hospital (IRB no., 2018-12-013-011), which waived the requirement for informed consent because of the retrospective design. We retrospectively analyzed patients who underwent VATS as treatment for PSP at a single institution from January 2010 to December 2016. This study included patients who had ipsilateral recurrence after surgery. Patients who underwent pleural drainage with chemical pleurodesis were compared with patients who only underwent pleural drainage. Demographic data included sex, age, smoking status, treatment types, duration of hospital stay, and the time period until recurrence. The treatments included observation with oxygen supply, pleural drainage alone with a chest tube, pleural drainage with chemical pleurodesis, and repeated VATS. Oxygen therapy was performed using a 5 L/min flow via a nasal cannula. For pleural drainage, we inserted a 24F chest tube. If the air leak continued for 2 days, we considered chemical pleurodesis using tetracycline or repeated VATS. No chemical pleurodesis was performed during repeated VATS. For tetracycline pleurodesis, 1,000 mg of tetracycline powder was mixed with 40 mL of normal saline and 10 mL of 2% lidocaine, and the resulting solution was infused into the pleural cavity through a 24F thoracostomy chest tube. In the VATS procedure, 3 classical incision ports were made. Wedge resection using a linear endoscopic stapler covered not only the targeted bullae, but also the surrounding degenerated tissues. As in the first VATS, after wedge resection, the air leakage test was performed routinely, and no leakage was confirmed in the staple line or elsewhere. Chest X-ray examinations were conducted daily, and if there was no air leakage, the chest tube was extracted and the patient was discharged the next day. Categorical variables were described as counts and proportions, and compared using the chi-square test. A p-value <0.05 was regarded as indicating statistical significance. Statistical analyses were conducted using IBM SPSS ver. 25.0 for Windows (IBM Corp., Armonk, NY, USA).

Results

The records of all 932 patients who underwent VATS for PSP were analyzed, and ipsilateral recurrence after surgery occurred in 67 patients (7.1%). Since most of the patients had PSP in adolescence for no particular reason, postoperative air leakage was well controlled and all patients were discharged without any noteworthy complications. Patients' demographic characteristics are reported in Table 1. Fifty-six out of the 67 patients (83.5%) were male and there were 4 ex-smokers and no current smokers. The median age was 17 years. The mean follow-up time was 60 months, and the median time of recurrence after surgery was 10.5 months. The treatments for recurrence after surgery were observation (n=12), pleural drainage alone (n=16), pleural drainage with chemical pleurodesis (n=34), and repeated VATS (n=5). The mean duration of hospital stays was 5.3 days in patients treated with only pleural drainage, and 7.1 days in patients treated with pleural drainage and chemical pleurodesis. Patients who underwent pleural drainage with chemical pleurodesis were compared with those who had pleural drainage alone. Eight out of 16 patients (50%) with pleural drainage alone had recurrence again, and 15 out of 34 patients (44.1%) with pleural drainage and chemical pleurodesis had another recurrence. Chemical pleurodesis

Table 1. The characteristics of patients with recurrence after surgery (n=67)

Characteristic	Value
Male	56 (84)
Age (yr)	17 (13–38)
Smoking	4 (5.9)
Current smoker	0
Ex-smoker	4 (5.9)
Follow-up time (mo)	60 (14–88)
Interval until recurrence after surgery (mo)	10.5 (1–45)
Treatment of recurrence	
O_2 management	12 (17.9)
Chest tube	16 (23.8)
Chemical pleurodesis	34 (50.7)
VATS	5 (7.4)
Hospital stay (day)	
O_2 management	4.3 (2–10)
Chest tube	5.3 (3–10)
Chemical pleurodesis	7.1 (4–20)
VATS	4.4 (3–5)

Values are presented as number (%) or median (range).
VATS, video-assisted thoracic surgery.

https://doi.org/10.5090/jcs.23.006

Table 2. Comparison of results between pleural drainage alone and pleural drainage with tetracycline pleurodesis

Variable	Pleural drainage alone (n=16)	Pleural drainage with tetracycline pleurodesis (n=34)	p-value
Age (yr)	18.3 (13–38)	17.1(13–24)	0.446
Hospital stay (day)	5.3 (3–10)	7.1 (4–20)	0.034*
Interval until second recurrence (mo)	21.1 (1–68)	10.7 (1–45)	0.077
Smokers (ex-smoker+ current)	0	1	0.498
Second recurrence (%)	8 (50)	15 (44.1)	0.332

Values are presented as median (range) or number (%).
*p<0.05 (statistically significant).

with tetracycline did not reveal a meaningful difference in the re-recurrence rate in comparison with pleural drainage alone (p=0.332) (Table 2).

Discussion

In patients treated using conservative therapy for PSP, the recurrence rate is reported to be 23%–50%, and it increases to 60% after further events [4]. These high rates have encouraged advances in various therapeutic applications, ranging from simple aspiration to invasive procedures. In 1990, the first thoracoscopic approach for the surgical treatment of PSP was described by Levi et al. [7], and the application of this method has increased over the last 2 decades. VATS for PSP is a representative and reasonable treatment that is increasing in popularity and is the preferred treatment at many centers. More recently, the Japanese Association for Thoracic Surgery issued revised guidelines, suggesting that VATS should be the first choice for surgical access [8]; however, some studies have reported fairly high recurrence rates of up to 10%–16% after VATS [9,10]. This high recurrence rate prompted the development of further methods, such as partial pleurectomy, chemical pleurodesis, pleural abrasion, and coverage with a surgical sealant [11].

Among these procedures, the treatment of choice has not yet been established. Some studies reported additional chemical pleurodesis during VATS for PSP [12]. However, published guidelines suggest that chemical pleurodesis should be undertaken only if the patient is either reluctant or unable to undergo surgery because the recurrence rate of pneumothorax after surgery such as VATS, with or without surgical pleurodesis, is significantly fewer after chemical pleurodesis [13]. The ipsilateral recurrence rate after surgery was 7.1% in our patients with PSP, and we focused on the treatment of pneumothorax recurrence after VATS. Since few published papers have dealt with the management of pneumothorax recurrence after VATS, the choice of treatment should perhaps be determined by experienced clinicians, and our study of chemical pleurodesis may yield helpful insights in this regard.

Several chemical materials (e.g., tetracycline, minocycline, and talc) have been applied to alleviate prolonged air leaks or to improve the recurrence rate in the nonsurgical treatment of spontaneous pneumothorax. Chemical pleurodesis is feasible because it is easy and noninvasive, and can effectively reduce the duration of air leaks [14]. Talc pleurodesis is safe and efficient in PSP management, but it was not accessible to us. The application of talc as a pleurodesis agent also has been restricted to young patients with PSP, despite its greater benefits in malignant pleural effusions. Although talc pleurodesis has been proven safe, there have been historical apprehensions related to acute respiratory distress syndrome [15]. Tetracycline is widely available, safe, and inexpensive. Tetracycline pleurodesis has been used to reduce the recurrence of primary or secondary spontaneous pneumothorax. Light et al. [16] performed a randomized trial that demonstrated that tetracycline pleurodesis reduced the pneumothorax recurrence rate from 41% to 25% over 5 years in hospitalized patients treated with tube thoracostomy in comparison to those who only underwent chest-tube drainage. One of the mechanisms of pneumothorax recurrence after surgery has been reported to be the development of new bullae surrounding the staple line. The insufficient resection of bullae or emphysematous changes along the staple line has also been discovered to be a risk factor for postoperative air leaks [11].

In our study, chemical pleurodesis with tetracycline for the management of recurrence after surgery of PSP did not reduce the recurrence rate in comparison with pleural drainage alone. Following this study, we decided to try pleural drainage alone for the treatment of recurrences after VATS, and we are attempting to identify new effective drugs for chemical pleurodesis.

Our study had some limitations. In particular, the number of patients with recurrence after VATS was relatively small (67 patients), suggesting that further studies might yield different results in the future. No chest computed tomography scans were taken of patients after VATS, so the homogeneity of lung conditions between the group with and without chemical pleurodesis was not guaranteed.

In conclusion, chemical pleurodesis with tetracycline did

not significantly reduce the recurrence rate compared with pleural drainage alone in the management of recurrence after VATS. Further studies are required to identify alternative drugs that can significantly reduce the recurrence rate, and if chemical pleurodesis is performed for the management of recurrence after VATS, drugs that are more effective than tetracycline should be considered.

Article information

ORCID

Jun Tae Yang: https://orcid.org/0000-0002-6677-1102
Sahri Kim: https://orcid.org/0000-0003-2662-6469
Hyoung Soo Kim: https://orcid.org/0000-0001-6023-0818
Hee Sung Lee: https://orcid.org/0000-0002-2615-8346
Yong Joon Ra: https://orcid.org/0000-0003-2153-504X
Hong Kyu Lee: https://orcid.org/0000-0002-9087-7783

Author contributions

Conceptualization: HKL. Investigation: JTY, SK, HKL. Project administration: HKL. Supervision: HKL. Visualization: JTY. Writing–original draft: JTY. Writing–review & editing: all authors. Final approval of the manuscript: all authors.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

References

1. Davis AM, Wensley DF, Phelan PD. Spontaneous pneumothorax in paediatric patients. Respir Med 1993;87:531-4. https://doi.org/10.1016/0954-6111(93)90009-o
2. Gu BM, Ko HH, Ra YJ, Lee HS, Kim HS, Lee HK. Correlation of primary spontaneous pneumothorax and air pollution in adolescents. J Chest Surg 2021;54:53-8. https://doi.org/10.5090/kjtcs.20.073
3. Baumann MH, Strange C. The clinician's perspective on pneumothorax management. Chest 1997;112:822-8. https://doi.org/10.1378/chest.112.3.822
4. MacDuff A, Arnold A, Harvey J; BTS Pleural Disease Guideline Group. Management of spontaneous pneumothorax: British Thoracic Society Pleural Disease Guideline 2010. Thorax 2010;65 Suppl 2:ii18-31. https://doi.org/10.1136/thx.2010.136986
5. Massard G, Thomas P, Wihlm JM. Minimally invasive management for first and recurrent pneumothorax. Ann Thorac Surg 1998;66:592-9. https://doi.org/10.1016/s0003-4975(98)00621-3
6. Cardillo G, Bintcliffe OJ, Carleo F, et al. Primary spontaneous pneumothorax: a cohort study of VATS with talc poudrage. Thorax 2016;71:847-53. https://doi.org/10.1136/thoraxjnl-2015-207976
7. Levi JF, Kleinmann P, Riquet M, Debesse B. Percutaneous parietal pleurectomy for recurrent spontaneous pneumothorax. Lancet 1990;336:1577-8. https://doi.org/10.1016/0140-6736(90)93351-o
8. Goto T, Kadota Y, Mori T, et al. Video-assisted thoracic surgery for pneumothorax: republication of a systematic review and a proposal by the guideline committee of the Japanese association for chest surgery 2014. Gen Thorac Cardiovasc Surg 2015;63:8-13. https://doi.org/10.1007/s11748-014-0468-9
9. Ohno K, Miyoshi S, Minami M, et al. Ipsilateral recurrence frequency after video-assisted thoracoscopic surgery for primary spontaneous pneumothorax. Jpn J Thorac Cardiovasc Surg 2000;48:757-60. https://doi.org/10.1007/BF03218248
10. Haraguchi S, Koizumi K, Hioki M, et al. Postoperative recurrences of pneumothorax in video-assisted thoracoscopic surgery for primary spontaneous pneumothorax in young patients. J Nippon Med Sch 2008;75:91-5. https://doi.org/10.1272/jnms.75.91
11. Sakamoto K, Takei H, Nishii T, et al. Staple line coverage with absorbable mesh after thoracoscopic bullectomy for spontaneous pneumothorax. Surg Endosc 2004;18:478-81. https://doi.org/10.1007/s00464-003-8918-y
12. Chen JS, Hsu HH, Chen RJ, et al. Additional minocycline pleurodesis after thoracoscopic surgery for primary spontaneous pneumothorax. Am J Respir Crit Care Med 2006;173:548-54. https://doi.org/10.1164/rccm.200509-1414OC
13. Henry M, Arnold T, Harvey J; Pleural Diseases Group, Standards of Care Committee, British Thoracic Society. BTS guidelines for the management of spontaneous pneumothorax. Thorax 2003;58(Suppl 2):ii39-52. https://doi.org/10.1136/thorax.58.suppl_2.ii39
14. Liberman M, Muzikansky A, Wright CD, et al. Incidence and risk factors of persistent air leak after major pulmonary resection and use of chemical pleurodesis. Ann Thorac Surg 2010;89:891-8. https://doi.org/10.1016/j.athoracsur.2009.12.012
15. Janssen JP, Collier G, Astoul P, et al. Safety of pleurodesis with talc poudrage in malignant pleural effusion: a prospective cohort study. Lancet 2007;369:1535-9. https://doi.org/10.1016/S0140-6736(07)60708-9
16. Light RW, O'Hara VS, Moritz TE, et al. Intrapleural tetracycline for the prevention of recurrent spontaneous pneumothorax: results of a Department of Veterans Affairs cooperative study. JAMA 1990;264:2224-30. https://doi.org/10.1001/jama.1990.03450170072025