

THERAPEUTIC EFFECT OF WHOLE LUNG LAVAGE ON PNEUMOCONIOSIS

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ABSTRACT

Pneumoconiosis as an occupational disease is a serious threat to the health of workers. Patients with pneumoconiosis are mainly engaged in dust-related work such as gold, coal, or iron mining, electric welding, or road work, and present with miliary nodules, fuse mass-like opacities, and cavity lesions on chest imaging. Clinical manifestations of pneumoconiosis include progressive chest tightness, dyspnoea, chest pain, coughing, expectoration, fever, and hypodynamia. Pneumoconiosis patients are prone to respiratory tract infections (including bacterial pneumonia and tuberculosis) because of poor disease resistance and will eventually lose the ability to work and fully function in daily life completely. Patients can lose their life because of complications such as pulmonary heart disease and respiratory failure. Disease prevention is the main method to control pneumoconiosis.

We retrospectively analysed 516 cases of pneumoconiosis patients receiving whole lung lavage (WLL) procedure from May 2009–January 2015. The symptoms, pulmonary function, chest computed tomography manifestations, and living status were reviewed carefully. The improvement rate of chest tightness, chest pain, and dyspnoea was 99%, 90%, and 98%, respectively, 7 days after WLL procedure. The symptoms had improved in 235 patients at 3–6 months postoperatively. The therapeutic effect remained stable in 56 cases after 4–5 years. Chest tightness, chest pain, and dyspnoea were improved significantly, and pulmonary diffusion function and small airway resistance also improved. There was no progress in 62 patients 4–5 years postoperatively, as indicated by the chest computed tomography examination. Overall, WLL treatment is an effective method for treating pneumoconiosis.

Keywords: Whole lung lavage (WLL), pneumoconiosis, therapeutic effect.

INTRODUCTION

Pneumoconiosis as an occupational disease is a serious threat to the health of workers.¹ Clinical

manifestations of pneumoconiosis include progressive chest tightness, dyspnoea, chest pain, cough, and expectoration.² Pneumoconiosis patients are prone to respiratory tract infection because of

poor disease resistance and can ultimately lose the ability to work and engage in daily life. Patients may lose their lives because of such complications as pulmonary heart disease and respiratory failure. Disease prevention is the main method by which pneumoconiosis is controlled.³ Once symptomatic pneumoconiosis develops, only a few therapies are available,⁴ including drug treatment (such as tetrandrine), whole lung lavage (WLL), and avoiding work in a dusty environment. Therapies can also treat the various complications associated with pneumoconiosis, for example infection control, oxygen therapy, and ventilator support.

In this study, we reported on 582 patients with pneumoconiosis who were treated at our hospital from May 2009–January 2015. Of these, 38 patients had severe restrictive pulmonary dysfunction, 16 patients complicated with pneumothorax, 10 patients complicated with tuberculosis infection, and 2 patients complicated with bacterial pneumonia. After the exclusion of 66 patients who could not undergo WLL, a total of 516 cases of pneumoconiosis were treated with WLL in our hospital from May 2009–January 2015.

METHODS

General Information

Study patients were selected from the inpatients of our hospital; all were male (22–68 years) with an average age of 54.6 ± 5.8 years. Of these cases of pneumoconiosis, 322 were coal worker's pneumoconiosis, 150 were gold mining-induced pneumoconiosis, 3 were cement-induced pneumoconiosis, 8 were foundry worker's pneumoconiosis, 2 were electric welder's pneumoconiosis, 27 were turquoise-induced pneumoconiosis, and 4 were mixed pneumoconiosis.

Diagnosis and Staging of Pneumoconiosis

The diagnosis of pneumoconiosis was made by the Occupational Disease Diagnosis Agency of the local Disease Control Center. In our study, 482 patients were suffering with Stage I pneumoconiosis, 24 with Stage II pneumoconiosis, and 10 with Stage III pneumoconiosis. Chest X-ray was the main test to diagnose pneumoconiosis and its stages.

Stage I pneumoconiosis

- a) I: Small round opacities at profusion Level 1 which are distributed in at least one zone of each

- lung and the size is ≥ 2 cm in diameter, or small irregular opacities with profusion Level 1 and the distribution reaches at least two lung zones
- b) I*: Small opacities are significantly increased but the intensity or distribution of opacities are not sufficient to classify as Stage II pneumoconiosis

Stage II pneumoconiosis

- a) II: Small round or irregular opacities at profusion Level 2 and the distribution range exceeds four lung zones, or small irregular opacities at profusion Level 3 and the distribution range reaches four lung zones
- b) II*: Small irregular opacities at profusion Level 3 and the distribution range exceeds four lung zones, or large opacities that are not enough to be diagnosed as Stage III pneumoconiosis

Stage III pneumoconiosis

- a) III: Large opacities appear which are ≥ 2 cm long and 1 cm wide
- b) III*: One large opacity area, or the sum of several large opacities, exceed the area of the right upper lung zone

There were 135 cases complicated by chronic bronchitis, 68 cases by pulmonary emphysema, and 32 cases by hypertension. All included patients had smoked.

Indications for Whole Lung Lavage

WLL was considered for patients with coal worker's pneumoconiosis, silicosis, and other pneumoconiosis caused by various inorganic dusts. For patients with complications before the procedure, WLL was not performed until the complications were under control and conditions became stable. Pulmonary function test results were used as an indicator for WLL, with lung function indices determined for 155 patients before and after lavage. Results indicative of WLL being an appropriate procedure were:

- Vital capacity (VC) and maximal voluntary ventilation (MVV) reaching 70% of predicted values
- Peak expiratory flow, forced expiratory flow at 25–75% of forced VC (FEF_{25-75}), forced expiratory volume in 1 second (FEV_1), and diffusing capacity of the lung for carbon monoxide (DL_{CO}) reaching 70% of predicted values
- Partial pressure of oxygen in arterial blood exceeding 9.3 kPa (70 mmHg)

- Heart, liver, kidney function, and relevant test indices all normal

For patients >55 years old:

- VC and MVV reaching 70% of predicted values
- FEF₂₅₋₇₅, FEV₁, and DL_{CO} reaching 80% of predicted values
- The partial pressure of oxygen in arterial blood exceeding 10.0 kPa (75 mmHg)

WHOLE LUNG LAVAGE THERAPY

Treatment Before Anaesthesia

It is necessary to visit patients before anaesthesia to fully determine their state of illness. Full consideration should be given to anaesthesia-related risks and the anaesthesia should be meticulously prepared. The left-sided double-lumen endotracheal tubes, which can pass through the glottis and have a large enough diameter, were selected for intubation. This will help reliable management during WLL. The depth of the double-lumen endotracheal tube was determined

by referring to a 170 cm adult male, for whom the front end of the double-lumen endotracheal tube is 29 cm off the incisor. The depth should increase by 1 cm for every 10 cm increase in height. Ensuring the accurate insertion of the endotracheal tube is a critical step in anaesthetising patients for WLL. Bilateral lungs must be effectively isolated and the isolation effect should be examined repeatedly by listening to respiratory sounds. WLL can be conducted when the location of the endotracheal tube and the isolation of bilateral lungs are satisfactory. It is recommended that the left lung with a smaller capacity or the lung with poor compliance should be lavaged first. Ventilation pressure is generally 4-5 kPa and it should be controlled <4 kPa for patients with pulmonary bullae. During the negative pressure suction, the silicone tube should be marked to indicate the length of the suction tube. For patients with pulmonary bullae, the negative pressure suction should be <4 kPa. Clinically, a mode of alternating positive pressure ventilation and negative pressure suction, which is synchronous with the ventilated lung, has been developed for the lavaged lung.

Table 1: Symptom improvement of pneumoconiosis patients at 7 days, 3-6 months, and 4-5 years after whole lung lavage.

Symptom	7 days postoperatively (n=516)		3-6 months postoperatively (n=235)		4-5 years postoperatively (n=56)	
	Improvement (n)	Improvement rate (%)	Improvement (n)	Improvement rate (%)	Improvement (n)	Improvement rate (%)
Chest tightness	511	99.1	219	93.2	51	90.5
Dyspnoea	507	98.3	215	91.4	50	89.2
Chest pain	465	90.4	208	88.5	48	86.3
Physical strength changes	464	89.9	190	80.7	39.0	70.5

Table 2: Lung function changes of 56 pneumoconiosis patients at 4-5 years after whole lung lavage (measured value/expected value, %).

	FVC	FEV ₁	MVV	FEF ₂₅	FEF ₅₀	DL _{CO}
Pre-treatment	90.6±7.2	87.3±5.2	89.4±6.2	53.7±4.9	59.4±5.3	80.7±6.3
Post-treatment	80.3±6.7 [†]	79.3±7.1 [†]	73.8±5.9 [†]	59.4±4.8 [†]	69.0±6.9 [†]	88.6±5.2 [†]

[†]indicates p<0.05 compared with the pre-treatment condition.

FVC: forced vital capacity; FEV₁: forced expiratory volume in 1 second; MVV: maximal voluntary ventilation; FEF₂₅: forced expiratory flow at 25% of forced vital capacity; FEF₅₀: forced expiratory flow at 50% of forced vital capacity; DL_{CO}: single breath diffusing capacity of the lungs for carbon monoxide.

This study adopted a high-frequency jet ventilation mode. The ventilation mode with low tidal volume not only achieves a certain ventilation, but also maintains low intratracheal and intrathoracic pressure. Additionally, this mode can prevent pulmonary overexpansion and improve the oxygenation of patients, and has less influence on circulation.

Method of Anaesthesia

All participants received combined intravenous-inhalational general anaesthesia under rapid induction and double-lumen endotracheal intubation. Each patient was intramuscularly injected with 10.0 mg of diazepam and 0.5 mg of atropine 30 minutes before the procedure. The following anaesthetics were then administered successively: 3-5 mg of midazolam, 10 mg of dexamethasone, 1.5-2 mg/kg of propofol, 25 mg of atracurium besilate, and 0.1-0.2 mg of fentanyl. After 3 minutes of oxygen supply by mask, the left-sided double-lumen endotracheal tube was inserted. The tube location and the isolation of both lungs were examined by respiratory sound auscultation, silicone tube detection, fibrobronchoscopy, and airway pressure observation. If the examination result was satisfactory, propofol was continuously pumped at the dosage of 4-12 mg/kg/hour to maintain anaesthesia. Meanwhile, atracurium besilate and fentanyl were administered intermittently and isoflurane inhalation was also provided. The depth of anaesthesia was adjusted according to surgical requirements and the patient's vital signs. One-lung ventilation parameters are as follows: pure oxygen inhalation, tidal volume 8-12 mL/kg, 12-14 times/min, end-tidal carbon dioxide 35-45 mmHg, airway pressure <40 cm H₂O. One side of the double-lumen endotracheal tube was connected with the anaesthesia machine for one-lung ventilation. The other side was connected with the WLL device. After vital signs became stable WLL was conducted, during which a multifunction electrocardiogram monitor was used.

Method of Whole Lung Lavage

The patient lay supine on the operating table to receive the intravenous anaesthesia combined with the double-lumen endobronchial intubation (Robertshaw tube). After it was confirmed that two lungs were effectively isolated, WLL began. Generally, the lung with more serious lesions would be lavaged first, with 37°C normal saline. At first,

the normal saline of the volume equivalent to single-lung functional residual capacity (around 1,000 mL for adults) was injected. If the patient kept calm, with no obvious variations of electrocardiogram and oxygen saturation, repeated lavages were allowed to begin. In the following lavages, ~500-1,000 mL of normal saline was injected each time, and then the bronchoalveolar lavage fluid of the same volume was sucked out at a negative pressure of 4-5 kPa. At the end of the third, sixth, and ninth drainage, pressurised ventilation was performed with the maximum pressure kept below 4 kPa. WLL was performed repeatedly until the recovered bronchoalveolar lavage fluid became clear. However, WLL would not exceed 12 times for a single lung in general. Oxygen supply continued for another 12 hours after operation. The patients should be kept warm to avoid hypothermia. Routine antibiotics and potassium supplementation were given for 1 day. Hypokalaemia may occur in some patients after the WLL procedure, which can cause serious complications, so prevention of hypokalaemia requires particular attention after WLL. Supplementation of potassium after catheterisation during the operation and 1-2 g potassium supplementation after operation can prevent the occurrence of hypokalaemia.

Observation of Therapeutic Effect

The clinical symptoms of all patients were analysed after 7 days of treatment. The clinical characteristics were analysed of 235 patients were analysed for 3-6 months postoperatively and 56 patients 4-5 years postoperatively, including clinical symptoms, physical strength, physical changes, pulmonary function, and chest computed tomography (CT) manifestations. The changes in chest CT manifestations of 62 patients receiving WLL treatment were analysed for 4-5 years postoperatively.

Statistical Methods

Lung function data are shown as $x \pm SD$ and treated by t-test. The difference in incidence rate was evaluated using the chi-square test, where $p < 0.05$ was considered statistically significant.

RESULTS

Improvement in Symptoms

Dyspnoea was eased immediately after single lung lavage. Chest tightness was found in 496 patients, chest pain in 482 patients, and

dyspnoea in 502 patients. The improvement rate of these symptoms 7 days after WLL was 99%, 90%, and 98%, respectively. Symptoms improved in 235 patients 3-6 months postoperatively and the therapeutic effect remained stable in 56 patients 4-5 years postoperatively (Table 1). The pulmonary function and chest CT findings had no significant changes on 235 cases 3-6 months postoperatively. The pulmonary function examination showed improvements in both small airway resistance and dispersion function, and the decline in ventilatory function on 56 patients 4-5 years postoperatively (Table 2). As indicated by the chest CT examination, pneumoconiosis presented with interlobular septal thickening, nodules, round or irregular large mass-like opacities, and pulmonary emphysema. There was no obvious progress in 62 patients 4-5 years postoperatively compared with their preoperative conditions. A comparison of chest CT manifestations showed that 56 patients (90.3%) remained unchanged and 6 patients (9.7%) showed progress.

Complications

In recent years, complications in WLL procedures have decreased gradually following the development of WLL technology and the introduction of a standardised operation procedure. The complication rate was as high as 47% in 134 patients receiving WLL before 2012, including 28 cases of hypoxaemia, 10 cases of bronchospasm, 8 cases of postoperative fever, 10 cases of hypokalaemia, 5 cases of atelectasis, and 1 mortality. The complication rate was 2.8% in 382 patients receiving WLL from 2012-2015, including 7 patients with hypoxaemia, 2 patients with postoperative fever, and 2 patients with atelectasis. The complication incidence has shown an obvious decrease.

DISCUSSION

Pneumoconiosis is the most common occupational disease in China that has definite aetiology. WLL was first successfully applied to a patient with mixed pneumoconiosis in 1982 by Mason et al.⁵ WLL was applied to a basic experimental and clinical research in 1986 in China.⁶ The WLL procedure can physically remove residual dust in alveoli and phagocytose alveolar macrophages to improve clinical symptoms and lung function.⁷ Research shows that the occurrence of silicosis and dust concentration had an obvious dose-response relationship and the severity of silicosis

and the amount of dust deposition had a dose-effect relationship.⁸ So the occurrence of pulmonary fibrosis can be reduced by a WLL procedure removing dust from the lungs. As an effective supplement to aetiological treatment WLL can remove the dust deposits, dust cells in the lungs, and a variety of fibrosis-related active substances.⁹ WLL can eliminate silicon dioxide and macrophages not only in the alveoli but also within the pulmonary interstitial tissue, so as to improve the patient's clinical symptoms and delay the development of pneumoconiosis, as demonstrated in a study by Morgan et al.¹⁰

In our study, the symptoms of chest tightness, chest pain, and dyspnoea were significantly alleviated after the WLL, and chest CT manifestations and pulmonary function had no obvious change after 3-6 months. The improvements were still maintained 4-5 years after the WLL. There was no further development of disease shown in the chest CT examination. The pulmonary function examination showed that both small airway resistance and diffusion function improved, and pulmonary ventilation declined. WLL can improve pulmonary diffusing capacity because it can wash out a lot of dust and reduce diffusion distance. The reason for pulmonary ventilation decline may be relative to natural lung hypofunction and ageing. Our study showed that WLL does improve symptoms and delays the deterioration of patients with pneumoconiosis.

The safety of WLL has always been a concern. The key to ensuring safety is good control of anaesthesia and the effective separation between ventilated lung and lavaged lung. Leaking of the ventilated lung is the main cause of hypoxaemia. In recent years, we have used an ultrafine bronchoscope which was inserted by double-lumen catheter to ensure the catheter gasbag was in place. This improvement reduced gasbag leaks after displacement and the occurrence of hypoxaemia.

Complications of WLL were significantly reduced from 2012-2015 in our hospital, which was due to continuous technological improvement in the practice, careful consideration of the indications and contraindications, complete preparation of the preoperative examination, and standardisation of the operation procedure. At the time we used furosemide, anisodamine, dexamethasone, aminophylline, and other drugs to promote residual liquid discharge and absorption according to the intraoperative situation. The indication of second

lung lavage was strictly selected. The anaesthesia duration was extended and the indication of stopping anaesthesia and extubation was selected carefully. At the same time, we strengthened the intraoperative and postoperative nursing care, expectorant treatment, and the respiratory function exercise.

CONCLUSION

WLL, as a safe and effective treatment for pneumoconiosis, can remove the dust and alveolar macrophages in the respiratory tract and alveolar cavity, improve symptoms, and delay

disease development. Strict conformation to the operation procedures, as well as strengthening of the anaesthetic, intraoperative, and postoperative care is necessary in its application. As to further research, a multicentre, large sample investigation is needed to accurately evaluate the effects of WLL because of the small sample size and short observation duration at present. Pneumoconiosis therapy should also include the avoidance of dusty work environments, tetrandrine administration (which can be administered orally), and the treatment of various complications such as active infection control, oxygen therapy, and ventilator support.

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