

ORIGINAL ARTICLE

Assessing the efficacy and outcomes of oxytetracycline pleurodesis in the management of malignant pleural effusion.

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ABSTRACT... Objective: To determine the outcome of OTC pleurodesis in patients with MPE in terms of efficacy, safety, and complications. **Study Design:** Quasi-experimental study. **Setting:** Department of Pulmonology, Jinnah Hospital, Allama Iqbal Medical College Lahore. **Period:** September, 1st 2025 to February, 28th 2026. **Methods:** A total of 127 patients diagnosed with MPE full filling the inclusion criteria were selected through non-probability consecutive sampling. Written informed consent was taken from all the patients. Pleurodesis was performed using a dose of 35 mg/kg OTC. All the patients were followed up to 30 days after the procedure. Statistical analysis was performed using SPSS version 20.0. Descriptive statistics were calculated for baseline characteristics, including mean (M) $\pm$ standard deviation (SD) for continuous variables while percentages and frequencies for categorical variables. The Independent t-test was used to compare continuous variables. For categorical variables, the Chi-square test was applied to assess the association with pleurodesis success. A p-value of ≤ 0.05 was considered statistically significant. **Results:** The cohort consisted of 67 males (52.76%) and 60 females (47.24%), with mean age of 58.4 ± 6.3 years. The duration of malignancy was 1.8 ± 0.4 years. The overall post pleurodesis success rate was 66.15%. Post-procedural complications included chest pain in 24.40% and fever in 17.32% of patients. Statistical analysis showed no significant associations between pleurodesis success and patient demographics or disease characteristics. **Conclusion:** These findings support OTC pleurodesis as a viable and effective option for MPE management, especially in resource-limited settings.

Key words: Lung Cancer, Malignant Pleural Effusion, Oxytetracycline, Pleurodesis, Sclerosing Agent.

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INTRODUCTION

Cancer is one of leading causes of death worldwide due to multiple complications, including pleural effusion (PE). PE is defined as the accumulation of fluid in the pleural cavity, the space between the chest wall and lungs caused by different conditions such as pneumonia, tuberculosis, congestive heart failure, and malignancy.¹ Pleural effusion caused by malignancy is a debilitating and often life-threatening condition secondary to neoplastic diseases. Among them, Lung/bronchogenic carcinoma, breast cancer, ovarian cancers, lymphomas, and gastrointestinal cancers are in descending trends. In United states, the incidence of malignant pleural effusion (MPE) is estimated around one lac 50 thousand cases per year.² Neoplastic diseases cause 13% to 40% of all PE and accounts for 70% of all massive effusions. PE develops in nearly one half of all the patients with metastatic cancer.³

This condition primarily results from the metastasis of cancer cells to the pleura, the membrane that surrounds the lungs, leading to the release of fluid from both cancerous and inflammatory processes.^{4,5} The pathophysiology of MPE is multifactorial and arises primarily from the progression of underlying malignancies. Malignant cells can infiltrate the pleura through hematogenous or lymphatic routes or by direct extension from the primary tumor. Once cancer cells infiltrate the pleura, they incite an inflammatory response characterized by the release of proinflammatory cytokines, chemokines, and growth factors. These mediators trigger the accumulation of fluid in the pleural space by increasing capillary permeability and inhibiting fluid reabsorption, leading to a disruption in the delicate balance between pleural fluid production and reabsorption.^{6,7}

PE restricts ventilation, causing progressive

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shortness of breath, orthopnea, tachycardia, dry cough, and chest pain. Additionally, it reduces physical activity of patients that has overall negative impact on quality of life.⁸ The management of MPE is challenging in terms of diagnosis and treatment. Several palliative treatment options are available, including repeated needle thoracentesis, tube thoracostomy, indwelling pleural catheters, chemical or biologic pleurodesis, pleurectomy, and pleuroperitoneal shunt.⁹ The gold standard procedure for the management of MPE is pleurodesis.^{3,10,11} Pleurodesis aims to achieve a symphysis between parietal and visceral pleural surfaces to prevent fluid or air accumulation in the pleural space, relieve symptoms, thereby avoiding the need for frequent hospitalization. This procedure typically involves the instillation of sclerosing agents to eliminate the pleural space by formation of fibrous adhesions that can lead to permanent cessation of fluid collection between visceral and parietal pleura. It is particularly useful in patients with recurrent effusions.¹²

There are different sclerosing agents available for chemical pleurodesis, including oxytetracycline (OTC) derived from tetracycline, nitrogen mustard, bleomycin, iodopovidone mitoxantrone, silver nitrate, and talc powder. These agents have their own benefits and drawbacks, with selection criteria based on availability, cost effectiveness, agent's efficacy, safety profile and ease of administration.¹ OTC, a tetracycline derivative, is a relatively inexpensive and readily available sclerosing agent. Its advantages include availability, cost-effectiveness, ease of administration, excellent safety, and a generally well-tolerated side effect profile. The direct effects of this drug are similar to growth factors released by fibroblasts.¹³

Several studies have reported variable success rates with OTC pleurodesis in patients with MPE. One study indicated a success rate of only 9.1%¹⁴, while others reported success rates of 66%¹⁵ and 73.68%.³ Post-pleurodesis complications such as chest pain (18%) and fever (21%) have also been noted.³ Given its widespread use as a sclerosing agent due to its accessibility and safety profile, it is imperative to determine the true efficacy of OTC pleurodesis in MPE patients. As no local data are available, and given the variation in international

findings, this study will set a baseline for the use of OTC in Pakistan. The results will also help build physician confidence in using OTC, a safer and more readily available agent with additional antibiotic properties, compared to other cytotoxic agents that have several potential side effects.

OBJECTIVE

To determine the outcome of OTC pleurodesis in patients with MPE in terms of efficacy, safety, and complications associated with OTC pleurodesis, thereby providing valuable data for clinical decision-making and improve management strategies for MPE in Pakistan.

METHODS

Data Collection

This quasi-experimental study was carried out at Pulmonology Department, Allama Iqbal Medical College (AIMC) / Jinnah Hospital, Lahore, from September 1st, 2025 to February 28, 2026. The study received approval from the hospital's ethical review board (ERB264/16/15-09-2025/AIMC/JHL) prior to initiation. A total of 127 patients with clinically diagnosed MPE were enrolled. Sample size calculation was performed using the WHO sample size calculator, based on a 95% confidence level, 5% absolute precision, and an anticipated success rate of pleurodesis with OTC of 9.1%. Participants were selected using a non-probability consecutive sampling technique. All participants provided written informed consent prior to procedure and inclusion in study.

Inclusion and Exclusion Criteria

Patients aged 25 to 80 years of either gender who had a confirmed diagnosis of malignancy and presented with clinically diagnosed pleural effusion and scheduled for pleurodesis were enrolled for the study. Exclusion criteria consisted of patients with fibrotic lung disease, cardiac disease, bronchial obstruction (as assessed from prior medical records and radiology reports), hypersensitivity to OTC, prior pleurodesis treatment with other agents, or a history of poor lung expansion after pleural fluid drainage.

Baseline Data Collection

Baseline demographic data, including age, gender,

duration of malignancy, type of malignancy (primary lung cancer vs. metastatic malignancy), and the volume of PE, were recorded. PE volume was determined by a consultant radiologist using ultrasound imaging. Pretreatment assessments included a detailed history of all the patients, clinical examination, complete blood profile, and baseline posteroanterior (PA) and lateral chest radiographs.

Pleurodesis Procedure

Pleurodesis was performed by two consultant pulmonologists with over 5 years of post-fellowship experience. The procedure began with the insertion of a 24F-32F chest tube into the midaxillary line at the 5th intercostal space, under local anesthesia. Pleural fluid was drained via gravity using an underwater-sealed drainage system. Once the drainage output decreased to less than 100 ml over 24 hours, PA chest radiographs were obtained to confirm sufficient fluid evacuation, the absence of loculated collections, and full lung re-expansion.

Following this, pleurodesis was performed using a mixture of 50 ml of fluid, prepared by combining 12.5 ml of 2% lidocaine with normal saline. OTC, derived from oxytetracycline capsules (35 mg/kg body weight), was added to this fluid. The resulting mixture was instilled into the pleural cavity via chest tube and clamped for two hours to allow for optimal contact. After this period, the clamp was released.

Post-procedural Monitoring

When the drainage fluid volume dropped to less than 100 ml per day after pleurodesis, chest tube was taken out. If drainage fluid exceeded 300 ml per day, pleurodesis was repeated. Posteroanterior and lateral chest X-rays were obtained following chest tube removal and again one month after pleurodesis to evaluate the success of the procedure.

Outcome Measures

The primary outcome measure was the success of pleurodesis, defined as the absence of pleural fluid accumulation within the first 30 days following the procedure. Secondary outcomes included the occurrence of post-pleurodesis chest pain, measured using the Visual Analog Scale (VAS ≥ 1) within 24 hours of the procedure, and the development of fever (temperature $> 100^{\circ}\text{F}$) during

the same period.

All data were systematically recorded in a pre-designed proforma for subsequent analysis.

Statistical Analysis

Statistical analysis was performed using SPSS version 20.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were calculated for baseline characteristics, including mean (M) $\pm$ standard deviation for continuous variables with frequencies and percentages for categorical variables. Continuous variables, such as age, duration of malignancy, and pre-pleurodesis PE volume, between patients with successful and unsuccessful pleurodesis outcomes were compared by using independent t test. Chi-square test was applied for categorical variables, such as gender and type of malignancy to assess the association with pleurodesis success. A value of ≤ 0.05 (p-value) was considered as statistically significant.

RESULTS

A total of 127 patients diagnosed with MPE were enrolled in this study (Table-I). The cohort consisted of 67 males (52.76%) and 60 females (47.24%), with mean age of participants was 58.4 ± 6.3 years. The duration of malignancy varied, with a mean duration of 1.8 ± 0.4 years. The most prevalent malignancies identified were lung carcinoma (52 patients, 40.94%), followed by breast carcinoma (40 patients, 31.50%), malignant ovarian cancer (18 patients, 14.17%), small intestine cancer (10 patients, 7.87%), and lymphoma (7 patients, 5.51%). Dyspnea was the predominant symptom, reported by all 127 patients (100%). Weight loss was observed in 60 patients (47.24%), while 31 patients (24.41%) presented with a cough. The average pre-pleurodesis volume of pleural fluid, as determined by ultrasound, was 850 ± 30 ml, with the average volume of pleural fluid being drained was 654 ± 26 ml.

Regarding pleurodesis outcomes, a successful procedure was achieved in 84 patients (66.15%), as detailed in Table-II. However, 19 patients (14.96%) required a repeat pleurodesis, and 24 patients (18.89%) experienced reaccumulation of pleural fluid (greater than 100 ml) within 30 days, resulting in unsuccessful pleurodesis. Post-procedural

complications included chest pain (VAS ≥ 1) in 31 patients (24.40%), and fever ($>100^{\circ}\text{F}$) in 22 patients (17.32%). No mortality was reported during the study period.

Statistical analysis revealed no significant association between pleurodesis success rates and clinical characteristics, including gender, age, duration of malignancy, type of malignancy, and the volume of pleural fluid in the pleural cavity, with a p-value of 0.894, 0.452, 0.325, 0.697, and 0.732 respectively. These findings suggest that, despite variability in patient characteristics, these factors did not significantly impact the likelihood of successful pleurodesis in this cohort.

TABLE-I**Baseline characteristics of patients (n = 127)**

Characteristics	Value
Age (M $\pm$ SD)	58.4 $\pm$ 6.3 years
Gender (n, %)	
Males	67 (52.76%)
Females	60 (47.24%)
Duration of malignancy (M $\pm$ SD)	1.8 $\pm$ 0.4 years
Type of malignancy (n, %)	
Lung carcinoma	52 (40.94%)
Breast carcinoma	40 (31.50%)
Ovarian carcinoma	18 (14.17%)
Small intestine cancer	10 (7.87%)
Lymphomas	7 (5.51%)
Symptoms (n, %)	
Dyspnea	127 (100%)
Weight loss	60 (47.24%)
Cough	31 (24.41%)
Pre-pleurodesis volume on ultrasound (M $\pm$ SD, ml)	850 $\pm$ 30 ml
Pleurodesis volume drainage (M $\pm$ SD, ml)	654 $\pm$ 26 ml

TABLE-II**Outcome of OTC pleurodesis (n = 127)**

Outcome	Value
Successful pleurodesis (n, %)	84 (66.15%)
Repeat pleurodesis (n, %)	19 (14.96%)
Unsuccessful pleurodesis (n, %)	24 (18.89%)
Post-pleurodesis chest pain (VAS ≥ 1) (n, %)	31 (24.40%)
Post-pleurodesis fever ($>100^{\circ}\text{F}$) (n, %)	22 (17.32%)

Mortality after fleurodesis (n, %) 0 (0%)

TABLE-III**Statistical analysis of clinical characteristics and pleurodesis success rates**

Clinical Characteristic	Successful Pleurodesis (n = 84)	Unsuccessful Pleurodesis (n = 43)	p
Gender			
Males (%)	44 (52.38%)	23 (53.49%)	0.894
Females (%)	40 (47.62%)	20 (46.51%)	
Age (M $\pm$ SD)	58.3 $\pm$ 6.1	58.5 $\pm$ 6.5	0.452
Duration of malignancy (M $\pm$ SD, years)	1.7 $\pm$ 0.3	1.9 $\pm$ 0.5	0.325
Type of malignancy			
Lung carcinoma (%)	35 (41.67%)	17 (39.53%)	0.697
Breast carcinoma (%)	30 (35.71%)	10 (23.26%)	
Ovarian carcinoma (%)	8 (9.52%)	10 (23.26%)	0.732
Small intestine cancer (%)	5 (5.95%)	5 (11.63%)	
Lymphomas (%)	4 (4.76%)	3 (6.98%)	0.732
Pre-pleurodesis volume of effusion (M $\pm$ SD, ml)	850 $\pm$ 30	860 $\pm$ 40	

Note: Chi-square for categorical variables and Independent t-test for continuous variables; $P^* \leq 0.05$

DISCUSSION

MPE is a major complication in patients with advanced malignancies, especially lung and breast cancer. It occurs when there is an imbalance between pleural fluid secretion and reabsorption, leading to fluid accumulation in the pleural space. MPE is recognized as one of the leading causes of exudative PEs, particularly in patients with metastatic cancers. This condition often results in significant clinical symptoms, including dyspnea, orthopnea, and reduced physical activity, ultimately impacting patients' quality of life.¹⁶

Among the various management strategies for PE, pleurodesis remains the cornerstone for preventing recurrent fluid accumulation in patients with MPE. Pleurodesis involves obliterating the pleural space

by causing adhesion between the visceral and parietal pleura, which prevents the re-accumulation of fluid. While pleurodesis can be performed using mechanical or chemical methods, chemical pleurodesis has become a preferred option in resource-limited settings. This procedure is minimally invasive, requires no general anesthesia, and can be performed at a lower cost, which makes it especially suitable for settings with limited healthcare resources.¹⁷

In the present study, we evaluated the effectiveness of OTC, a tetracycline derivative, as a sclerosing agent for pleurodesis. Our findings showed a success rate of 66.15%, which aligns closely with the success rates reported in previous studies. For instance, a study by the American Thoracic Society reported a 67% success rate with tetracycline pleurodesis, with complications such as chest pain (14%) and fever (10%) occurring within 24 hours post-procedure.¹⁸ Similarly, Şenyiğit et al., in their review of 117 cases, found an 81% success rate with OTC pleurodesis in patients with malignant pleural mesothelioma.¹⁹

Other comparative studies have also demonstrated comparable outcomes. In a study that compared talc and OTC in 47 patients, a 67% success rate was observed with OTC at a dose of 70 mg/kg, which is similar to our findings, though our study utilized a lower dose of 35 mg/kg.²⁰ Additionally, a recent trial in Pakistan reported a 76% success rate with tetracycline pleurodesis, reinforcing the effectiveness of this approach in different regional settings.²¹

Despite its efficacy, OTC pleurodesis is not without its complications. In our study, chest pain (24.40%) and fever (17.32%) were the most commonly observed adverse effects, which are consistent with findings from a Ghanaian series that reported complications such as fever and chest pain occurring in 20–25% of patients, with most cases being self-limiting.²² A literature review documented complications of chest pain (30.4%) and fever (23.1%) with OTC pleurodesis, which further supports our observations.²³

One notable finding of our study is that the success

of pleurodesis with OTC appears to be largely independent of patient demographics and disease characteristics. No significant differences were observed in the success rates based on factors such as age, gender, type of malignancy (primary vs. metastatic), disease duration, or effusion volume. This suggests that OTC can be an effective treatment for a wide range of patients with MPE, regardless of these variables.

LIMITATIONS

Although the results of current study provide meaningful insights into the effectiveness of OTC pleurodesis, there are several limitations that can be considered when interpreting the results. First, the sample size of 127 patients may be insufficient to generalize the findings to a larger population. Additionally, the study was conducted at a single center with a short follow-up period, which limits the ability to assess the long-term outcomes of OTC pleurodesis. Moreover, the exclusion of patients with poor lung expansion may have introduced selection bias. Finally, we did not evaluate quality-of-life metrics or patient-reported outcomes, which would be crucial to understand the full impact of this treatment. Future studies should include larger, multicenter cohorts with longer follow-up periods and consider assessing patient-reported outcomes and quality of life to further substantiate the findings.

CONCLUSION

OTC pleurodesis proves to be a cost-effective, safe, and reliable method for managing MPE in patients with advanced malignancies. Our findings indicate that OTC is a viable alternative to other more expensive sclerosing agents, with a low complication rate and effective outcomes. Given its accessibility, affordability, and demonstrated efficacy, OTC can be particularly beneficial in resource-limited settings. However, further research with larger, multicenter trials and a focus on patient-reported outcomes is needed to fully establish its role in the treatment of MPE and optimize its use in clinical practice.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHORSHIP AND CONTRIBUTION DECLARATION

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3	Mirza Muhammad Ayub Baig: Drafting, literature search.
4	Muhammad Bilal Liaqat: Literature search, revision of manuscript.