Original Article

Outcome of Tetracycline Pleurodesis in Patients with Malignant Pleural Effusion

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Abstract

Background: Malignant pleural effusion commonly complicates advanced malignancies which significantly impact patient quality of life. Tetracycline pleurodesis is frequently utilized in resource-limited settings due to its availability and cost-effectiveness. However, recent local data regarding its efficacy and safety remain sparse.

Objective: To determine the outcome of tetracycline pleurodesis in patients with malignant pleural effusion.

Methods: This descriptive study was conducted over six months at Lady Reading Hospital, Peshawar. A total of 89 patients aged 31–77 years with cytologically confirmed MPE underwent chemical pleurodesis using tetracycline. Data were collected on demographics, malignancy type and duration, effusion volume, and pleurodesis outcomes. The primary outcome of this study was pleurodesis success (no effusion recurrence at 30 days). Secondary outcomes included post-procedure chest pain and fever. Stratified analysis was performed by age, sex, malignancy type, duration, and effusion volume.

Results: Pleurodesis was successful in 67 of 89 patients (75.3%). Post-procedural chest pain and fever were found in 22.5% and 20.2%, respectively; all episodes were short term. Stratified analysis showed no statistically significant predictors of pleurodesis outcome ($p > 0.05$ for all variables). No mortality or serious complications were observed.

Conclusion: Tetracycline pleurodesis achieved successful short-term control of MPE in approximately three-quarters of patients with low complication rates. These findings support the use of tetracycline as an effective and accessible sclerosant in palliative care settings, especially where other options are unavailable.

Keywords: Malignant pleural effusion; pleurodesis; tetracycline

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Introduction

Malignant pleural effusion (MPE) is a debilitating and often life-threatening condition characterized by the accumulation of fluid in the pleural cavity, which is the space between the lungs and the chest wall. 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.[1,2] The pathophysiology of MPE is multifactorial, and it primarily arises 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 have infiltrated 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.[3,4]

There are three primary approaches to MPE management including palliation, chemical pleurodesis and indwelling pleural catheters. Amongst these, chemical pleurodesis seeks to obliterate the pleural space, preventing the re-accumulation of fluid. This procedure typically involves the instillation of sclerosing agents such as talc or tetracycline into the pleural cavity, promoting pleural adhesion and is typically useful in patients with recurrent effusions.[5] When it comes to outcome of tetracycline pleurodesis in patients with malignant pleural effusion, literature is not only quite outdated but also shows a high degree of variability. A study reported that frequency of successful pleurodesis with tetracycline in patients with MPE was 86.6%.[6] Contrarily, in another study, it was reported that successful pleurodesis with tetracycline in patients with MPE was obtained only in 66% of patients.[7] Similarly, in another study it was reported that tetracycline pleurodesis was successful in 77.8%, post-pleurodesis chest pain occurred in 20% and post-pleurodesis fever occurred in 14% of the patients.[8] Since tetracycline is a widely used sclerosing agent used for pleurodesis due to its easy availa-

bility and safety, it is imperative to determine the efficacy of this agent to achieve successful outcomes of pleurodesis to improve patient's quality of life. However, there is a lack of contemporary data from South Asia, particularly Pakistan, where tetracycline remains widely used due to its low cost and easy availability Therefore, this study is conducted to determine the outcome of tetracycline pleurodesis in patients with malignant pleural effusion. Results from this study will help building the confidence of physicians regarding the use of tetracycline, a much safer and easily available agent with additional antibiotic properties compared to other cytotoxic agents for pleurodesis which have many potential side effects.

Methods

This single-centre descriptive study was conducted in the Department of Pulmonology, Lady Reading Hospital, Peshawar, from 1st November 2024 to 30th April 2025 following approval from the College of Physicians and Surgeons Pakistan (CPSP) with Ref No: CPSP/REU/PUL-2023-022-825 and Institutional Review Board, Lady Reading Hospital(Ref: No. 153/LRH/MTI). Non-probability consecutive sampling technique was used including adult patients (31–77 years, either sex) with symptomatic, confirmed malignant pleural effusion (MPE). MPE was defined as a recurrent effusion > 300 mL in a patient with known malignancy, classified as exudate by Light's criteria and containing malignant cells on cytologic examination. Patients with fibrotic lung disease, significant cardiac disease, endobronchial obstruction, poor post-drainage lung expansion, drug hypersensitivity, or a previous pleurodesis attempt were excluded. Using an anticipated post-pleurodesis chest-pain frequency of 18 %, an absolute precision of 8 %, and a 95 % confidence level, the WHO sample -size calculator yielded a target of 89 participants. After written informed consent, baseline demographics (age, sex), disease characteristics (malignancy type, duration), and ultrasound-measured effusion volume were recorded. Pretreatment work-up included history, physical examination, full blood count, and baseline postero-anterior and lateral chest radiographs.

Under local anesthesia a 24–32 Fr chest tube was inserted in the 5th intercostal space, mid-axillary line, and attached to an underwater seal. When drainage fell below 100 mL in 24 h and follow-up radiographs confirmed full lung re-expansion without loculation, pleurodesis was performed. The sclerosing mixture comprised 12.5 mL of 2 % lidocaine diluted to 50 mL with saline; tetracycline powder (35 mg kg^{-1}) freshly opened from oral capsules was suspended in this solution and instilled intrapleural. The tube was clamped for two hours, then returned to free drainage. If subsequent output remained < 100 mL d^{-1} the tube was removed; if > 300 mL d^{-1}, the procedure was repeated once. Patients were reassessed 30 days later with chest radiography. Outcomes were defined as a priori: success—no radiographic re-accumulation within 30 days; failure—recurrent effusion within 30 days. Immediate complications were recorded as post-pleurodesis chest pain (visual-analogue scale ≥ 1 within 24 hours) and fever (temperature > 100 °F within 24 hours).

Data were entered into a pre-designed proforma and analysed in SPSS v20. Continuous variables (age, malignancy duration, effusion volume) are presented as mean ± SD; categorical variables (sex, malignancy type, outcomes, complications) as frequencies and percentages. Pleurodesis success was stratified by age group (≤ 60y/>60y), sex, malignancy type (primary vs metastatic), malignancy duration (≤12mo />12mo) and effusion volume (≤1300mL/>1 300mL). Post-stratification comparison employed the χ^2 test; $p \leq 0.05$ was considered statistically significant. Patient confidentiality was maintained throughout by omitting personal identifiers from all study records.

Results

A total of 89 patients underwent tetracycline pleurodesis for malignant pleural effusion during the six-month study period. The mean age was 54.5 ± 14.7 years (range 31–77); 50 were male (56.2 %) and 39 female (43.8 %). Most effusions were secondary to primary lung malignancy (n=66;74.2%), whereas 23 (25.8 %) arose from metastatic disease. The mean duration of malignancy at presentation was 15.2 ± 8.4 months, and the mean volume of fluid drained before sclerosant instillation was 1171 ± 432 mL. Pleurodesis was successful in 67 patients (75.3%); 22 (24.7%) developed radiographic recurence within 30 days. Chest pain occurred in 20 patients (22.5%) and fever in 18 (20.2%); all episodes were transient and conservatively managed. Stratified analysis showed no variable associated with

outcome: age ≤ 60 y vs > 60 y (74.1 % vs 77.1 %, $\chi^2 = 0.01$, p = 0.94); male vs female (80.0 % vs 69.2 %, $\chi^2 = 0.85$, p = 0.36); primary vs metastatic malignancy (75.8 %vs 73.9 %,$\chi^2 \approx 0$, p ≈ 1.00); malignancy duration ≤ 12 mo vs > 12 mo (78.4 % vs 73.1 %, $\chi^2 = 0.10$, p = 0.75); effusion volume ≤ 1 300 mL vs > 1 300 mL (75.8 % vs 73.9 %, $\chi^2 \approx 0$, p ≈ 1.00). Although subgroup analyses were performed, none of the comparisons reached statistical significance (all p > 0.05). Thus, tetracycline pleurodesis showed consistent success rates across age, sex, malignancy type, disease duration, and effusion volume. Tetracycline pleurodesis achieved durable pleural symphysis in approximately three quarters of patients with low transient morbidity and no procedure related mortality.

Table 1: *Baseline Characteristics*

Characteristic	Value	%
Age, mean ± SD, y	54.5 ± 14.7	
Male	50	(56.2%)
Female	39	(43.8%)
Primary lung malignancy	66	(74.2%)
Metastatic malignancy	23	(25.8%)
Duration, mean ± SD, mo	15.2 ± 8.4	
Effusion volume, mean ± SD, mL	1171 ± 432	
Abbreviations: SD, standard deviation; mo, months; mL, milliliter; Y, year		

Table 2: *Pleurodesis Outcome by Subgroups*

Subgroup	Category	Success, n (%)	Failure, n (%)	P value
Age	≤60 y	40 (74.1%)	14 (25.9%)	0.94
	>60 y	27 (77.1%)	8 (22.9%)	
Gender	Male	40 (80.0%)	10 (20.0%)	0.36
	Female	27 (69.2%)	12 (30.8%)	
Malignancy	Primary	50 (75.8%)	16 (24.2%)	1.00
	Metastatic	17 (73.9%)	6 (26.1%)	
Duration	≤12 mo	29 (78.4%)	8 (21.6%)	0.75
	>12 mo	38 (73.1%)	14 (26.9%)	
Volume	≤1300 mL	50 (75.8%)	16 (24.2%)	1.00
	>1300 mL	17 (73.9%)	6 (26.1%)	
Abbreviations: y, years; mo, months; mL, milliliter				

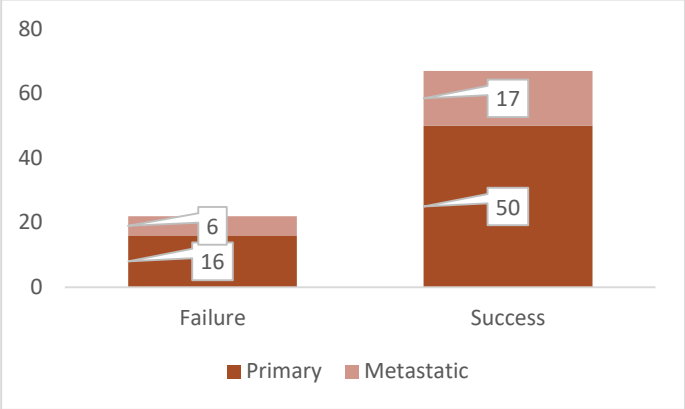

Figure 1: *Pleurodesis Outcome by Malignancy Type*

Success = no radiographic recurrence ≤ 30 days;
Failure = recurrence within 30 days.
Primary = primary lung malignancy (n = 67);
Metastatic = secondary deposits (n = 22). Total n = 89.

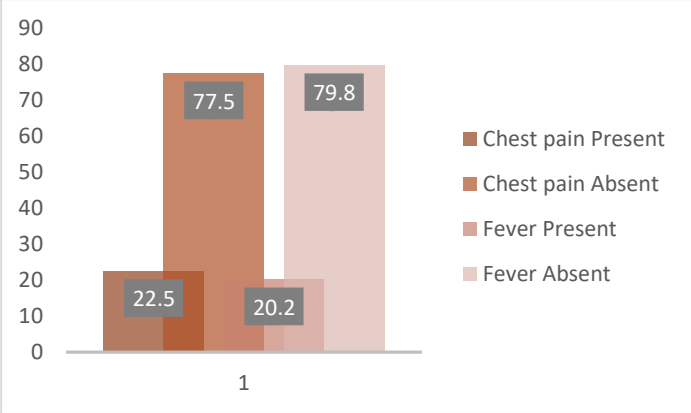

Figure 2: *Post-Pleurodesis Complications Among Patients*

Complications were recorded within 24 hours post-procedure. Chest pain was defined as VAS ≥ 1 and fever as temperature > 100 °F. Both were self-limiting and required only conservative management.

Discussion:

Malignant pleural effusion represents advanced disease with limited survival, and palliation remains the primary therapeutic goal. Our study demonstrated that tetracycline pleurodesis is effective and well-tolerated, with outcomes comparable to those reported in recent literature.

We found a pleurodesis success rate of 75.3% at 1 month (67 of 89 patients), indicating that no re-accumulation of effusion occurred in about three-quarters of patients after tetracycline instillation. This outcome is consistent with the efficacy range reported in prior studies. Notably, a large randomized trial

of talc slurry pleurodesis similarly achieved about a 75% success rate at 1 month, and success rates in many modern series of pleurodesis (with various agents) generally fall below 80%.[11] Our result also closely mirrors the 76% success rate observed specifically with tetracycline pleurodesis in a recent randomized trial from Pakistan. In that trial, tetracycline via chest tube had 76% success, significantly lower than the 94% success with thoracoscopic talc poudrage, highlighting talc's superior efficacy.[12] Likewise, a Nigerian study comparing tetracycline with iodopovidone reported high pleurodesis efficacy in both groups (~93% in each).[13] Our success rate is slightly lower, which may reflect differences in patient selection or definitions (the Nigerian study included "partial" responses as successes, potentially inflating their rate). Overall, our findings reinforce that tetracycline (and its analogues) can achieve roughly 70–80% success in MPE pleurodesis, which aligns with the middle of the range reported for other agents in the literature.[11,12] Some variability is expected across studies due to heterogeneous populations and methods for instance, malignant pleural effusion is known to respond less favorably to pleurodesis (success ~73% vs ~85% in other malignancies).[11,15] Importantly, we excluded patients with non-expandable ("trapped") lung, which is a major cause of pleurodesis failure; this likely contributed to our reasonably high success rate. Taken together, our results demonstrate that tetracycline pleurodesis produces an efficacy comparable to that reported with talc in many circumstances (around 70–80% short-term success), though talc poudrage may still yield higher success in optimally selected cases.[12]

The procedure was found to be safe and well-tolerated in our cohort. We observed no procedure-related mortality, consistent with other contemporary studies of pleurodesis.[12,14] Malignant pleural effusion with advanced disease, affecting up to 15% of cancer patients and carrying a median survival of only 4–12 months.[2,9,10] Chemical pleurodesis is generally considered a low-risk palliative intervention; serious complications like acute respiratory distress syndrome (ARDS) are very rare. In our series, the most frequent side effects were transient chest pain (22.5%) and fever (20.2%) following tetracycline instillation. These rates are in line with reported figures. Transient pleuritic pain and low-grade fever are well-known common adverse effects of pleurodesis due to the acute pleural inflammation provoked.[11] For instance, few studies[8,16] documented post-pleurodesis fever and pain in ~20% of patients using tetracycline, and a recent review confirms that fever and pain are the most common pleurodesis-related events generally.[11] Another meta-analysis also found chest pain as the most common complaint post procedure.[17] Thus, tetracycline can be considered a safe sclerosing agent, with side effect rates comparable to other agents.

Another notable finding in our study was that patient factors and effusion characteristics did not significantly influence pleurodesis outcomes. We observed no statistically significant difference in success rates when stratified by age or sex of the patient, the type of malignancy (primary lung cancer vs. metastatic cancer to pleura), the volume of effusion, or the duration of the underlying malignancy. This suggests that tetracycline pleurodesis can be effective across a wide range of patient demographics and disease characteristics, as long as the lung can re-expand. Our results align with the observations of other investigators who found that baseline patient factors often do not predict pleurodesis success.[13,15] For example, Omoregbee et al.[13] noted no difference in pleurodesis efficacy between breast cancer and lung cancer patients in their series (both responded equally well). Similarly, a secondary analysis of the TIME1 trial by Mercer et al[15] did not identify age or gender as significant predictors of pleurodesis outcome. Another prospective RCT also align with study about no relation of patient factors with tetracycline pleurodesis.[18] On the other hand, certain disease-related factors are known to affect success in specific contexts: as noted above, malignant mesothelioma tends to have lower success rates than metastatic pleural effusions, presumably due to diffuse tumor burden impairing lung re-expansion.[11,20]

Technical factors can also play a role – adequate drainage of fluid and use of sufficiently large chest tubes are thought to facilitate better pleural apposition. In our protocol, we used large-bore chest tubes (24–32 Fr) for drainage; previous literature[21,22] suggests small-bore catheters (<12 Fr) may be associated with slightly lower success, so our use of larger tubes may have contributed to the high success rate by ensuring complete lung re-expansion. Overall, our findings suggest that within an appropriately selected population (expandable lung, no extensive pleu-

ral fibrosis), tetracycline pleurodesis works reliably across various subgroups. We did not find any subgroup that fared significantly worse, though our sample may not be large enough to detect small differences. Regional South-Asian guidelines likewise list tetracycline and doxycycline as acceptable sclerosants when talc is unavailable, emphasi-zing that agent choice should follow local availability and clinician experience.[19] This uniform efficacy is a positive feature, indicating the procedure's broad applicability in MPE patients.

This study has some limitations that must be acknowledged. First, the sample size (n=89) was modest and drawn from a single tertiary center. While our cohort provides valuable insight, a larger multicenter sample would improve the statistical power to detect differences between subgroups and increase the generalizability of the results. We originally calculated a larger sample size requirement based on an expected 66% success rate (from prior data), but logistical constraints limited enrollment; the study may therefore be underpowered for subgroup analyses. Second, our study was a descriptive observational study without a control group or randomization. We did not compare tetracycline to another pleurodesis agent or to an alternative management (such as IPC), so conclusions about relative efficacy cannot be made. It would strengthen the evidence to compare tetracycline in a randomized trial against the gold-standard talc (or against newer agents like iodopovidone or others). Third, our follow-up period for defining success was 30 days. While a 1-month success outcome is standard in pleurodesis studies, longer-term follow-up (3–6 months) might have identified late recurrences of effusion. It's known that some patients who appear successfully pleurodesed at 1 month can have effusion recur later as disease progresses; our study did not capture longer-term durability of pleurodesis. Additionally, we focused on clinical success (no re-drainage needed) and did not quantify improvements in symptoms or quality of life, which are important outcomes in MPE management. Another limitation is that we excluded patients with non-expandable lung or very advanced disease (e.g. expected survival <1 month). While this ensured we only treated those likely to benefit, it may introduce selection bias our results apply to relatively fit MPE patients with expandable lungs, and not to the sickest patients. Finally, there is an inherent heterogeneity in malignancies causing MPE in our sample (including both primary lung cancers and metastases from various primaries), and we did not stratify outcomes by specific tumor type beyond the broad "primary vs metastatic" categorization. It is possible that certain tumor types (e.g. ovarian cancer, lymphoma, etc.) could respond differently to pleurodesis, but our sample size precluded detailed analysis by cancer subtype. Despite these limitations, our study addresses a gap in up-to-date data on tetracycline pleurodesis. The effectiveness we observed in our study helps affirm that this older agent remains relevant. Future studies could build on this by involving multiple centers, including a comparator arm (talc or other agent), and extending follow-up to assess long-term efficacy and patient-centered outcomes.

Conclusion:

Tetracycline pleurodesis proved to be a safe and effective option for malignant pleural effusion, with favorable short-term outcomes and minimal complications. Its low cost and wide availability make it a practical choice in resource-limited settings where talc or newer agents are not accessible. Morever, this study also highlights the importance of conducting larger multicenter trials with longer follow-up to confirm durability and refine patient selection for pleurodesis in diverse populations.

Ethical Permission: The Institutional Review Board of Lady Reading Hospital-MTI approved this study vide reference No. 153/LRH/MTI..

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Authors' contribution:

IUK: Concept & design, acquisition of data, drafting of article

ZI: Final approval of the version to be published

WU: Analysis & interpretation,

MD: Acquisition of data

SER: Analysis & interpretation

MA: Critical revisions of the version to be published

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