Original Article

# Efficacy and Safety of Povidone-iodine Pleurodesis in Malignant Pleural Effusions

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## Abstract

**Background:** Malignant pleural effusion (MPE) is a known complication of advanced malignancy. It leads to recurrent pleural fluid accumulation and progressive dyspnea. Pleurodesis is one of the palliative treatment methods for preventing recurrent effusion. Previously, talc was the commonly used sclerosant; however, it is not commonly available in resource-constrained settings. Povidone-iodine is another sclerosant that is easily available and can be used as an alternative in these cases. The present study aimed to evaluate the efficacy and safety of povidone-iodine pleurodesis in patients with malignant pleural effusions. **Material and Methods:** This prospective interventional study included 40 patients with recurrent symptomatic malignant pleural effusion cases. Following complete drainage of pleural fluid and radiological confirmation of adequate lung expansion, pleurodesis was performed using 20 mL of 10% povidone-iodine diluted with 80 mL of normal saline and 10 mL of 2% lignocaine instilled through an intercostal drainage tube. Patients were followed up at one month and three months. The primary outcome was successful pleurodesis, defined as complete or partial response without the need for repeat pleural intervention. Secondary outcomes included improvement in dyspnea, duration of chest tube placement, hospital stay, radiological lung expansion, and procedure-related complications. **Results:** The mean age was 58.4 ± 12.3 years, with males comprising 60% of the study population. Lung carcinoma was the most common primary malignancy, accounting for 50%. The overall pleurodesis success rate was 90% at one month and 80% at three months. Complete response was achieved in 70% of patients at one month and 60% at three months, while partial response was observed in 20% of patients at both follow-up visits. The mean Visual Analogue Scale (VAS) dyspnea score improved significantly from 7.2 ± 1.5 before pleurodesis to 3.0 ± 1.2 at one month ($p < 0.001$). The mean time to chest tube removal was 4.5 ± 1.8 days, and the mean hospital stay was 6.5 ± 2.0 days. Chest radiograph expansion scores improved significantly from 2.8 ± 0.9 before pleurodesis to 8.5 ± 1.3 after the procedure ($p < 0.001$). **Conclusion:** Povidone iodine pleurodesis appears to be an effective and safe method for the management of recurrent malignant pleural effusions. It provides good pleurodesis success rates, significant symptomatic relief, satisfactory lung re-expansion, and minimal serious complications. Given its low cost, easy availability, and favorable safety profile, povidone-iodine represents a practical alternative to conventional sclerosants, particularly in resource-constrained healthcare settings.

**Keywords:** Malignant pleural effusion, Povidone-iodine, Pleurodesis, Dyspnea, Pleural sclerosis, Palliative care.

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## Introduction

Malignant pleural effusion (MPE) is a frequent complication of advanced malignancy and is linked to high morbidity and poor prognosis. It occurs due to the buildup of fluid in the pleural cavity caused by metastatic involvement of the pleura, blockage of lymphatics, increased vascular permeability, and the release of inflammatory mediators by the tumour cells. Overall, MPE occurs in about 15% of cancer patients, and the most common primary malignancies associated with the development of MPE are the lung, breast, lymphoma, and ovarian carcinoma.[1,2] Malignant pleural effusion is found in advanced disease and has a median survival of between 3 and 12 months, depending on the underlying malignancy and the general clinical condition of the patient.[2,3] As the fluid builds up, the patient will suffer from progressive dyspnea, chest pains, cough, decreased exercise tolerance, and impairment of quality of life. For patients with MPE, treatment aims to palliate symptoms, as many such patients will have a short life expectancy. Therapeutic thoracentesis provides only short-term relief, and in most patients, there is a recurrence of pleural fluid, requiring repeated thoracentesis. Recurrent aspirations lead to more hospital visits, patient discomfort, higher healthcare costs, and complications like pneumothorax, infection, and bleeding.[2,4] Pleurodesis has become an established palliative treatment for recurrent malignant pleural effusions. It aims to obliterate the pleural space by inducing adhesion between the visceral and parietal pleurae through inflammation and fibrosis to prevent

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fluid accumulation. For pleurodesis to be effective, sufficient expansion of the lungs must be achieved, and adequate apposition of the pleural surfaces after the causative fluid is removed.[5]

Previously, several sclerosing agents were employed for this purpose, including sterile talc, doxycycline, bleomycin, tetracycline derivatives, silver nitrate, and povidone-iodine. Talc is considered the standard sclerosant due to its high success rate, but it may be limited in many resource-limited populations, and concerns about systemic inflammatory reactions and acute respiratory distress syndrome have been reported, especially for small-particle talc.[5,6] Povidone-iodine has proven to be a promising alternative sclerosant because it is cheap, readily available, easy to administer, and antiseptic. The mechanism of pleurodesis created by povidone-iodine remains unclear, but it is thought that it is caused by the inflammatory response, the low pH, and the oxidative properties of povidone-iodine.[7] In the last 20 years, there have been several clinical studies that have shown success rates of pleurodesis from 80% to more than 90% in patients, which are similar to the success rates in selected patients.[7–9] Moreover, povidone-iodine has a good safety profile, with the most frequently reported adverse effects being chest pain and temporary fever. When careful patient selection and procedural precautions are used, serious complications are rare.[8,9] Povidone-iodine is considered the best agent for pleurodesis in low- and middle-income countries where medical-grade talc is not always available. Povidone-iodine is readily available in the operating room and intensive care units, making it very useful in facilities with limited financial resources. Although some studies have proven it to be effective, different studies report different success rates, methods, and complications associated with the procedure. Further clinical studies are therefore needed to better outline its place in the treatment of MPE and to support its routine use. With this background, the present study aimed to determine the efficacy and safety of povidone-iodine pleurodesis in patients with malignant pleural effusions.

## Materials and Methods

This prospective interventional study was conducted in the Department of Pulmonary Medicine at a tertiary care teaching hospital. Institutional ethical approval was obtained for the study. Written consent was obtained from all the participants of the study after explaining the nature of the study and possible outcomes in the vernacular language. Care was taken to maintain the anonymity of the patients as per protocol.

**Inclusion Criteria**

1. Patients aged 18 years.
2. Proven malignant pleural effusion by pleural fluid cytology and pleural biopsy.
3. Symptomatic recurrent pleural effusion requiring pleurodesis.
4. Complete or near-complete lung expansion following intercostal tube drainage, confirmed radiologically.
5. Patients willing to provide written informed consent.

**Exclusion Criteria**

1. Non-expandable (trapped) lung after pleural fluid drainage.
2. Active pleural infection or empyema.
3. Massive endobronchial obstruction preventing lung expansion.
4. Known allergy or hypersensitivity to povidone-iodine or iodine-containing preparations.
5. Significant thyroid disease.
6. Severe renal impairment.
7. Patients with poor performance status who were considered unfit for pleurodesis.

Based on the inclusion and exclusion criteria during the study period, a total of 40 cases with recurrent symptomatic malignant pleural effusion were included in the study. All patients underwent detailed clinical evaluation, including history taking and complete physical examination. The laboratory investigations included hematological and biochemical investigations, chest radiography, and contrast-enhanced computed tomography of the thorax wherever indicated. The diagnosis of malignant pleural effusion was established by pleural fluid cytology and pleural biopsy. An intercostal chest drain (24–28 Fr) was inserted under aseptic precautions under local anesthesia. Pleural fluid was drained gradually until daily drainage was less than 100–150 mL over 24 hours. Clinically and radiologically, the lungs were checked for satisfactory re-expansion.

Intravenous analgesic was given as needed before pleurodesis. Under sterile conditions, 20 mL of 10% povidone-iodine was diluted with 80 mL of normal saline and 10 mL of 2% lignocaine. The solution was instilled through the intercostal drainage tube, which was then clamped for two hours. Patients were asked to turn every 15 to 30 minutes during this time to allow the sclerosant to be distributed evenly in the pleural cavity. After two hours, the chest tube was reopened and placed on underwater seal drainage. The removal of the drain was performed when daily drainage was less than 100 mL and chest radiography revealed good lung expansion without any significant residual pleural collections.

**Outcome Measures:** The primary outcome was the success of pleurodesis, defined as the absence of clinically significant recurrence of pleural effusion requiring therapeutic aspiration during the follow-up period. The secondary outcome measures were assessed by improvement in dyspnea after pleurodesis. Estimation of time to chest tube removal and duration of hospital stay. Recurrence of pleural effusion and complications such as chest pain, fever, hypotension, allergic reactions, infection, respiratory distress, and thyroid-related adverse effects were analyzed. Follow-up of patients was done at intervals of 1 month and 3 months after pleurodesis. At each visit, clinical assessment and chest radiography were performed to evaluate symptom relief and detect recurrence of pleural effusion.

**Statistical Analysis:** The data were entered into a Microsoft Excel spreadsheet and analyzed using Statistical Package for the Social Sciences (SPSS) software version 29.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation or median with interquartile range, depending on data distribution. Categorical variables were presented as frequencies and percentages. The paired t-test was

used to compare continuous variables before and after pleurodesis, as appropriate. Associations between categorical variables were analyzed using the Fischer's Exact test. A p-value less <0.05 was considered statistically significant.

## Results

The baseline demographic and clinical characteristics of the study population are given in Table 1. Analysis of the table showed that the mean age was 58.4 ± 12.3 years, with ages ranging from 34 to 79 years. The male population predominated with 60% of the study cases. The diagnosis revealed that lung carcinoma was the common cause in 50% of cases, followed by breast carcinoma in 20%. The other malignancies were ovarian carcinoma in 10.0%, lymphoma in 5.0%, and other malignancies, including mesothelioma and gastrointestinal cancers, in 15.0% of patients. Right-sided pleural effusion was found in 55% of cases, bilateral in 5% of cases, and the remaining 40% were left-sided pleural effusion. According to the Eastern Cooperative Oncology Group (ECOG) performance status, 28 (70.0%) patients had a performance status of 0–1, whereas 12 (30.0%) had a score of 2. The mean pre-procedure dyspnea score measured using the Visual Analogue Scale (VAS) was 7.2 ± 1.5.

**Table 1: Baseline demographic and clinical characteristics of study participants**

| Characteristic | Value |
|---|---|
| Age (years) | |
| Mean ± SD | 58.4 ± 12.3 |
| Range | 34 - 79 |
| Gender | |
| Male | 24 (60.0%) |
| Female | 16 (40.0%) |
| Primary Malignancy | |
| Lung Cancer | 20 (50.0%) |
| Breast Cancer | 8 (20.0%) |
| Ovarian Cancer | 4 (10.0%) |
| Lymphoma | 2 (5.0%) |
| Others (Mesothelioma, GI) | 6 (15.0%) |
| Side of Effusion | |
| Right | 22 (55.0%) |
| Left | 16 (40.0%) |
| Bilateral | 2 (5.0%) |
| Performance Status (ECOG) | |
| 0-1 | 28 (70.0%) |
| 2 | 12 (30.0%) |
| Pre-pleurodesis Dyspnea Score (VAS 0—10) | |
| Mean ± SD | 7.2 ± 1.5 |

Pleurodesis Outcomes assessment at one month and three months is given in Table 2. Analysis of the table showed that at one month, a complete response with no recurrence of pleural effusion was achieved in 70.0% of patients, while 20.0% of patients demonstrated a partial response with minimal fluid re-accumulation that did not require intervention. Pleurodesis failed in 10.0% of patients due to symptomatic recurrence requiring further therapeutic intervention. The overall pleurodesis success rate, complete plus partial response at one month, was 90.0%. At the three-month follow-up, complete response was maintained in 60.0% of patients. A partial response was observed in 20.0%, and pleurodesis failure increased to 8 20.0% patients. Consequently, the overall pleurodesis success rate at three months was 80.0%.

**Table 2: Pleurodesis Outcome at 1- and 3-Month Follow-up**

| Outcome Category | 1 Month Follow-up (n=40) | 3 Months Follow-up (n=40) |
|---|---|---|
| Complete Response (No reaccumulation) | 28 (70.0%) | 24 (60.0%) |
| Partial Response (Minimal reaccumulation, no intervention) | 8 (20.0%) | 8 (20.0%) |
| Failure (Symptomatic recurrence requiring intervention) | 4 (10.0%) | 8 (20.0%) |
| Overall, Success Rate (Complete + Partial Response) | 36 (90.0%) | 32 (80.0%) |

Secondary Outcome Measures are depicted in [Table 3]. The mean duration to chest tube removal following pleurodesis was 4.5 ± 1.8 days, with a median duration of 4 days [IQR]: 3–6 days. The mean hospital stay was 6.5 ± 2.0 days, with a median of 6 days (IQR: 5–8 days). Following pleurodesis, there was a marked improvement in dyspnea.

The mean VAS dyspnea score decreased from 7.2 ± 1.5 before the procedure to 3.0 ± 1.2 at one month. The mean reduction in dyspnea score was 4.2 ± 1.8, which was statistically significant ($p < 0.001$).

**Table 3: Secondary Outcome Measures**

| Parameter | Value |
|---|---|
| Time to Chest Tube Removal (days) | |
| Mean ± SD | 4.5 ± 1.8 |
| Median (IQR) | 4.0 (3.0 - 6.0) |
| Duration of Hospital Stay (days) | |
| Mean ± SD | 6.5 ± 2.0 |
| Median (IQR) | 6.0 (5.0 - 8.0) |
| Post-pleurodesis Dyspnea Score (VAS) at 1 Month | |
| Mean ± SD | 3.0 ±1.2 |
| Change in Dyspnea Score (Pre vs. Post at 1 Month) | |
| Mean ± SD | 4.2 ± 1.8 |
| p-value* | <0.001 |
| *Using paired t-test. | |

Procedure-related Complications in this study are presented in [Table 4]. Analysis of the table shows that povidone-iodine pleurodesis was generally well tolerated. Chest pain was the most frequently observed complication, occurring in 30.0% of patients. Among these, 20.0% experienced mild pain that responded to oral analgesics, while 10.0% required parenteral opioid analgesia. Transient fever developed in 20.0% of patients, and hypotension was observed in 5.0% of patients. One patient 2.5% experienced transient respiratory distress that resolved with conservative management. No allergic reactions, empyema, or thyroid-related adverse effects were reported during the study period.

**Table 4: Procedure-related Complications and Adverse Events**

| Complication / Adverse Event | Number of Patients (n=40) | Percentage (%) |
|---|---|---|
| Chest Pain | 8 | 20.00% |
| Mild (requiring oral analgesics) | 4 | 10.00% |
| Severe (requiring parenteral opioids) | 4 | 10.00% |
| Fever (Temperature > 38°C, transient) | 8 | 20.00% |
| Hypotension (Systolic BP < 90 mmHg) | 2 | 5.00% |
| Respiratory Distress (transient, self-limiting) | | 2.50% |
| Allergic Reactions | 0 | 0.00% |
| Infection Empyema | 0 | 0.00% |
| Thyroid-related Adverse Effects (clinical or biochemical) | 0 | 0.00% |

Pleurodesis outcome according to primary malignancy is given in Table 5. Subgroup analysis demonstrated successful pleurodesis in 70.0% of patients with lung cancer, 87.5% of patients with breast cancer, all 100.0% of patients with ovarian cancer, and 83.3% of patients with other malignancies at the three-month follow-up. Although the highest success rate was observed among patients with ovarian malignancy, the differences in pleurodesis success among the different malignancy groups were not statistically significant (Chi-square test, p = 0.38) [Table 5].

**Table 5: Subgroup Analysis Pleurodesis Outcome vs. Primary Malignancy (at 3 Months)**

| Primary Malignancy | Total (n) | Success (Complete/PartiaI) | Failure | p-value* |
|---|---|---|---|---|
| Lung Cancer | 20 | 14 (70.0%) | 6 (30.0%) | |
| Breast Cancer | 8 | 7 (87.5%) | 1 (12.5%) | |
| Ovarian Cancer | 4 | 4 (100.0%) | 0 (0.0%) | |
| Lymphoma | 2 | 1(50.00%) | 1(50.00%) | |
| Other Malignancies | 6 | 5 (83.3%) | 1 (16.7%) | |
| Total | 40 | 31 (77.5%) | 9 (22.5%) | 0.38 |
| *Using the Fischer's Exact test (no statistically significant difference between groups). | | | | |

**Table 6: Comparison of Pleural Fluid and Radiological Parameters**

| Parameter | Before Pleurodesis (n=40) | After Pleurodesis (n=40) | p-value* |
|---|---|---|---|
| Pleural Fluid Protein (g/dL) Mean ± SD | 4.6 ± 0.9 | N/A | |
| Pleural Fluid LDH (U/L) Mean ± SD | 540 ± 160 | N/A | |
| Daily Drainage Volume at Removal (mL/24hrs) Mean ± SD | N/A | 80 ± 25 | |
| Chest Radiograph Expansion Score (0-10) scale, O=complete collapse, 10=full expansion) Mean ± SD | 2.8 ± 0.9 | 8.5 ± 1.3 | <0.001 |
| *Using paired t-test. | | | |

Pleural Fluid and Radiological Parameters of the cases are given in Table 6. The mean pleural fluid protein concentration before pleurodesis was 4.6 ± 0.9 g/dL, while the mean pleural fluid lactate dehydrogenase (LDH) level was 540 ± 160 U/L. The mean daily drainage volume at the time of chest tube removal was 80 ± 25 mL per 24 hours. Radiological assessment demonstrated significant improvement in lung expansion following pleurodesis. The mean chest radiograph expansion score increased from 2.8 ± 0.9 before pleurodesis to 8.5 ± 1.3 after the procedure, and this improvement

was statistically significant ($p < 0.001$) [Table 6].

## Discussion

Malignant pleural effusion (MPE) remains a common presentation of advanced malignancy. It is linked to a high symptom burden, especially worsening dyspnea, decreased functional capacity, and loss of quality of life. The main goal of pleurodesis is to prevent the accumulation of fluid in the space between the lung and the chest wall, and to avoid repeated thoracentesis and hospitalizations, which are common in this condition. In the present study, we tested the effectiveness and safety of povidone-iodine pleurodesis in 40 patients with recurrent MPE and found that povidone-iodine pleurodesis was effective and safe in the short term. The mean age of the study population was 58.4 ± 12.3 years, and there was a male preponderance with 60% of all cases being males. The malignancies associated showed 50% of cases were lung carcinoma, 20% were breast carcinoma, and 10% were ovarian carcinoma. This distribution is similar to the known epidemiology of malignant pleural effusion, which accounts for the majority of effusions due to the high incidence of lung and breast malignancies and the predilection for pleural metastasis.[2,3,10] In similar studies, Olivares-Torres et al,[8] and Agarwal et al,[7] reported that in their experience, the most frequently observed primary tumor in patients undergoing iodopovidone pleurodesis was lung cancer, in accordance with the results of this study. The overall pleurodesis success rate observed in the present study was 90% at one month, decreasing to 80% at three months. A few patients had a recurrence during their follow-up period, but in most patients, the success rate at three months was satisfactory with respect to pleural symphysis. The results of these studies favorably compare with earlier studies showing povidone-iodine as a useful sclerosant. Iodopovidone has been reported to be effective in approximately 89% of patients,[7] treated with pleurodesis, and generally causes a favorable response.

Olivares-Torres et al,[8] reported high rates of success (85%). Walker-Renard et al,[10] performed a systematic review that found iodopovidone achieves efficacy comparable to other commonly used sclerosants in appropriately selected patients. The difference in success rate over time in the current study is within range, although it occurs due to the progression of the disease in advanced malignancy despite initial pleural adhesion. One of the major findings of this study was that dyspnea was greatly improved after pleurodesis. VAS scores were significantly reduced at 1 month following the procedure (7.2 ± 1.5 preoperatively vs 3.0 ± 1.2 at 1 month; $p < 0.001$). Symptom control was an important therapeutic goal in MPE, especially in patients with a short life expectancy. The same results and reduction in dyspnea after successful pleurodesis with either talc or povidone-iodine pleurodesis have been reported in previous pleurodesis trials. [5,7,11] The significant decrease in the patient's respiratory symptoms in the present study may be due to improvement in lung expansion after drainage and to successful adhesion of the pleura. The average time until the chest tube was removed was 4.5 ± 1.8 days, and the average hospital length of stay was 6.5 ± 2.0 days. These findings are similar to those from previous studies, and chest drains are normally removed after pleurodesis is successful within 4-6 days.[7,12] This is because reducing the drainage time will lead to less patient discomfort, lower risk of complications associated with the drainage, and potentially lower hospitalisation costs, which makes povidone-iodine a viable choice in resource-challenged healthcare environments. The adverse events in this study were mostly procedure-related and mild and limited. The most common complications were chest pain in 30% of patients and transient fever in 20%. Hypotension developed in only 5% of patients and was transient in one case, which responded to conservative treatment. Importantly, there were no cases of empyema, allergic reaction, or thyroid dysfunction noted. These complication rates are similar to those reported in previous clinical trials, in which fever and transient chest pain were reported as the most frequent adverse effects of iodopovidone pleurodesis. [7,8] Povidone-iodine has been used in standard doses without significant problems.

No statistically significant difference in success rates was found between cancers of the breast, ovary, and lung ($p = 0.38$) when analysed by the type of primary malignancy. This discovery indicates that the primary tumour type also does not significantly affect the effectiveness of pleurodesis using povidone-iodine. These findings are in keeping with earlier reports, which found that sufficient lung expansion and the general condition of the patient seemed to be more likely predictors of the success of pleurodesis than the location of the primary malignancy.[8,11,13] There was an excellent improvement in lung expansion after pleurodesis, with the mean expansion score rising from 2.8 ± 0.9 to 8.5 ± 1.3 ($p < 0.001$). Before instilling sclerosant into the pleural space, it is recognized that adequate lung re-expansion is one of the best predictors of pleurodesis success since the visceral and parietal pleura should be in contact for the process and should be in symphysis.[2,5] Patients' radiological outcomes are favourable in the present study, which is consistent with the high success rate of pleurodesis overall. There are some limitations in the present study. It was performed at one center, and the sample size was limited, and there was no control group treated with a different sclerosant (talc or bleomycin). Moreover, the follow-up period was only three months, and long-term recurrence was not assessed due to study constraints.

## Conclusion

In conclusion, the results of the present study suggest povidone-iodine pleurodesis is effective in controlling a recurrent MPE and offers substantial symptomatic benefit while having a low risk of serious adverse events. Given its affordability, accessibility, and adequate effectiveness, povidone-iodine could be an effective and viable alternative to talc, especially in low-resource health care environments.

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### Conflicts of interest

There are no conflicts of interest.

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