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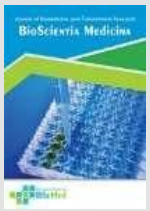

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Comparison of Outcomes in Patients with Malignant Pleural Efusion et Causa Breast Cancer Metastase Thought of Pleurodesis with Talc Poudrage and Talc Slurry at Dr. M. Djamil General Hospital, Padang, Indonesia

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A B S T R A C T

Background: Breast cancer accounts for about 50-65% of malignant pleural effusions. Talc pleurodesis is one of the definitive procedures for pleural effusions in which the route of administration is divided into poudrage and slurry. This study aimed to compare the differences of outcomes in malignant pleural effusion patients et causa breast cancer metastase who receive pleurodesis therapy with talc poudrage and talc slurry. **Methods:** This study has a cross-sectional design, which was conducted at Dr. M. Djamil General Hospital in May – July 2023. This study used medical records of patients diagnosed with malignant pleural effusion due to metastases of breast cancer at Dr. M. Djamil General Hospital Padang from January 2019 – July 2023. The outcomes assessed included drain production in 24 hours, drain release time, and in-hospital mortality. **Results:** In this study, 12 respondents who have talc poudrage and talc slurry pleurodesis were included. In the talc poudrage group, the mean of 24-hour drain production was 259.17 ± 46.79 ml, the mean of drain release time was 4.08 ± 0.66 days, and there was one respondent who died during hospitality. In the talc slurry group, the mean of 24-hour drain production was found to be more (420.83 ± 78.21 ml), drain release time was found to be much longer (5.67 ± 0.98 days), and 3 respondents died in hospital. The bivariate analysis found a significant difference between the 24-hour drain production and drain release time of patients who underwent talc slurry and talc poudrage meanwhile there was no difference in hospital mortality. **Conclusion:** Talc poudrage has a better outcome than talc slurry regarding drain production and drain release time in patients with malignant pleural effusion due to metastases of breast cancer.

1. Introduction

Pleural effusion is an accumulation of fluid between the parietal and visceral pleura, the pleural cavity. This could occur by itself or as the result of surrounding parenchymal diseases such as infection, malignancy, or inflammatory conditions. Pleural effusion is one of the main causes of mortality and pulmonary morbidity.[1]

Malignant pleural effusion is a condition in which cancer causes an abnormal amount of fluid to collect between the thin layer of tissue (pleura) that covers the outside of the lungs and the walls of the chest cavity. Lung cancer and breast cancer account for approximately 50-65% of malignant pleural effusions. Other common causes include pleural mesothelioma and lymphoma.[2]

The target management of MPE is to eliminate symptoms quickly and effectively with minimal discomfort, does not interfere with daily activities, and is cost-effective. Treatment options consist of routine thoracocentesis, chest tube, or catheter drainage with pleurodesis, as well as pleurectomy.[3] In the majority of patients with MPE who are managed with thoracocentesis, recurrent pleural effusions occur during disease progression. Therefore, in patients with a poor prognosis, complete pleural intervention may be indicated. This ensures the long-term elimination of symptoms of pleural effusion. These include chemical pleurodesis (tetracycline, doxycycline, and bleomycin), talc pleurodesis via thoracoscopy (talc poudrage) or chest tube (talc slurry), mechanical pleurodesis in surgery, pleurectomy and installation of an indwelling pleural catheter (IPC). Pleurodesis is a method for combining the parietal and visceral pleura, which aims at attaching the two pleural layers (parietal and visceral), thereby preventing the accumulation of pleural effusion and preventing the accumulation of air or fluid in the pleural space.[4,5]

Pleurodesis Video-assisted thoracoscopy surgery (VATS) is talc poudrage pleurodesis performed with video thoracoscopy under general anesthesia and selective one-lung ventilation. Any remaining fluid is aspirated, loculations are divided, a pleural biopsy is performed if necessary, and lung reexpansion is confirmed.[2]

In patients with poor general conditions and who cannot tolerate the risks of general anesthesia, it is preferred to undergo bedside talc slurry procedures where this procedure does not require general anesthesia. However, this action still had weakness because of the blind action that cannot ensure the correct blockage of fluid leaking. A study by Beltsios et al. that included 130 patients with talc pleurodesis revealed that there was a statistically significant difference in the success rate of pleurodesis in patients in the talc slurry group compared to the control group. The analysis showed a statistically significant superiority of talc pleurodesis.[8] In a study by Xia H et al., in a trial involving 1,525 patients with malignant pleural effusion, the success rate of talc pleurodesis was significantly higher than the control group with similar side effects. However, it is stated that thoracoscopic talc powder is more effective than talc slurry because it can block the right leakage through pleurodesis, whereas in talc slurry, the procedure is carried out blindly, even though the risk of general anesthesia is not present in this group, other morbidities such as pleural empyema due to pleurodesis fluid are still present.[9]

Pleurodesis is important in the management of malignant pleural effusion, and the results of previous studies regarding the method of applying pleurodesis still vary. Besides that, the study of pleurodesis on malignant pleural effusion due to metastases of carcinoma mammae has never been carried out at Dr. M. Djamil General Hospital. This study aimed to determine the differences in outcomes of patients with malignant pleural effusion due to carcinoma mammae metastasis who underwent pleurodesis with talc poudrage and talc slurry at Dr. M. Djamil General Hospital Padang.

2. Methods

This is an analytical study using a cross-sectional design. The study was conducted at Dr. M. Djamil General Hospital Padang in May – July 2023, which included all patients diagnosed with malignant pleural effusion due to metastases of carcinoma mammae at Dr. M. Djamil General Hospital Padang in January 2019 – July 2023. Inclusion criteria were age > 18 years, diagnosed with malignant pleural effusion due to metastases of carcinoma mammae, which was confirmed by cytology examination, and the patient had undergone pleurodesis. Patients with unclear or incomplete medical records were excluded from the study. The primary results were drain production, duration for drain removal, and hospital mortality. The independent T-test was used to assess the comparison of drain production and duration for drain removal, while the Chi-Square test was used to assess the comparison of hospital mortality between the two groups. A normality test for numerical data was

carried out with Shapiro-Wilk. If it is not normally distributed, then the T-test cannot be used, and an alternative test (the Mann-Whitney test) is carried out.

3. Results

In Table 1, the clinical characteristics of the patients are shown. The mean age of respondents in the talc slurry group was higher than in the talc poudrage group (51.83 ± 9.16 years vs. 46.33 ± 13.00 years). Most respondents in both groups have moderate education levels. The majority of respondents in both groups were normoweight. All respondents in both groups had a pleural fluid cytology examination and were diagnosed with malignant pleural effusion due to metastases of carcinoma mammae.

Table 2 shows a comparison of drain production in patients who underwent talc poudrage and talc slurry pleurodesis. In the talc poudrage group, the mean of drain production was 259.17 ± 46.79 ml, while in the talc slurry group, the mean of drain production was 420.83 ± 78.21 ml. Mann-Whitney test was used because the data was not normally distributed. The p-value was 0.000 ($p<0.05$), so it was concluded that there was a significant difference between the drain production of both groups.

Table 3 shows a comparison of drain removal time between the two groups. In respondents who underwent pleurodesis with talc poudrage, the drain removal time was shorter (4.08 ± 0.66 days), while in respondents who underwent pleurodesis using talc slurry, the drain removal time was longer (5.67 ± 0.98 days). Mann-Whitney test was used because the data was also not normally distributed. The results of the Mann-Whitney test obtained a p-value of 0.001 ($p<0.05$), so it was concluded that there was a significant difference in drain removal duration between the two groups.

In Table 4, it was found that in the talc powder group, eleven respondents lived, and one respondent died during hospitalization. Of the respondents who underwent pleurodesis using talc slurry, 9 people lived, and 3 people died during hospitalization. The analysis was carried out using Fisher Exact because there were cells with <5 samples and the test results obtained a p value of 0.59 so it was concluded that there was no significant difference between hospital mortality in both groups.

Table 1. Clinical characteristics.

Characteristics	Talc poudrage			Talc slurry		
	Mean±SD	f	%	Mean ± SD	f	%
Age (years)	46.33 ± 13.00			51.83 ± 9.16		
Education						
Primary school		1	8.3		1	8.3
Secondary school		1	8.3		1	8.3
High School		8	66.7		9	75.0
Bachelor		2	16.7		1	8.3
BMI						
Underweight		-	-		2	16.7
Normoweight		8	66.7		10	83.3
Overweight		4	33.3		-	-
Obese		-	-		-	-
Pleural cytology						
Metastases of Ca Mammae		12	100		12	100
Other malignancies		0	0		0	0

Table 2. Comparison of drain production in patients with malignant pleural effusion due to metastases of carcinoma mammae who underwent pleurodesis with talc poudrage and talc slurry at Dr. M. Djamil General Hospital.

Group	Drain production (ml) Mean±SD	*P-value
Talc poudrage	259,17 ± 46,79	0,000
Talc slurry	420,83 ± 78,21	

*Mann Whitney test.

Table 3. Comparison of the length of drain removal time in patients with malignant pleural effusion due to metastases of carcinoma mammae who underwent pleurodesis with talc poudrage and talc slurry at Dr. M. Djamil General Hospital.

Group	Length of drain removal time (days) Mean±SD	*P-value
Talc poudrage	4,08 ± 0,66	0,001
Talc slurry	5,67 ± 0,98	

*Mann Whitney test.

Table 4. Comparison of hospital mortality in patients with malignant pleural effusion due to metastases of carcinoma mammae who underwent pleurodesis with talc poudrage and talc slurry at Dr. M. Djamil General Hospital.

Group	Hospital death		*P-value
	Alive	Death	
Talc poudrage	11 (91,7%)	1(8,3%)	0,59
Talc slurry	9 (75%)	3 (25%)	

*Fisher exact test.

4. Discussion

In the talc slurry group, the mean age of respondents was higher than in the Talc powder group, namely 51.83 ± 9.16 years vs. 46.33 ± 13.00 years. The different ages between the two groups may also be a factor in selecting the pleurodesis procedure, where older patients tend to undergo talc slurry because there is no risk of general anesthesia in this procedure. Most of the respondents in both groups have moderate education levels, so it can be concluded that both groups could understand the disease, which leads to choosing the right decision for treatment, including the pleurodesis method. The majority of respondents in both groups were normoweight. Because these variables are similar, it did not affect the study results.

All subjects with pleural effusion, whether pleurodesis with talc powder or talc slurry, had a pleural fluid cytology examination and were diagnosed with malignant pleural effusion due to metastases of carcinoma mamae. Malignant pleural effusion in carcinoma mamae is the result of impaired lymphatic flow by pleural metastasis and increased permeability of the pleural vessels and tumor. Tumor cells metastasize to the pleura mainly through the bloodstream and invade the visceral pleura. After that, they spread to the parietal pleura.[5,10] Malignant pleural effusions caused by breast cancer metastases had significantly worse survival.[11]

This study assessed three outcomes: drain production, length of drain removal, and hospital mortality. In the talc poudrage group, the mean of drain production was 259.17 ± 46.79 ml, while in the talc slurry group, the mean of drain production was 420.83 ± 78.21 ml. The less productive drains in 24 hours indicate that less fluid remained, indicating a higher rate of successfullness in the talc poudrage group. Moreover, in the talc poudrage group, the drain

removal time was found to be shorter than the talc slurry group (4.08 ± 0.66 days vs 5.67 ± 0.98 days). A previous study by Stefani et al. also found shorter drainage duration in the talc poudrage group (9 days vs 6 days) with longer effusion-free survival.[12] D'ambrosio et al., in 2022, also conducted a study on 86% of patients with malignant pleural effusion who underwent talc slurry pleurodesis. They found that the median drainage time was quite long (9 days), with 23.3% of respondents having empyema following the procedure.[13]

In the talc poudrage group, 11 people lived, and 1 respondent died during hospitalization. Of the respondents who underwent pleurodesis using talc slurry, 9 people lived, and 3 people died during hospitalization. These results are similar to the study by Bhatnagar et al. in 2019 on 330 patients who underwent pleurodesis with talc poudrage and talc slurry. They found a higher mortality rate in the talc slurry group (34 patients, 21%) than the talc poudrage group (27 patients, 17%). Similar to this study, although there was a difference in mortality, this difference was not statistically significant.[14] This may be affected by a similar risk of death where in talc poudrage there is anesthesia risk and complications from the talc itself, whereas, in the talc slurry group, the chemical substances are more massive with uncertain occlusion of the leakage.[15]

Watanabe et al. 2019 conducted a study on elderly patients who experienced pneumothorax and found that 1 patient died after pleurodesis with talc slurry due to complications of acute exacerbation of interstitial pneumonia and stated that talc poudrage was quite safe and effective for patients who could tolerate the risks of general anesthesia.[16]

Pleurodesis with talc poudrage was found to be more effective than other contemporary treatments for malignant pleural effusion. However, it is important to know that pneumothorax, pneumonia, emphysema, prolonged air leak, pulmonary embolism, arrhythmia, re-expansion pulmonary edema, and empyema are complications that need to be considered when administering talc poudrage.[17] Cardillo et al. conducted a study on 611 patients who underwent VATS procedure and found that 0.81% (5 cases) of patients who underwent pleurodesis with talc poudrage died during surgery due to pulmonary embolism, pulmonary edema, myocardial infarction, and acute renal failure.[18]

Chemical pleurodesis causes an inflammatory response that results in fibrin adhesion and fibrosis, thereby obliterating the pleural space. Bedside pleurodesis (talc slurry) is easier to perform and cheaper than operative pleurodesis (talc poudrage). However, there are several disadvantages of talc slurry pleurodesis, such as the complication of permanent small loculations due to uneven distribution of talc and a higher risk of empyema. A study of Champion et al in 2021 on animal models and cadavers regarding the administration of talc slurry stated that the distribution of talc slurry in the pleural cavity was found to be poor with the single tube method. This is likely to cause loculation after administration of talc slurry.[15] Studies by Bellini et al. in 2020 on 52 patients stated that improvement after talc slurry pleurodesis was not optimal. Patients often experience residual loculated effusion that could become permanent if not drained aggressively, and sometimes, this incomplete pleurodesis requires repeated pleurodesis.[19] A study by Bhatnagar et al. in 2018 on 154 patients found that only 43% of patients who received talc slurry experienced successful pleurodesis on the 35th day of follow-up, although in this study, this success was higher compared to the control group who did not undergo pleurodesis with talc (only with an indwelling catheter).[20] This study has limitations because it only assessed patient outcomes in a short time, so the long-term recurrence rate or survival cannot be determined.

5. Conclusion

There was a significant difference in the drain production and the length of drain removal time between the talc slurry group and the talc poudrage group, where the drain production was less and the drain removal time was shorter in the talc poudrage

group. However, regarding hospital mortality, this study did not find any significant differences between the two groups. Longer term studies are needed to assess the survival, success, and recurrence rate of patients with malignant pleural effusion due to metastases of carcinoma mammae who underwent pleurodesis with talc slurry and talc poudrage.

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