



Original Article

Rapid Pleurodesis: Single Agent Single Session Vs. Multiple Sessions Using Multiple Agents in the Treatment of Recurrent Malignant Pleural Effusion

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Abstract

Background: One prevalent, upsetting side effect of several oncological conditions is malignant pleural effusion. Pleurodesis is one of the most effective ways to reduce symptoms, stop recurrence, and enhance quality of life. This prospective study aimed at evaluating the performance of three rapid pleurodesis procedures and determine which modality achieved the most positive results, the fewest problems, and the most cost-efficiency.

Methods: This study included 91 patients with recurrent and rapidly collecting malignant pleural effusion. They were distributed into three groups: Group A (single session, single agent), Group B (single session, combined agents), and Group C (multiple sessions, multiple agents) pleurodesis through a catheter which was closed for 2 hours and then opened to drain. The catheter was then removed, and the patient was discharged to continue outpatient follow-up.

Results: Group A included 28 patients, Group B included 29 patients, and Group C included 34 patients. The most common primary malignancy was breast cancer in Group A (46.4 %), and lung cancer in Group B (48.3%) and Group C (47.1 %). Frequently encountered complications following pleurodesis were fever (7.1%, 10.3% and 11.8 % for group A, B and C respectively); and dyspnea (7.1 % in Group A), (13.8% in Group B), and (8.8% in Group C). Hospital stay was longer in the third group with ($p < 0.001$) without significant difference in the outpatient follow-up for lung inflation and recurrence as in one week was (3.6 % in Group A), (0 % in Group B and Group C), in one month was (10.7 % in Group A), (6.9 % in Group B), and (2.9 % in Group C), in 3 months was (14.3 % in Group A), (17.2 in Group B), and (11.8% in Group C).

Conclusion: Rapid pleurodesis – either with a single agent in a single session, a combined agent in a single session, or multiple sessions using multiple agents – is an effective treatment to avoid the recurrence of malignant pleural effusion with minimal side effects. Since the first protocol is equally successful and requires only a short hospital stay at a moderate cost, we recommend it.

KEYWORDS

Rapid pleurodesis;
Malignant Pleural Effusion; Talc Powder; Doxycycline

Article History

Submitted: 14 Apr 2024
Revised 1: 25 Apr 2024
Revised 2: 16 June 2024
Accepted: 22 June 2024
Published: 1 Nov 2024



Introduction

One of the most frequent complications for cancer patients is malignant pleural effusion. The patient's quality of life is negatively impacted by the severe symptoms it creates [1]. Different approaches to supportive care in these instances include chemical or biological pleurodesis, pleurectomy, pleuro-peritoneal shunt, and repeated needle thoracocentesis. The procedure known as pleurodesis involves sealing the pleural cavity and creating adhesions between the two pleural layers to stop recurrence [2].

Rapid pleurodesis is a variant of pleurodesis that helps improve the quality of life for malignant patients by decreasing hospital stays and clinic visits [3,4]. Most patients can heal quickly after rapid pleurodesis without hospital admission. The goal of the procedure is complete radiographic lung inflate and pleural fluid evacuation; after this, pleurodesis is performed [1]. Additionally, quick pleurodesis reduces the risk of needless thoracocentesis procedures, puncture site infections, and infections acquired during hospital stays [5].

This study aims to compare the effectiveness of three rapid pleurodesis protocols: single session single-agent protocol, multiple sessions using multiple agents, and single session using combined agents. The goal is to determine which modality produces the best results, causes the fewest complications, and is most cost-effective.

Patients and Methods

This two-year prospective research was carried out at the Department of Cardiothoracic Surgery at Menoufia University hospital. After obtaining the required permission from the local ethics committee of the Faculty of Medicine, Menoufia University, the study was conducted on ninety-one patients who had recurring and rapidly developing malignant pleural effusion.

Patients included in the study had recurrent malignant pleural effusion with metastatic oncological diseases. Both sexes over 16 years old were included after confirming lung inflation following evacuation of pleural effusion.

We excluded critically ill unstable patients with recent fever within the last 24 hours, empyema, entrapped lung, and respiratory distress despite successful drainage.

After giving their informed permission, patients who met the requirements had a thorough examination and history collection. Prior to drainage, radiology was completed using an X-ray scan or a CT if needed.

Complications following pleurodesis, including fever, allergies, dyspnea, and ICU stay, were evaluated in every group. Additionally, a three-month outpatient follow-up was used to evaluate the recurrence of pleural effusion. One week, one month, and three months later.

Procedure Details

Pleural effusion drainage by insertion of 12-14 Fr dialysis Catheter under local anesthetics. Gradual evacuation over 4-8 Hours of injected substance with monitoring of vital signs. Post evacuation, a Chest X-ray scan was done to confirm lung inflation. We wait until the evacuation is complete, and the radiology is inflated, and then we start pleurodesis. Initiation of Pleurodesis according to assigned protocol. Patients were randomly divided into three groups:

1. Group A: Single Injection of 5 gm. of Talc Powder mixed with 20 cc of local anesthetic and 30 cc of Normal Saline.
2. Group B: Single Injection of 5 gm. of Talc Powder Mixed with 0.5gm of Doxycycline 20 cc of local anesthetic, and thirty cc of Normal Saline.
3. Group C: First Session: Injection of 5 gm. of Talc Powder Mixed with 20 cc of local anesthetic and 30 cc of Normal Saline. Second Session: Injection of 1 gm. of Doxycycline mixed with 20 cc of local anesthetic and 30 cc of Normal Saline.

After each session, the catheter was closed for two hours, and every 15 minutes, the patient was taught to alter their position. Then the catheter was opened, and fluid was allowed to be drained. The catheter was then removed, and the patient

Table 1: Comparing the Three Studied Groups According to Different Parameters

	Group 1 (n = 28)	Group 2 (n = 29)	Group 3 (n = 34)	p
Sex				
Male	20 (71.4%)	17 (58.6%)	17 (50.0%)	0.231
Female	8 (28.6%)	12 (41.4%)	17 (50.0%)	
Age				
Mean ± SD.	53.3 ± 13.0	51.5 ± 10.5	55.5 ± 12.6	0.427
Median (Min. – Max.)	55.0 (4.0 – 70.0)	50.0 (35.0 – 76.0)	56.5 (30.0 – 78.0)	
Malignancy primary				
Unknown	3 (10.7%)	2 (6.9%)	3(8.8%)	MCp= 0.944
Lung	9 (32.1%)	14 (48.3%)	16(47.1%)	
Breast	13 (46.4%)	9 (31.0%)	12(35.3%)	
Ovary	1 (3.6%)	1 (3.4%)	1(2.9%)	
Uterus	2 (7.1%)	3 (10.3%)	2(5.9%)	
Pre maneuver chemotherapy				
Done	28 (100.0%)	29 (100.0%)	34 (100.0%)	–
Dyspnea	28 (100.0%)	29 (100.0%)	34 (100.0%)	–
Cough	16 (57.1%)	13 (44.8%)	21 (61.8%)	0.388
Chest pain	15 (53.6%)	15 (51.7%)	18 (52.9%)	0.990
Pre-maneuver thoracocentesis				
Mean ± SD.	4.3 ± 1.6	4.4 ± 1.8	4.1 ± 2.0	0.819
Median (Min. – Max.)	4.0 (2.0 – 7.0)	4.0 (1.0 – 8.0)	4.0 (1.0 – 8.0)	
Recollection				
Mean ± SD.	5.5 ± 2.3	7.3 ± 7.3	6.3 + 3.1	0.066
Median (Min. – Max.)	5.5 (2.0 – 10.0)	7.0 (2.0 – 14.0)	5.5 (2.0 – 15.0)	
Cytology +ve	15 (53.6%)	16 (55.2%)	17 (50.0%)	0.914
Preoperative chest radiography				
Moderate effusion	13 (46.4%)	16 (55.2%)	19 (55.9%)	0.722
Massive effusion	15 (53.6%)	13 (44.8%)	15 (44.1%)	
Post pleurodesis complications				
Fever	3(10.3%)	2(6.9%)	4(11.8%)	MCp=0.828
Pain	2(7.1%)	3(10.3%)	4(11.8%)	MCp=0.910
Dyspnea	2(7.1%)	4(13.8%)	3(8.8%)	MCp=0.748
Allergy to agent	0(0.0%)	1(3.4%)	2(5.9%)	MCp=0.772
ICU stay	2(7.1%)	3(10.3%)	2(5.9%)	MCp=0.887
Total hospital stay				
Mean ± SD.	2.1 ± 0.8	2.2 ± 0.9	3.0 ± 0.7	<0.001*
Median (Min. – Max.)	2.0 (1.0 – 4.0)	2.0 (1.0 – 4.0)	3.0 (2.0 – 4.0)	
Sig. bet. groups.	p ₁ =0.640, p ₂ <0.001*, p ₃ <0.001*			

was informed to avoid NSAIDs or other anti-inflammatory drugs for one week.

An outpatient follow-up for three months was scheduled; x-ray scans of the chest – and CT scans as well, if necessary – were done after one week, one month, and three months.

Statistical analysis

Data were analyzed using IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp). Categorical data were represented as numbers and percentages. The chi-square test was applied to compare between two groups. Alternatively, the Monte Carlo correction test was applied when more than 20% of the cells had an expected count of less than 5. For continuous data, they were assessed for normality by the Shapiro-Wilk test.

Quantitative data were expressed as range (minimum and maximum), mean, standard deviation, and median normally distributed quantitative variables, while the ANOVA test was used to compare the three studied groups and followed by the Post Hoc test (Tukey) for pairwise comparison. However, for non-normally distributed quantitative variables, the Post Hoc test (also known as Dunn's multiple comparisons test) was employed for pairwise comparisons after the Kruskal-Wallis test was used to compare different groups. The results' significance was assessed at the 5% level.

Results

We started this study with three groups, each with 35 patients. However, 14 patients were missed during follow-up: 7 in Group A, 6 in Group B, and 1 in Group C.

Table 1 displays specific demographic information as well as symptoms that are currently present. The research population comprised 91 patients who were separated into three groups. In Group A, the most frequent primary malignancy was breast (46.4%), followed by lung (32.1%), however in Groups B and C, the most common primary malignancy was lung (48.3%) and followed by breast (31.0%) and (35.3%). The main complaint in all groups with 100% was dyspnea. There was no significant variance between groups in post-procedure complications as the most common complaint was

fever in Group A (10.3%), followed by dyspnea, chest pain, and ICU stay; and in Group B it was dyspnea (13.8%) followed by chest pain, ICU stay, fever, and allergy to the agent; but in Group C, fever (11.8%) and pain (11.8%) were the most common complaint, followed by dyspnea then allergy to agent, and then ICU stay.

Table 2 indicates that there was no statistically significant variation in the recurrence of the patients' follow-ups after one week, one month, and three months. Within one week, recurrence occurred in 3.6 % of Group A with no recurrence in Group B and Group C. Within one month, recurrence occurred in 10.7 % of Group A, 6.9 % of Group B, and 2.9% of Group C. Within three months, recurrence occurred in 14.3 % of Group A, 17.2 % of Group B, and 11.8 % of Group C.

Discussion

Whether using a single agent in a single session, a combination of agents in a single session, or multiple sessions and agents, the rapid pleurodesis approach effectively avoids the recurrence of malignant pleural effusion with few problems.

Malignant and/or recurrent pleural effusions are associated with significant morbidity [1]. The key point to accomplishing effective pleurodesis is draining the pleural space fully and re-expanding the lung. Treatment response for MPE is extremely variable [6].

Table 2: Comparing the Three Studied Groups According to Recurrence with Follow-up

Recurrence with follow-up	Group 1 (n = 28)	Group 2 (n = 29)	Group 3 (n = 34)	^{MC} p
One week				
No	27 (96.4%)	28 (96.6%)	33 (97.1%)	0.826
Yes	1 (3.6%)	0 (0.0%)	0 (0.0%)	
Died	0 (0.0%)	1 (3.4%)	1 (2.9%)	
One month				
No	24 (85.7%)	26 (89.7%)	31 (91.2%)	0.794
Yes	3 (10.7%)	2 (6.9%)	1 (2.9%)	
Died	1 (3.6%)	1 (3.4%)	2 (5.9%)	
3 months				
No	21 (75.0%)	22 (75.9%)	26 (76.5%)	0.958
Yes	4 (14.3%)	5 (17.2%)	4 (11.8%)	
Died	3 (10.7%)	2 (6.9%)	4 (11.8%)	

There is a wide variation of sclerosing agents existing, which include talc, antibiotics (Tetracycline), Cytotoxics, antimalarials (Quinacrine and Mepacrine), 50% glucose in water, immunomodulators, caustic substances, nitrates, and even biological agents. However, talc is the most widely used agent [7].

Ninety-one patients were included in our study, who were divided into three groups in which breast cancer was the most common primary malignancy in Group A (46.4%) then lung (32.1%), but in Group B and Group C, it was lung (48.3%) and (47.1%) then breast (31.0%) and (35.3%). Likewise, Figueiredo I. et al. reached similar results as they stated that breast cancer was the most common malignancy, present in (34%) of patients, and primary lung cancer was the second most common malignancy, present in (24%) of patients [7].

Patients usually complained of one or more of the following symptoms (dyspnea, cough, and chest pain). The primary complaint across all patient groups in our study was dyspnea, which is a requirement for our included patients to be symptomatic, unlike many other studies that only include symptomatic patients, such as those conducted by Farghaly AE, Figueiredo et al., and Reddy C., et al. [1,7,8].

Regarding post pleurodesis complications, there was no significant variance between groups as the most common complaint was fever in Group A (10.3%) followed by dyspnea, chest pain, and ICU stay; and in Group B, it was dyspnea (13.8%) followed by chest pain, ICU stay, fever, and allergy to the agent; but in Group C fever (11.8%) and pain (11.8%) were the most followed by dyspnea then allergy to agent, and then ICU stay. This is like the results of Wu-Huei Hsu et al., in which fever was the most common complaint (77%), then vomiting (14%), and then hiccups (5%) [9].

Allergy to the drug and ICU stays were among the least common problems in our research. A mild reaction to the drug might cause serious symptoms, such as hypotension or severe

dyspnea, that necessitate ICU admission for close observation.

However, Reddy C. et al.'s study of thirty patients revealed fewer complications than our study, including fever (two patients) and empyema (one patient). This difference in study size between our study and theirs may be explained by the smaller study group in their study compared to the total number of patients in our study [8].

In our study, there was a significant difference between the three groups in the mean hospital study, which was 2.1 days in Group A, 2.2 days in Group B, and 3 days in Group C, with no significant difference between Group A and Group B, but with significant difference between Group A and Group C and also between Group B and Group C.

We can explain such elongated time in Group C in comparison to Group A and Group B as we did two sessions of pleurodesis in Group C but only one in Group A and Group B. In Özkul S et al. (Rapid Pleurodesis with talc), the mean length of hospital stay was 2.2, which was the same in Group A and Group B in our study [6]. In Farrag, MA et al., the mean hospital stay was 4 days in Group B (Rapid Pleurodesis with Vibramycin), which is higher than our mean hospital stay even in Group C, and this is due to the different technique as pleural fluid was withdrawn every 6 h till negative suction was reached [10].

There was no significant variance between our studied groups in the follow-up in one week, one month, and three months with the low rate of recurrence of the pleural effusion.

- Within one week, recurrence occurred in 3.6 % of Group A, with no recurrence in Group B and Group C.
- Within one month, recurrence occurred in 10.7 % of Group A, 6.9 % of Group B, and 2.9% of Group C.
- Within three months, recurrence occurred in 14.3 % of Group A, 17.2 % of Group B, and 11.8 % of Group C.

In Farrag et al., pleurodesis failure was 15 % in one month and 15 % in three-month follow-up,

which is similar to our study results, even when using Vibramycin only and in one session [10].

In Wu-Huei Hsu et al., failure occurred in 23 % of patients in one-month follow-up, which is higher than our failure rate in the three groups, and this may be due to using a different agent (Bleomycin) [9].

In Reddy C et al., the success rate at 6 months was 92% with a failure rate of 8 %, which is lower than our study recurrence rate as they used a thoracoscope with talc, and thoracoscope may improve the results of pleurodesis in their study [8].

Study Limitation:

The small number of patients limits the current study.

Conclusion

For malignant patients, rapid pleurodesis with single agent single session, multiple agent single session, and multiple agent multiple session is an effective treatment to improve respiratory complaint with a shorter hospital stay, better quality of life, and minimal problems.

Rather than using the conventional pleurodesis approach, we recommend performing rapid pleurodesis using any of our protocols. Since the first protocol is equally successful as the others and requires only a short stay in the hospital at an affordable cost, we highly recommend it.

Funding: Self-funded

Conflict of interest: Authors declare no conflict of interest.

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