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Short comparison of talc poudrage and tetracycline pleurodesis within patients suffering from malignant pleural effusion.

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ABSTRACT… Objective: To compare talc poudrage and tetracycline pleurodesis within patients suffering from malignant pleural effusion. **Study Design:** Controlled Clinical Trial. **Setting:** Department of Pulmonology, Jinnah Hospital Lahore. **Period:** September, 2022 up until May, 2023. **Material & Methods:** 100 individuals, both male and female, ranging in age from 20 to 80 years, diagnosed with malignant pleural effusion confirmed on biopsy were included by nonprobability consecutive sampling. Patients with active pleural infection, hemodynamic instability, systemic infection, serum hematocrit < 25%, hemothorax, chylothorax, multiple etiologies of pleural effusion, prior chemical pleurodesis, sensitivity to study drugs, life expectancy < 1 month, pregnancy and chest X-ray displaying trapped lung post chest tube drainage on the affected side were excluded. The patients were allocated into two groups at random using a lottery system. In group 1, patients received pleurodesis with talc poudrage and in group 2, patients received pleurodesis alongside tetracycline. Success was assessed after 4 weeks of pleurodesis. **Results:** In this study, mean age in talc group was 58.94±13.6 years and in tetracycline group it was 59.26±13.7 years.65% patients were male and 35% were females.Success was 94% in talc group and 76% in tetracycline group with p-value = 0.012. In terms of adverse effects, there is no statistically significant difference between the two groups. **Conclusion:** Talc pleurodesis has a higher success rate than the tetracycline pleurodesis. Talc pleurodesis also has less adverse effects than tetracycline pleurodesis.

Key words: Chemical Pleurodesis, Hemothorax, Malignant Pleural Effusion, Pregnancy, Tetracycline.

INTRODUCTION

The most prevalent reason for hospitalization in the pulmonology and medical departments for minor operations is pleural effusion. It is a buildup of free fluid in the pleural cavity. Its occurrence varies internationally and nationally, depending on the conditions that cause it. Clinical symptoms include fatigue, fever, chest discomfort, heaviness, and shortness of breath with exertion.[1]

Malignant pleural effusion (MPE) is a common cancer consequence. It shows the advanced stage of primary tumors. MPE can be characterized as an aberrant accumulation of pleural fluid containing neoplastic cells, which can be detected through cytological investigation or pleural biopsy.[2] This occurs as a result of normal fluid dynamics being disturbed caused by the infiltration of tumor into thoracic lymph nodes and pleura. MPEs develop commonly in cancer of the lung, cancer of the breast, and lymphomas.[3] It is related to a poorer life expectancy. According to recent literature, patients diagnosed with lung cancer and MPE had a 5.5-month survival, despite the fact that survival overall for all types of cancer ranges from 3 to 12 months, depending on the kind of tumor as well as the patient's coexisting conditions. MPE is found in 15% of cancer patients.[4]

The ultimate goal of treatment for individuals with malignant pleural effusion (MPE) is to improve their life's quality over time. These people have recurring respiratory issues.[5] Foremost principle of the treatment of MPE is timely reprieve of symptoms, minimum discomfort, trifling nosiness in everyday activity and cost effectiveness.[6] A

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widely used surgery eliminating the pleural space by injecting a sclerosant into the pleural cavity is known as chemical pleurodesis. It causes pleural inflammation and fibrosis, which leads to wide adhesion among the parietal and visceral pleura.[2]

Even though the most favorable agent for chemical pleurodesis has not been acknowledged till now; there are two ways talc can be infiltrated. The first is via the thoracoscope tube with an aerosol canister (talc poudrage) or as a suspension (talc slurry) through an intercostal tube. Antibiotics (tetracycline, doxycycline, and bleomycin) as well as bacterial agents (Corynebacterium parvum, OK432), silver nitrate, and iodopovidone have also been used.[4] Each agent has advantages and disadvantages, and the success rate of pleurodesis varies per agent.[7]

At present, the most extensively utilized agent is talc as slurry or poudrage since it is affordable, easily accessible, as well as reputedly efficient. There are many consequences like severe pain, fever, dyspnea, pneumonitis, and acute respiratory distress syndrome and consequently, it is not always favourable.[8] Usage of tetracycline in chemical pleurodesis shows average success rate bus it has exceptional safety profile, rational effectiveness, economical and ease of administration.[6]

This study's aim is to compare talc poudrage with tetracycline for chemical pleurodesis in patients with malignant pleural effusion. There are very few studies on the comparison of these two pleurodesis agents.

MATERIAL & METHODS

From September 2022 to May 2023, this randomized controlled study was undertaken in the Pulmonology department of Jinnah Hospital Lahore after approval from ethical Review Board (ERB 146/6/18-7-2023/S1 ERB). 100 patients diagnosed with malignant pleural effusion took part in this investigation by taking prevalence of success of talc poudrage 87%[9], prevalence of success of tetracycline 65.2%[9], level of significance 5% and power of study 80%.

Inclusion Criteria

Patients of both sexes with age ranges from 20 to 80 years having malignant pleural effusion confirmed on biopsy were enrolled in this study. Patients were enrolled through consecutive sampling. All patients gave their informed consent.

Exclusion Criteria

Patients with active pleural infection, hemodynamic instability, systemic infection, serum hematocrit <25%, hemothorax, chylothorax, multiple etiologies of pleural effusion, prior chemical pleurodesis, sensitivity to study drugs, life expectancy < 1 month, pregnancy and chest X-ray showing trapped lung post chest tube drainage on the affected side were excluded.

Chest intubation was used to drain the malignant effusion from the patients until the output was less than 50 ml in 24 hours. Then, using a lottery technique, patients were divided into two groups at random. Those in group 1 had pleurodesis with talc poudrage, while those in group 2 received pleurodesis with tetracycline. In group A, a 50ml syringe with a 16-gauge needle is used to inject 50ml of 0.9% sterile saline into the sterile talc powder bottle (4grams). The bottle is swirled continuously. The two 50ml syringes (25ml each) are then refilled with the slurry suspension, which has been further diluted with 25ml of sterile saline. The talc is continuously shaken out of the syringes carrying the talc slurry. The slurry is administered intrapleurally using an injection into the chest tube after the injection site has been sterilised. The chest tube was inserted, clamped for two hours, then left unclamped and allowed to freely drain for four hours. When the drain flow was less than 50 mL, extubation was performed. After extubation and one month following the treatment, a chest X-ray was taken.

In Group B, through the drain, 1.5 to 2 g of tetracycline combined with 3 mg/kg lidocaine, and 50 ml of normal saline were administered. Following administration, for two hours, the chest tube was clamped, and after that, it was left unclamped in addition to being on free drainage for 4 hours. Extubation was done when

drain output is less than 50mL. Chest X-ray was done after extubation and one month after the procedure. Complete absence of pleural fluid after 1 month of pleurodesis was taken as success. Adverse events in terms of fever, chest pain, prolong drainage, dyspnea and death were also observed.

SPSS V-20 was used to analyze the data. All quantitative data, such as age and duration of effusion, were given a mean and standard deviation. The frequency and percentage of qualitative variables such as gender, site involved, primary malignancy, success and adverse effects. To compare qualitative variables between two groups, the chi-square test was utilized. The independent sample t-test and ANOVA were utilized to compare qualitative factors. P-values of 0.05 were considered significant.

RESULTS

One hundred patients presenting with MPE were equally divided into two groups (n = 50). Mean age in talc group was 58.94±13.6years and in tetracycline group it was 59.26±13.7 (p-value = 0.907). 13% patients belong to age between 20 – 40 years, 41% belong to 41-60 years and 46% were between 61-80 years. Duration of effusion in talc group was 4.2±1.98 weeks and in tetracycline group 4.08±1.86 weeks. 57% patients had duration of effusion < 1 month and 43% had duration > 1 month. 35% patients were male and 65% were females. 38% patients had right sided pleural effusion, 44% left sided pleural effusion and 18% had bilateral pleural effusion. Most common malignancy was mesothelioma (40%), breast cancer (27%), lung cancer (16%) and 17% patients fall in other cancer category. (Table-I)

DISCUSSION

The second most frequent global cause of exudative effusions is malignancy. Malignant pleural effusions (MPEs) are regularly linked to hematologic malignancies such as lymphoma as well as solid organ cancers like breast or lung cancer.

Variables	Talc Group (n = 50)	Tetracycline Group (n = 50)	P-Value
Gender			
Male	16 (32%)	19 (38%)	0.529
Female	34 (68%)	31 (62%)	
Age			
20-40 years	6 (12%)	7 (14%)	0.91
41-60 years	20 (40%)	21 (42%)	
61-80 years	24 (48%)	22 (44%)	
Site Involved			
Right	21 (42%)	17 (34%)	0.693
Left	21 (42%)	23 (46%)	
Bilateral	8 (16%)	10 (20%)	
Duration of Effusion			
< 1 month	28 (56%)	29 (58%)	0.84
>1 month	22 (44%)	21 (42%)	
Primary Malignancy			
Breast	14 (28%)	13 (26%)	0.881
Lung	8 (16%)	8 (16%)	
Mesothelioma	21 (42%)	19 (38%)	
Other	7 (14%)	10 (20%)	

Table-I. Showing the various demographics of the patients in this study

Variable	Talc Group (n = 50)	Tetracycline Group (n = 50)	P-Value
Success			
Yes	47 (94%)	38 (76%)	0.012
No	3 (6%)	12 (24%)	

Table-II. Showing the success rate among the patients in two groups

Variable	Talc Group (n = 50)	Tetracycline Group (n = 50)	P-Value
Chest Pain			
Yes	8 (16%)	12 (12%)	0.317
No	42 (84%)	38 (76%)	
Fever			
Yes	9 (18%)	7 (14%)	0.585
No	41 (82%)	43 (86%)	
Prolong Drainage			
Yes	3 (6%)	6 (12%)	0.295
No	47 (94%)	44 (88%)	
Dyspnea			
Yes	3 (6%)	4 (8%)	0.695
No	47 (94%)	46 (92%)	
Death			
Yes	2 (4%)	3 (6%)	0.646
No	48 (96%)	47 (94%)	

Table-III. Showing the various adverse effects

In the case of lung cancer, approximately 50% of patients will experience having an MPE at some point during their treatment, with 15% developing an effusion at the time of diagnosis.[10] During MPE development, tumor cells reach the pleural space via hematogenous, direct, or lymphatic dissemination. Fluid accumulation in the pleural space can be caused by tumor development that obstructs lymphatic outflow. Only 55 to 60% of patients with pleural or lymphatic metastases develop MPE.[11]

Pleurodesis refers to a procedure used to create a symphysis between the parietal and visceral pleura in order to diminish the pleural space. The term is derived from the Greek terms pleurá (pleura) and desmos (bond). The operation is used to stop repeated spontaneous pneumothoraxes or pleural effusions from happening. A variety of techniques have been proposed and tested in the over-a-hundred-year history of pleurodesis to achieve effective pleural symphysis. Among these are mechanical abrasion (first employed by an American surgeon, Edward Delos Churchill, in 1941) and several chemical sclerosants. The quest for the optimum sclerosing agent is still ongoing.[12]

Talc is inexpensive and widely available around the world. Prior to being administered as medicine, it undergoes transformation into a sterile product. Talc contains crystals of magnesium hydrosilicate. The presence of replacement elements in the crystalline structure distinguishes the various forms of talc. Aluminum replaces silicon in medical talc; aluminum, iron, and manganese replace magnesium; and calcite, magnesite, dolomite, chlorite, serpentine, and quartz could be pollutants. The talc particles' dimensions are determined by the proportions of the mineral filter holes during the manufacturing process (200, 325, or 400 mesh).Tetracyclines are antibiotics with a shared basic structure that are derived directly from numerous species of Streptomyces bacteria or partially synthetically generated from those isolated compounds. Many countries no longer have access to parenteral tetracyclines since production has halted. Doxycycline is a semi-synthetic tetracycline that is a low-cost medication, while Minocycline is another tetracycline that is less favored than doxycycline.[13]

Humayoun et al conceded a study on the comparison of tetracycline and talc poudrage pleurodesis within individuals diagnosed with MPE in which they found 87% success of talc poudrage and 65.2% success of tetracycline pleurodesis. No death occurred in both groups and mild chest pain was observed in both groups which was treated by NSAIDs.[9] Shouman et al compared tertracycline vs talc pleurodesis with other sclerosing agents and found 80% success of both talc and tetracycline pleurodesis. Chest pain was more common in tetracycline pleurodesis and dyspnea in talc pleurodesis.[14]

Keeratichananont et al compared autologous blood with tals pleurodesis for malignant pleural effusion. They found 87% success of talc poudrage, fever was observed in 28% patients and opioids for pain removal was used in 26% patients.[2] Zhang et alnoted the adverse effects of talc pleurodesis in their meta analysis. They observed 7% mortality in 30 days of pleurodesis, fever in 14%, dyspnea in 13%, pain in 20% and prolong drainage in 3% patients.[3]

In a study of malignant pleural effusion, Bhatnagar et al contrasted talc poudrage to talc slurry pleurodesis. They found the 30 day success of talc poudrage in 90% patients. They noticed death in 4.2% patients, dyspnea in 16.26% patients and prolong drainage in 5.42% patients.[15] Chang et al compared viscum pleurodesis with talc pleurodesis and found 93.3% success rate of talc pleurodesis in malignant pleural effusion.[5]

Shoukri conducted an investigation regarding tetracycline pleurodesis for malignant pleural effusion and found the 86.6% success rate of tetracycline. 13% patients suffered from fever, 26% patients had chest pain and 13% had prolonged drainage.[16] Tettey et al reviewed the tetracycline pleurodesis in malignant pleural effusion. They found success in 77% patients of malignant pleural effusion. 18% of patients indicated chest pain, while 21% reported fever.[17] Mohamed et al

investigated doxycline (tetracycline derivative) pleurodesis and found a success rate of 72.7% in malignant pleural effusion. They found pain in 45.5% patients and fever in 9.1% patients.[18]

CONCLUSION

Talc pleurodesis with more success rate than the tetracycline pleurodesis and less adverse effects in talc pleurodesis than the tetracycline pleurodesis. Talc poudrage can safely be used as a pleurodesis agent.

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AUTHORSHIP AND CONTRIBUTION DECLARATION

No.	Author(s) Full Name	Contribution to the paper	Author(s) Signature
1	Zeeshan Ashraf	Concept and study design, Data collection, Drafting of discussion, Literature review, Statistical analysis.	
2	Muhammad Ashraf	Concept and study design, Supervision of whole process, Critical review of intellectual content.