

ORIGINAL ARTICLE**SHORT TERM COMPARISON OF TALC POUDRAGE WITH TETRACYCLINE FOR MEDICAL PLEURODESIS IN MALIGNANT PLEURAL EFFUSION.**

Humayon GM, Mushtaq MA, Ayyaz S, Shahzad MI, Kamran MH, Hafeez A, Dogar LA, Shaheen MZ.

ABSTRACT

We conducted a study to compare the outcome of medical pleurodesis with Talc poudrage and Tetracycline in patients with malignant pleural effusion.

Forty six patients presenting with malignant pleural effusion were selected and divided randomly into two equal groups. Age range was 20 to 90 years with mean age of 52 years. Twenty five were females and 21 males. Group-A was given 5 gram purified medical grade Talc instilled through a pleuroscope and group-B was given 1 to 1.5 gram Tetracycline instilled through a chest drain. Radiological response was assessed in both the groups and compared using chi square table. Success rate among Talc Poudrage group was significantly better i.e. 87% as compared to Tetracycline group 65.2% ($p=0.04$). No significant serious side effects were noted except mild chest pain.

This study shows benefit of Talc Poudrage through pleuroscope over Tetracycline pleurodesis in malignant pleural effusions.

Key Words: Malignant Pleural effusion, Tetracycline Pleurodesis, Talc Poudrage.

INTRODUCTION:

Malignant pleural effusions remain a therapeutic challenge both to the pulmonologist and oncologist. It is a common problem in patients with metastatic malignancies. Fifty percent patients with breast cancer¹, 25% of those with lung cancer² and 35% of those with lymphoma³ have a malignant pleural effusion during the course of their illness.

Pleural effusions may be asymptomatic, although many patients develop dyspnea cough and chest pain^{2, 4}. Palliative treatment includes repeated thoracentesis, tube thoracostomy with sclerotherapy, pleural stripping, or rarely pleuroperitoneal shunt⁵⁻⁷. Traditionally the most common treatment for a recurrent malignant effusion has been a large bore chest tube drainage followed by instillation of a sclerosing agent.

Tetracycline, doxycycline, Talc and bleomycin are the most commonly used agents for pleurodesis. Tetracycline has been widely used as a pleurodesis agent which is cheap but success rates vary from 62% to 70%^{8, 9}. Its use has been declining due mainly to its unavailability^{8, 9}.

Talc is an alternative sclerosing agent used worldwide. Its use has been associated with fewer side effects due to its acceptable particle size (medical grade talc) and considered safe in terms of both causing ARDS as well as carcinogenicity¹⁰. Its availability, however, has been an issue in our part of the world.

Tetracycline has been the sole pleurodesing agent used so far in our institution. With the recent availability of medical grade talc along with a rigid pleuroscope, it was considered worthwhile to conduct a study comparing the results of tetracycline pleurodesis (instilled through chest tube) and talc Poudrage through rigid pleuroscope to see the outcome in our setting and to develop practice guidelines.

MATERIALS AND METHODS:

This study was carried out in the department of Pulmonology, Nishtar Hospital, Multan which is a tertiary care teaching hospital affiliated with Nishtar Medical College. Study was carried out from March 2011 to September 2011. There were a total of 46 cases divided into two equal groups. One group was treated with tetracycline pleurodesis and the other with talc poudrage through pleuroscope.

Sampling technique: Purposive (non probability) sampling.

Inclusion criteria: All patients presenting with symptomatic pleural effusion having histological diagnosis of malignancy.

Exclusion Criteria:

- Incomplete drainage of effusion because of loculations or partially expanded lung.
- Previous attempts of pleurodesis.
- Patients having expected survival less than one month.

Data Collection Procedure:

Forty six patients of malignant pleural effusion admitted through outpatients department of Pulmonology at Nishtar Hospital, Multan were included in the study. Malignancy was diagnosed on the basis of histopathology of the tissue. Pleural effusion was diagnosed on chest X-ray. Written, informed consent was taken from the patients. Confidentiality was ensured and the fact that there is no additional risk involved taking part in this study. Patients were assessed on chest X-ray at 4th week after pleurodesis. The absence of pleural effusion was considered as successful response.

Data Analysis and Statistical Tests:

All the data was entered using SPSS version 10. Frequencies (percentages) were calculated for gender and successful response to therapy. Descriptive statistics was applied to calculate mean and standard deviation of age of the patients. Chi-square test was applied to compare the outcome of response to therapy between the groups at 4th weeks. P value equal or less than 0.05 was considered significant.

PROCEDURE:

Talc Poudrage:

The procedure was explained to the patient and written informed consent was taken. The patient was shifted to pleuroscopy room. After aseptic measures, the chosen intercostal space was infiltrated with 2% Lidocaine. The patient was given intravenous diluted midazolam for gentle sedation and intravenous Nalbuphane, diluted in 10cc normal saline, as per requirement. Through standard operating procedure, pleuroscope was introduced into the pleural space and pleural fluid was

aspirated to dryness. Five gram sterilized Talc was instilled in to the pleural space with insufflator through pleuroscope in all the directions. Large bore (No.28) chest drain was passed and attached with under water seal which was attached to negative suction at the pressure of 10 cm of water for the period of 24 hours. After 24 hours, chest X-ray was done to see the expansion of lung. Drain was pulled out when the daily out put was less then 100 ml.

Tetracycline Pleurodesis:

The procedure was explained to the patient and written informed consent was taken. After aseptic measures, local anesthetic (lidocaine 2%) was infiltrated and a large bore chest drain (No. 28) was placed using standard operating procedure. This was attached with a drainage bag. After 24 hours chest X-ray was done to observe the expansion of lung. Then 1.5 to 2 g tetracycline mixed with 20ml lidocaine and 10ml normal saline was instilled through chest drain which was then attached to under water seal and connected to negative suction at the pressure of 10 cm of water for 24 hours. The patient was extubated when the daily out put was less than 100ml.

Effusion on Chest X-ray:

Presence of effusion on chest X-ray was seen between the two groups at the end of 4th week after pleurodesis. Only those patients with complete absence of pleural effusion on chest X-ray were considered as having successful response at the end of 4th week.

RESULTS:

Forty six patients were randomized with 23 in each group. The two groups were comparable in age, sex and duration of symptoms. The mean age of patients was 52 years (range 22 to 90 years). The mean length of pleural effusion history was 10 (range 5 to 15) days. All the patients inducted into the study were followed for one month after pleurodesis.

At the end of 4th week, 20 (87%) patients in the talc group showed a successful response while in tetracycline group only 15 (65.2%) patients showed successful response. This difference was statistically significant ($p < 0.05$). No deaths reported in both groups. Post procedure pain was mild, bearable and treated with NSAID in both groups.

DISCUSSION:

This study was initiated in the continuing effort to develop an optimal, effective treatment strategy that reduces morbidity and cost of procedure for the management of malignant pleural effusion. Effectiveness of pleurodesis can be studied with a 30 day post pleurodesis interval because most pleural effusions re-accumulate within this time¹¹ and it is the accepted standard when modes of therapy for pleural effusions are compared^{12, 13, and 14}.

Findings in this study support a role of pleuroscopic pleurodesis with talc and response rate better than tetracycline. Instillation of sclerosing agent when catheter output is approximately 100 ml is a common though arbitrary decision based on past experience. In some studies sclerosis is performed only when catheter output is below 100 ml per 24 hours^{12, 15, 16} and in others when catheter output is slightly higher^{17, 18}. We adopted last day catheter out put criteria of below 100ml.

Many sclerosing agents have been used for sclerotherapy. Tetracycline has been popular, safe, and effective with a 77% response rate, but the intravenous form of this drug for sclerotherapy is no longer manufactured and alternatives have been in use^{8, 9}. In our study the success rate of tetracycline pleurodesis is 65.2% which is comparable with published results. Doxycycline, a tetracycline analogue, has been reported with a success rate of 72 – 95 % in various studies but required repeated instillations in up to 72 % of patients^{27,28,29,30}. Bleomycin, an anti-neoplastic agent, has a 54% response rate, but adverse effects such as nausea, vomiting, bone marrow suppression, rash, diarrhea, and high cost have been major factors limiting its utility²¹.

Talc instillation into the pleural space has been used to treat recurrent pneumothorax and effusions since 1935²⁰; However reports of febrile reactions, granulomas, fibrothorax²¹, adult respiratory distress syndrome²², malignant mesothelioma and bronchogenic carcinoma^{23, 24} diminished its popularity. The problem of malignancy has been attributed to asbestos, which is found in non purified talc. Talc currently used for pleurodesis is purified and free of asbestos¹⁰ (medical grade talc. No case of malignant transformation with purified talc has been reported. Previous reports of patients who developed adult respiratory distress syndrome²² had been treated with 10 g of talc. With the currently recommended lower dose of 4-5 g of medical grade talc, no case of adult respiratory distress syndrome has been reported²². With the smaller dose, the frequency and severity of adverse reactions has declined. No incidence of ARDS occurred in our patients.

With the recent availability of a rigid thoracoscope and medical grade talc, we conducted this study to gain experience with this treatment as well as making new practice guidelines in our institution for the management of patients with malignant pleural effusion. Uniform distribution of powdered talc within the pleural space can be achieved with insufflation through the pleuroscope, with 90% response rates as achieved by Weisbrg D¹⁰, Hart Man DL²⁵ and Yim AP²⁶ et al. Our results, 87 % success rate at one month, are comparable with these studies.

There was no infective complication in both groups. Post procedure pain was controlled with routine analgesia and there were no reports of severe pain requiring systemic analgesics in both groups of patients.

Talc poudrage via a pleuroscope needs persons experienced with pleuroscopic techniques. With the growing demand and interest of pulmonologists in learning and setting up of pleuroscopy service, along with the recent availability of medical grade Talc, it is time to use Talc poudrage as the procedure of choice for the management of malignant pleural effusions. However in institutions where this service is not available, Talc slurry can be used with comparable results in published literature³¹.

CONCLUSION AND SUGGESTIONS:

In conclusion, talc pleurodesis through pleuroscope is successful for treating symptomatic malignant pleural effusions. Talc is more efficient than other sclerosing agents with no greater risk of complications.

REFERENCES:

1. Fraccia AA, Kapper WH, Carey JT, et al. Intrapleural Chemotherapy for effusion from metastatic breast carcinoma. *Cancer* 1970; 26:626-9.
2. Sahn SA. Pleural effusion in lung cancer. *Clin Chest Med* 1993; 14; 189-200
3. Bruneau R, Rubin P. The management of pleural effusions and chylothorax in lymphoma. *Radiology* 1965; 85: 1085-92.
4. Chernow B, Sahn S. Carcinomatous involvement of the pleura. *Am J Med* 1977; 63:695-702.
5. Andrews CO, Gora MI. Pleural effusions: pathophysiology and management. *Ann Pharmacother* 1994; 28: 894-903.
6. Walker-Renard PB, Vaughan LM, Sahn SA. Chemical pleurodesis for malignant pleural effusions. *Ann Intern Med* 1994; 120:56-64.
7. Windsor PG, Como JA, Windsor KS. Sclerotherapy for malignant pleural effusions: alternatives to tetracycline. *South Med J* 1994; 87: 709-14.
8. Walker-Renard PB, Vaughan LM, Sahn SA. Chemical pleurodesis for malignant pleural effusions. *Ann Intern Med* 1994; 120: 56-64.
9. Heffner JE, Unruh LC. Tetracycline pleurodesis: adios, farewell, adieu. *Chest* 1992; 101: 5-6.
10. Weisberg D, Ben-Zeev I. Talc pleurodesis: experience with 360 patients. *J Thorac Cardiovasc Surg* 1993; 106: 689-695.
11. Windsor PG, Como JA, Windsor KS. Sclerotherapy for malignant pleural effusions: alternatives to tetracycline. *South Med J* 1994; 87: 709-714.
12. Parker LA, Charnock GC, Delany DJ. Small-bore catheter drainage and sclerotherapy for malignant pleural effusions. *Cancer* 1989; 64: 1218-1221.
13. Keller SM. Current and future therapy for malignant pleural effusion. *Chest* 1993; 103(suppl): 63S-67S.
14. Robinson LA, Fleming WH, Galbraith TA. Intrapleural doxycycline control of malignant pleural effusions. *Ann Thorac Surg* 1993; 55: 1115-1122.

15. Morrison MC, Mueller PR, Lee MJ, et al. Sclerotherapy of malignant pleural effusion through sonographically placed small-bore catheters. *AJR* 1992; 158: 41-43.
16. Patz EF, McAdams HP, Goodman PC, Blackwell S, Crawford J. Ambulatory sclerotherapy for malignant pleural effusions. *Radiology* 1996; 199: 133-135.
17. Seaton KG, Patz EF, Goodman PC. Palliative treatment of malignant pleural effusions: value of small-bore catheter thoracostomy and doxycycline sclerotherapy. *AJR* 1995; 164: 589-591.
18. Ruckdeschel JC, Moores D, Lee JY, et al. Intrapleural therapy for malignant pleural effusions: a randomized comparison of bleomycin and tetracycline. *Chest* 1991; 100: 1528-1535.
19. Andrews CO, Gora ML. Pleural effusions: pathophysiology and management. *Ann Pharmacother* 1994; 28: 894-903.
20. Bethune N. Pleural poudrage: a new technique for deliberate production of pleural adhesions as a preliminary to lobectomy. *J Thorac Surg* 1935; 4: 251-261.
21. Gaesnsler EA. Parietal pleurectomy for recurrent spontaneous pneumothorax. *Surg Gynecol Obstet* 1956; 102: 293-308.
22. Rinaldo JE, Owens GR, Rogers RM. Adult respiratory distress syndrome following intrapleural instillation of talc. *J Thorac Cardiovasc Surg* 1983; 85: 523-526.
23. Jackson JW, Bennet MH. Chest wall tumor following iodized talc pleurodesis. *Thorax* 1973; 28: 788-793.
24. Jones RN. Asbestos exposures and thoracic neoplasms. *Semin Roentgenol* 1992; 27: 94-101.
25. Hartman DL, Gaither JM, Kesler KA, et al. Comparison of insufflated talc under thoracoscopic guidance with standard tetracycline and bleomycin pleurodesis for control of malignant pleural effusions. *J Thorac Cardiovasc Surg* 1993; 105: 743-748.
26. Yim AP, Chung SS, Lee TW, Lam CK, Ho JK. Thoracoscopic management of malignant pleural effusions. *Chest* 1996; 109: 1234-1238.
27. Walker-Renard PB, Vaughan LM, Sahn SA. Chemical pleurodesis for malignant pleural effusions. *Ann Intern Med* 1994; 120: 56-65.

28. Robinson LA, Fleming WH, Galbraith TA. Intrapleural Doxycycline control of malignant pleural effusions. *Ann Thorac Surg* 1993; 55: 1115-1122.
29. Seaton KG, Patz EF, Goodman PC. Palliative treatment of malignant pleural effusions value of small-bore catheter thoracostomy and Doxycycline sclerotherapy. *AJR* 1995; 164:589-591.
30. Mansoon T. Treatment of malignant pleural effusion with doxycycline. *Scand J Infect Dis* 1988; 53(suppl):29-34.
31. Web WR, Ozmen V, Moulder PV, Shabahang B, Breaux J. Iodized talc pleurodesis for the treatment of pleural effusions. *J Thorac Cardiovasc Surg* 1992; 103:881-886.