

**Research Article****Efficacy of Doxycycline in Pleurodesis for Malignant  
Pleural Effusion (MPE)****<sup>1</sup>Muhammad Rashid Abbas, <sup>2</sup>Anam Aslam****and <sup>3</sup>Ahmad Abdul Manan**<sup>1</sup>Teaching Hospital, DHQ Dera Ghazi Khan<sup>2</sup>Services Hospital Lahore<sup>3</sup>Nishtar Hospital Multan**ABSTRACT**

Pleural effusions are well-reported entities in Pulmonology department and malignant effusion poses a great difficulty not only for diagnosis but also in terms of its management.

**Objective:** To determine the efficacy of doxycycline in pleurodesis in cases of malignant pleural effusions (MPE).

**Subject and Methods;** This was a descriptive case series and it was done in Pulmonology Department of Services Hospital, Lahore from January 2016 to October 2016. In this study, 100 patients of both genders with age range of 20 to 80 years diagnosed with malignant pleural effusion (by fluid analysis) with primary from lung or any other metastasis were enrolled. The fluid was drained by intercostal chest drain (ICT). The cases with drain output less than 50 ml per 24 hour and no collection on X ray chest underwent pleurodesis using Doxycycline in capsule form. Ten capsules of this were mixed with 50 ml of normal saline and injected intra pleurally. The cases were then followed on next day and after one week and then one month by USG and CXR PA view. The failure of recollection of fluid more than 100 ml assessed on USG was labeled with positive efficacy.

**Results:** In the present study, there were 100 cases of malignant pleural effusion (MPE) out of which 58 (58%) were males and 42 (42%) females, with mean age of  $56.21 \pm 9.19$  years. There were 46 (46%) cases with breast malignancy, 24 (24%) with lung malignancy, and 30 (30%) having other malignancies. Out of 100 cases, 60 (60%) cases had effusion more than 1 liter at presentation. The efficacy was seen in 52 (52%) of cases. There was significant better efficacy ( $p=0.002$ ) in cases that had pleural effusion less than 1 liter at presentation where it was seen in 80% of the cases. It was also significantly better seen than had it for less than 1 month where it was seen in 44 (61.11%) of cases with  $p=0.001$ . **Conclusion:** Doxycycline is easily available sclerosing agent with successful pleurodesis in half of the cases with MPE. Its failure rate is significantly higher in case that had pleural effusion more than 1 liter at presentation.

**Key Words:** MPE, Pleurodesis, Doxycycline

**INTRODUCTION**

Pleural effusions are commonly encountered in outpatient and in patients departments. There is widely variety of etiology and the treatment is done accordingly. In cases of malignant pleural effusion (MPE), there is great concern for its management, as it can not only worsen the symptoms but also its recurrence increases the symptoms of the patients.<sup>1-2</sup>

Pleurodesis is the procedure by which the both pleural surfaces are glued to each other by creating an iatrogenic inflammatory response. It

can be done via surgical and medical methods. Among medical methods, chemical pleurodesis is the procedure of choice for recurrent pleural effusions.<sup>3-4</sup> The question is the choice of the sclerosing agent, which is determined by the efficacy of the agent, its cost, accessibility, safety, ease of administration and the number of administrations needed to achieve a complete response.<sup>5</sup>

Multiple agents were tried in the past for pleurodesis like talc slurry, Bleomycin,

tetracyclins, 5 fluorouracil. Talc had the best of results among them but there was issue with its cost and some doubts about its carcinogenicity. Contrary to this, tetracycline i.e. Doxycycline were cheaper but the efficacies were of question especially in cases of 5 fluorouracil and bleomycin. So there was a need for an agent, which is safer, easily available, cheaper and efficacious for the purpose of pleurodesis, that's why this study was planned to check it with doxycycline.<sup>6-7</sup>

### **OBJECTIVE:**

To determine the efficacy of pleurodesis in malignant pleural effusion done by Doxycycline.

### **MATERIALS AND METHODS:**

This was a descriptive case series and it was done in Pulmonology Department of Services Hospital Lahore from January 2016 to October 2016. In this study, 100 patients of either gender with age range of 20 to 80 years diagnosed with malignant pleural effusion (by fluid analysis) with primary from lung or any other metastasis were enrolled. The fluid was drained by an appropriate intercostal chest drain (ICT). The cases with drain output less than 50 ml per 24 hour and no collection assessed on X ray chest PA view, then underwent pleurodesis by using Doxycycline in capsule form. Ten capsules of doxycycline were mixed with 50 ml of normal saline and injected in intra pleural space. The tube was clamped for 2 hours and then re opened and negative suction applied for 24 hours. The cases were then followed on next day and after one week and then one month by USG and CXR PA view. The failure of recollection of fluid more than 100 ml assessed on USG was labeled with positive efficacy.

### **RESULTS;**

In the present study, there were 100 cases of malignant pleural effusion (MPE) out of which 58 (58%) were males and 42 (42%) females, with mean age of  $56.21 \pm 9.19$  years. There were 46 (46%) cases with breast malignancy, 24 (24%) with lung malignancy, and 30 (30%) having other malignancies. Out of 100 cases, 60 (60%) cases had effusion more than 1 liter at presentation. The efficacy was seen in 52 (52%)

of cases. There was significant better efficacy ( $p= 0.002$ ) in cases that had pleural effusion less than 1 liter at presentation where it was seen in 80% of the cases (table 1). It was also significantly better seen than had it for less than 1 month where it was seen in 44 (61.11%) of cases with  $p= 0.001$  (table 2).

### **DISCUSSION;**

Malignant pleural effusions are hard to cope with as they have the tendency to recur again and again and also there are thought to be the predictor of failure for pleurodesis procedures. They add further to the over all morbidity of the underlying malignancies. There is always a need for better, easily available and cheap agent for pleurodesis. Talc is thought to be highly efficacious but is very expensive considering the socioeconomic status of the study place.

In the present study the efficacy was seen in 52 (52%) of the cases with MPE. This was similar to few studies done in the past. In a study done by Porcel on 34 MPE cases and it was seen that the efficacy was seen in 55% of the cases.<sup>8</sup> But they used half of the dose as was used in our study. While in another study done by Costa et al, the efficacy was also near to our study with success rate around 60%.<sup>9</sup>

However, few studies have shown better results than this, as in a study done by Mohammed KH et al, the efficacy with doxycycline was seen in 72.7% of the cases.<sup>10</sup> They used the similar procedure and the follow up period like our study. the study by Heffner et al also had efficacy around 78%.<sup>11</sup> The reason of our efficacy less than the previous ones can be explained by the fact that the cases in present study had much advance disease than the comparative ones.

There was significant better efficacy ( $p= 0.002$ ) in cases that had pleural effusion less than 1 liter at presentation and duration less than one month with  $p= 0.001$ . This reveal same mechanisms to show the early stage with lesser degree of effusion and earlier presentation led to better efficacy rates. This was also noted by the studies done in the past.<sup>12-13</sup> But they did not use the same cut off values. The reason of higher degree of failure rate in cases with pleural effusion more than 1 liter can be explained by the fact that these cases had rapid re accumulation and

hence led to widening of the pleural spaces and also the dilution of the sclerosing agent and hence the lower success rate.

### CONCLUSION;

Doxycycline is easily available sclerosing agent

with successful pleurodesis in half of the cases with MPE. Its failure rate is significantly higher in case that had pleural effusion more than 1 liter at presentation.

**TABLE 1: EFFICACY WITH RESPECT TO AMOUNT OF PLEURAL EFFUSION**

n= 100

Amount of pleural effusion	Efficacy		Total
	Yes	No	
> 1 liter	20 (33.33%)	40 (66.67%)	60 (60%)
< 1 liter	32 (80%)	8 (20%)	40 (40%)
<b>Total</b>	<b>52 (52%)</b>	<b>48 (48%)</b>	<b>100 (100%)</b>

p= 0.002

**TABLE 2: EFFICACY WITH RESPECT TO DURATION OF PLEURAL EFFUSION**

n= 100

Duration of pleural effusion	Efficacy		Total
	Yes	No	
> 1 month	8 (28.57%)	20 (71.43%)	28 (28%)
< 1 month	44 (61.11%)	28 (38.89%)	72 (72%)
<b>Total</b>	<b>52 (52%)</b>	<b>48 (48%)</b>	<b>100 (100%)</b>

p= 0.001

### REFERENCES:

- Albert RK, Spiro SG, Jett JR. Clinical respiratory medicine. In: Pleural V. Effusion, emphysema, and pneumothorax. Philadelphia: Elsevier; 2008. P. 860-3.
- Antunes G, Neville E, Duffy J, Ali N. BTS Guidelines for the management of malignant pleural effusions. *Ann Intern Med.* 1994;120:56-64.
- Shaw P, Agarwal R. Pleurodesis for malignant pleural effusions. *Cochrane Database Syst Rev.* 2004;(I):CD 002916.
- Vargas FS, Teixeira LR, Antonangelo L, Vaz MA, Carmo AO, Marchi E, et al. Experimental pleurodesis in rabbits induced by silver nitrate or talc. *Chest.* 2001;119:1516-20.
- Agarwal R. Iodopovidone an inexpensive and effective agent for chemical Pleurodesis. *Lung Cancer.* 2007;55:253-54.
- Musani AI. Treatment options for malignant pleural effusion. *Curr Opin Pulm Med.* Jul 2009;15(4):380-87.
- Herrington JD. Chemical pleurodesis with doxycycline 1 g. *Pharmacotherapy.* 1996; 16(2) :280-85.
- Porcel JM, Salud A, Nabal M, et al. Rapid pleurodesis with doxycycline through a smallbore catheter for the treatment of metastatic malignant effusions. *Support Care Cancer.* 2006;14(5):475-78.
- Costa JS, Lombart ML, Chiner E, et al. Pleurodesis in patients with malignant pleural effusions: efficacy of doxycycline. *Chest (2006) 244S Poster Presentations Wednesday, October 25, 2006*
- Mohamed KH, Hassan OA. A new look at an old agent for pleurodesis. *Egypt J Chest Dis Tuberc.* 2013;62(4):617-20.
- Heffner JE, Standerfer RJ, Torstveit J, et al. Clinical efficacy of doxycycline pleurodesis. *Chest.* 1994;105:1743-47.
- Elnady M, Sakr A. Safety and efficacy of pleurodesis with thoracoscopic doxycycline poudrage in malignant pleural effusion. *Chest.* 2011;140(4):697A.
- Lee YCG, Baumann MH, Maskell NA, et al. Pleurodesis practice for malignant pleural effusions in five English speaking countries: survey of pulmonologists. *Chest.* 2003;124:2229-2238