



## Efficacy of Doxycycline as Pleuridising Agent in Cases of Malignant Pleural Effusion (MPE)

Javed Iqbal, Raja Yasser Shahbaz, Samina Fida\*, Ali Usman, Irfan Malik and Ghias ul Hassan

Department of Medicine, CMH Lahore Medical College, Lahore, Pakistan

\*Corresponding e-mail: [Samm.doc@hotmail.com](mailto:Samm.doc@hotmail.com)

### ABSTRACT

**Objective:** To determine the efficacy of doxycycline as pleuridising agent in cases of malignant pleural effusions (MPE). **Subject and methods:** This was a descriptive case series that was conducted at Medical and Pulmonology Department of Combined Military Hospital Lahore from January 2018 to August 2018. In this study, the cases of malignant pleural effusion assessed on history and proven by histopathology on any biopsy of either gender falling in range of 30 years or more were included. The pleural fluid was drained by appropriate size intercostal chest tube (ICT). These cases then underwent pleurodesis with Doxycycline. For pleurodesis 10 capsule of Doxycycline each carrying 100 mg in it were taken and mixed with 50 ml of normal saline. A repeat chest X-ray and USG chest was done to see for presence of fluid, complete absence of fluid was labelled as efficacious pleurodesis. **Results:** In this study, there were total 60 cases of malignant pleural effusion (MPE) included, out of which 35 (58.33%) were females and 25 (41.67%) males. The mean age of the subjects was  $57.32 \pm 7.28$  years. There were 29 (48.33%) cases with CA breast, 22 (36.67%) with CA lung and 9 (15%) had the other miscellaneous malignancies. The efficacy of pleurodesis with Doxycycline was seen in 26 (43.33%) of cases. There was significant better efficacy ( $p=0.001$ ) in cases that had pleural effusion less than 1 liter at presentation where it was seen in 14 (63.64%) of cases as compared to 12 (31.58%) cases that had effusion less than 1 liter. There was no significant difference in terms of duration of pleural effusion with  $p=0.21$ . **Conclusion:** Doxycycline is efficacious in almost half of the cases and it is significantly better in cases that had effusion less than 1 liter.

**Keywords:** Pleurodesis, Doxycycline, MPE

### INTRODUCTION

Pleural effusion is defined as the accumulation of the free fluid in the pleural cavity and is often reported in medical and pulmonology departments. It shades a wide range of etiologies which range from benign diseases that are curable to malignant ones that can be life threatening [1,2].

Pleural effusion is common in cases of malignancies especially due to lung and the breast malignancies. It can either be caused due to pneumonia or it can be due to metastatic spread. Malignance pleura effusion (MPE) has the property of recurring again and again even after drainage because sometimes disease is un-cure-able and palliation is the only option left. Pleurodesis is a modality that is used to decrease the recurrent accumulation of the pleural fluid. It causes by creating an inflammatory response in the pleural cavity and potentiate the inflammation and hence scarring process to adhere the parietal and the visceral pleura and leave no space for this accumulation [3,4].

There are two main ways to do pleurodesis i.e. medical and surgical. In medical method various sclerosing agents have been used in the past. These include tetracycline, bleomycin, talc, 5-fluorouracil and iodopovidone. Talc has been reported the most widely used and most efficacious in the developed world, but is expensive and is not the one of choice in developing countries like Pakistan. Doxycycline, on the other hand is easily available and is very cheap and used as antibiotic. The data has shown good efficacies as well with this agent. The other agents are also easily available but their safety profile, lesser efficacy and degree of side effects are also of concern [5-7].

## METHODS

### Study Settings

Combined Military Hospital Lahore.

### Study Duration

January 2018 to August 2018.

### Study Design

Descriptive case series.

### Sampling Technique

Non-probability consecutive sampling.

This was a descriptive case series that was conducted at Medical and Pulmonology Department of Combined Military Hospital Lahore from January 2018 to August 2018. In this study, the cases of malignant pleural effusion assessed on history and proven by histopathology on any biopsy of either gender falling in range of 30 years or more were included. The pleural fluid was drained by appropriate size intercostal chest tube (ICT). These cases then underwent pleurodesis with Doxycycline. For pleurodesis 10 capsule of Doxycycline each carrying 100 mg in it were taken and mixed with 50 ml of normal saline. This mixture was injected in the pleural space and then tube was clamped for at least 2 hours, afterwards negative suction was applied. A repeat chest X-ray and USG chest was done to see for presence of fluid, complete absence of fluid was labelled as efficacious pleurodesis.

## RESULTS

In this study, there were total 60 cases of malignant pleural effusion (MPE) included, out of which 35 (58.33%) were females and 25 (41.67%) males. The mean age of the subjects was  $57.32 \pm 7.28$  years. There were 29 (48.33%) cases with CA breast, 22 (36.67%) with CA lung and 9 (15%) had the other miscellaneous malignancies. The efficacy of pleurodesis with Doxycycline was seen in 26 (43.33%) of cases. There was significant better efficacy ( $p=0.001$ ) in cases that had pleural effusion less than 1 liter at presentation where it was seen in 14 (63.64%) of cases as compared to 12 (31.58%) cases that had effusion more than 1 liter (Table 1). There was no significant difference in terms of duration of pleural effusion with  $p=0.21$  as shown in Table 2.

**Table 1 Efficacy vs amount of pleural effusion (n=60, p=0.001)**

Amount of PE	Efficacy		Total
	Yes	No	
>1 liter	12 (31.58%)	26 (68.42%)	38
<1 liter	14 (63.64%)	08 (36.36%)	22
Total	26 (43.33%)	34 (56.67%)	60 (100%)

**Table 2 Efficacy vs duration of pleural effusion (n=60, p=0.21)**

Duration of PE	Efficacy		Total
	Yes	No	
>3 months	17 (40.47%)	25 (59.53%)	42
<3 months	09 (50%)	09 (50%)	18
Total	26 (43.33%)	34 (56.67%)	60 (100%)

## DISCUSSION

Pleural effusions especially malignant effusions need to be drained at any cost. The left over fluid can be a source of infection and can compress the normal lung parenchyma and further deteriorate the clinical scenario. The concern of

the malignant pleural effusion is the recurrence and hence successful drainage and later pleurodesis to prevent re accumulation is the treatment of choice specially in cases where the definitive treatment is not the first choice and need palliation.

In this study the efficacy of Doxycycline as pleuridising agent was seen in 26 (43.33%) of the cases in cases of malignant pleural effusion (MPE). These results were close the finding of the study conducted by Porcel et al., which conducted over 34 cases of MPE and the efficacy in their study was observed in 55% of the cases [8]. The reason of the difference results in their study can be explained by the different dose protocols as were used in the present study. Costa et al, also had the slight better results and the efficacy in their study approached to 60% of the cases [9].

The studies conducted by Mohammed KH et al., and Heffer et al., also revealed the efficacies better than our and observed as 72.7% and 78% respectively [10,11]. The reason of this difference can be the different degree of severity in both the studies.

The efficacy was seen significantly better in cases that had pleural effusion of less than 1 liter where it was observed in 14 (63.64%) cases as compared to 12 (31.58%) cases that had effusion more than 1 liter with  $p=0.001$ ). These findings were according to the other studies as well where they revealed the lesser the degree of fluid in the pleural cavity and higher are the chances of successful pleurodesis. However, these studies stratified according to the mean pleural fluids as compared to these cut off values used by our study [12,13]. The reason of this significant difference can be explained by the lesser severity of the disease and also by the fact that better drainage led to dry surface and better facing of the pleural surfaces leading to higher inflammation and scarring.

### CONCLUSION

Doxycycline is efficacious in almost half of the cases and it is significantly better in cases that had effusion less than 1 liter.

### DECLARATIONS

#### Conflicts of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

### REFERENCES

- [1] Albert RK, Spiro SG, Jett JR. *Clinical respiratory medicine. In: Pleural V. Effusion, emphysema, and pneumothorax*. Philadelphia: Elsevier, 2008. p. 860-63.
- [2] Antunes, G., et al. "BTS guidelines for the management of malignant pleural effusions." *Thorax*, Vol. 58, No. 2, 2003, p. ii29.
- [3] Shaw, Paul HS, and Roshan Agarwal. "Pleurodesis for malignant pleural effusions." *Cochrane Database of Systematic Reviews*, Vol. 1, 2004.
- [4] Vargas, Francisco S., et al. "Experimental pleurodesis in rabbits induced by silver nitrate or talc: 1-year follow-up." *Chest*, Vol. 119, No. 5, 2001, pp. 1516-20.
- [5] Agarwal, Ritesh. "Iodopovidone: An inexpensive and effective agent for chemical pleurodesis." *Lung Cancer*, Vol. 55, No. 2, 2007, pp. 253-54.
- [6] Musani, Ali I. "Treatment options for malignant pleural effusion." *Current Opinion in Pulmonary Medicine*, Vol. 15, No. 4, 2009, pp. 380-87.
- [7] Herrington, Jon D., Mary Lea Gora-Harper, and Robert K. Salley. "Chemical pleurodesis with doxycycline 1 g." *Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy*, Vol. 16, No. 2, 1996, pp. 280-85.
- [8] Porcel, José Manuel, et al. "Rapid pleurodesis with doxycycline through a small-bore catheter for the treatment of metastatic malignant effusions." *Supportive Care in Cancer*, Vol. 14, No. 5, 2006, pp. 475-78.

- [9] Signes-Costa, Jaime, et al. "Pleurodesis in patients with malignant pleural effusions: efficacy of doxycycline." *Chest*, Vol. 130, No. 4, 2006, p. 244S.
- [10] Mohamed, Khaled H., and Osama A. Hassan. "A new look at an old agent for pleurodesis." *Egyptian Journal of Chest Diseases and Tuberculosis*, Vol. 62, No. 4, 2013, pp. 617-20.
- [11] Heffner, John E., et al. "Clinical efficacy of doxycycline for pleurodesis." *Chest*, Vol. 105, No. 6, 1994, pp. 1743-47.
- [12] Elnady, Mohamed, and Amr Sakr. "Safety and efficacy of pleurodesis with thoroscopic doxycycline poudrage in malignant pleural effusion." *Chest*, Vol. 140, No. 4, 2011, p. 697.
- [13] Lee, YC Gary, et al. "Pleurodesis practice for malignant pleural effusions in five English-speaking countries: survey of pulmonologists." *Chest*, Vol. 124, No. 6, 2003, pp. 2229-38.