

# Povidone-iodine effectiveness as chemical pleurodesis for malignant pleural effusion in comparison to Bleomycin

Ahmed Muhi Fahad<sup>1</sup>, Laith Fathi Flayyh Sharba<sup>2</sup>, Hayder Noaman Rabeea<sup>3</sup>, Ashraf Sami Mohammed<sup>2</sup>, Saja Museser Abbood<sup>3</sup>,  
Ahmed Salih Alshewered<sup>4</sup>

<sup>1</sup> Department of Cardiovascular Surgery, Najaf Health Directorate, Al-Sadder Teaching Medical City, Ministry of Health/Environment, Najaf, Iraq

<sup>2</sup> Department of Surgery, Faculty of Medicine, Jabir Ibn Hayyan Medical University, Najaf, Iraq

<sup>3</sup> Radiation Oncology Department, Najaf Health Directorate, Middle Euphrates Cancer Center, Ministry of Health/Environment, Najaf, Iraq

<sup>4</sup> Misan Radiation Oncology Center, Misan Health Directorate, Ministry of Health/Environment, Misan, Iraq

SUMMARY

Malignant Pleural Effusion (MPE) is occurred in about 15% of all patients with cancer especially in lung cancer. Pleurodesis using Bleomycin and povidone-iodine to palliate symptoms of MPE. This study aimed to compare the efficacy, safety, and outcome of Bleomycin pleurodesis with Povidone-Iodine Pleurodesis (PIP) by injection through a chest tube as a palliative preventive management of recurrent MPE. This is a retrospective cross-sectional cohort study that includes fifty-four patients diagnosed with malignant pleural effusion. The patients were classified into two groups, G1 who received povidone-iodine for pleurodesis (total number 21 patients), and G2 who received Bleomycin for pleurodesis (total number 33 patients). The mean age of patients in G1 is 62 ± 11.31 years (range from 44-81), while in G2 is 58 ± 10.89 years (range from 43-83). In G1, the total number of males is 13 patients (61.9%) and female patients are 8(38.09%), while in G2, the male patients are 20 (60.6%) and females are 13(39.4%). In G1, there are 11(52.38%) patients with right-side involvement, 9 (24.85%) patients with left-side involvement, and one (4.76%) the patient is bilateral. In G2, there are 15 patients (45.45%) with right side involvement and 18 patients (54.54%) with left side involvement. There are 3 patients (14.28%) who have postoperative chest pain in G1, while in G2, there are 2 patients (6.06%) with postoperative chest pain and 2 patients (6.06%) with fever. All the complications in both groups are subsided gradually over 1<sup>st</sup> 1 hours-4 hours later on. The primary tumor in G1 is lung in 9 cases (42.85%), breast in 5 cases (23.8%), colon in 3 cases (14.28%), thyroid in one case (4.76%), prostate in two cases (9.52%) and lymphoma in one case (4.76%). In G2, the primary tumor is lung in 14 cases (42.42%), breast in 7 cases (21.21%), colon in 7 cases (21.21%), lymphoma in 4 cases (12.12%), and prostate in one case (3.03%). Regarding the following three months, the recurrence is present in one case in G1 (4.76%) and 7 cases in G2 (21.21%). The death rate is present in one case in G1 (4.76%) and two cases in G2 (6.06%). In conclusion, the older age and male gender cancerous patients are the more complicated with MPE. Left sided MPE is the common observed. The most postoperative complications are chest pain and fever. Lung cancer is the major cause of MPE over other types of cancer. Povidone-iodine is superior to Bleomycin as a sclerosing agent for pleurodesis because of its cheapness, high efficacy, availability, and least side effects.

**Key words:** malignant pleural effusion, pleurodesis, Bleomycin, povidone-iodine, sclerosing agent

## Address for correspondence:

Ahmed M Fahad, Department of Cardiovascular Surgery, Najaf Health Directorate, Al-Sadder Teaching Medical City, Ministry of Health/Environment, Najaf, Iraq, Zipcode: 54001, e-mail: ahmedsalihdr2008@yahoo.com

Word count: 2621 Tables: 02 Figures: 01 References: 19

Received: - 23 September, 2021

Accepted: - 06 October, 2021

Published: - 13 October, 2021

## INTRODUCTION

Malignant Pleural Effusion (MPE) has occurred in tumors of late stages [1]. It occurs in about 15% of all patients with cancer (commonly in the lung, breast cancer, lymphoma, gynecological malignancies, and malignant mesothelioma) [2]. The commonest symptom of patients is shortness of breath [3]. About 95% of MPE cases are caused by metastases in the pleural space and 70%-77% the cause is adenocarcinoma [4]. Palliation of symptoms start with systemic or local chemotherapy treatments [5]. When MPE continues or re-accumulates after chemotherapy, treatments like pleural aspiration, pleurodesis (the commonest way), or pleuro-peritoneal shunting are indicated [6]. Many decades ago, several drugs are used like Bleomycin, silver nitrate, tetracycline derivatives, talc, erythromycin, and povidone-iodine (an antiseptic agent) to create pleurodesis after injection inside the pleural cavity [7]. Povidone-iodine is a water-soluble iodine-releasing agent that consists of a complex between iodine and a solubilizing polymer carrier, polyvinylpyrrolidone [8]. About 120 micrograms of iodide are taken up by the thyroid gland for the synthesis of thyroid hormones, from the capillary vessels into the follicular cell of the gland by an active transport system [9,10].

This study aimed to compare the efficacy, safety, and outcome of Bleomycin pleurodesis with Povidone-Iodine Pleurodesis (PIP) by injection through a chest tube as a palliative preventive management of recurrent MPE.

## MATERIALS AND METHODS

This is a retrospective cross-sectional cohort study that was done in AL-Sadder Teaching Medical City of Najaf government of Iraq for two years' duration from January of 2019 to January of 2020. This includes fifty-four patients diagnosed with malignant pleural effusion. All patients were referred from the oncology center of the Najaf government. All patients received specific systemic chemotherapy. The patients were diagnosed with clinical features, chest radiograph, and computer tomography of the chest. All patients underwent a procedure of tube thoracostomy to the side of MPE under local anesthesia through the fifth intercostal space. The evacuated fluid was sent for cytology, AFB, and gram stain with culture and specificity. The effusion was drained gradually over many days later on.

After confirmation of the total evacuation of pleural effusion with a chest radiograph and computer tomography of the chest, the pleurodesis was done. The patients were classified into two groups, G1 who received povidone-iodine for pleurodesis (about 21 patients), and G2 whose received Bleomycin for pleurodesis (about 33 patients). In the G1 group, injection of 40 ml of povidone-iodine of 10% with 20 ml xylocaine of 2% and 10 ml of 0.9% normal saline slowly was done, while in the G2 group, 60 mg of Bleomycin was injected along with 30 ml of normal saline and 10% xylocaine. The chest tube then, clamped for two hours. Then, the tube was kept open on low-pressure suction about 10 mmHg, and then, it was removed after 24 hours later on. All patients are followed for 6 months later on. All patients in G1 send for thyroid function test and ensure it is normal before instillation of povidone-iodine. The success rate

was means complete response without reaccumulation of fluid during a period of follow-up. Oral consent was taken from all patients to be included in this study and the data were analyzed using Microsoft Excel version 2009. The data were given as numbers, mean, standard deviation, and percentage Figure 1. The p-value was considered significant if it is <0.05.

## RESULTS

This study includes 54 patients with MPE that was treated with tube thoracostomy and pleurodesis. The patients were subdivided into two groups, G1 (21 patients treated with povidone-iodine pleurodesis) and G2 (33 patients treated with bleomycin pleurodesis). The mean age of patients in G1 is 62 ± 11.31 years (range from 44-81), while in G2 is 58 ± 10.89 years (range from 43-83). In G1, the total number of males is 13 patients (61.9%) and female patients are 8(38.09%), while in G2, the male patients are 20 (60.6%) and females are 13(39.4%). In G1, there are 11(52.38%) patients with right-side involvement, 9(42.85%) patients with left-side involvement, and one (4.76%) the patient is bilateral. In G2, there are 15 patients (45.45%) with right side involvement and 18 patients (54.54%) with left side involvement as in Table 1.

Regarding the postoperative complications, there are 3 patients (14.28%) who have postoperative chest pain in G1, while in G2, there are 2 patients (6.06%) with postoperative chest pain and 2 patients (6.06%) with fever. All the complications in both groups are subsided gradually over 1<sup>st</sup> 1 hours-4 hours later on. The primary tumor in G1 is lung in 9 cases (42.85%), breast in 5 cases (23.8%), colon in 3 cases (14.28%), thyroid in one case (4.76%), prostate in two cases (9.52%) and lymphoma in one case (4.76%). In G2, the primary tumor is lung in 14

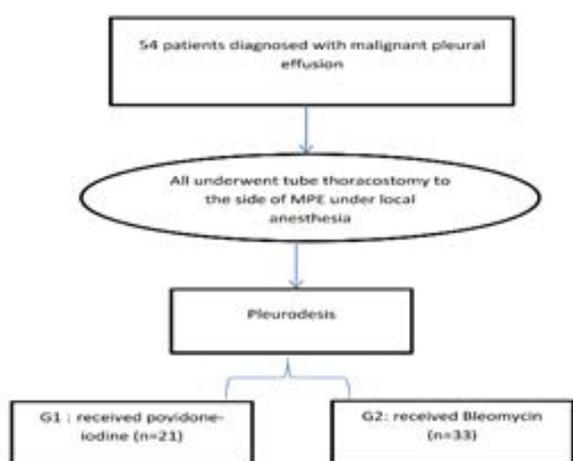


Fig. 1. Flow chart for the methods of the study.

Tab. 1. Demographic features of both groups

	G1	G2	P-value
Age (years)	62 ± 11.31	58 ± 10.89	0.532
<b>Gender</b>			
Male	13 (61.9%)	20 (60.6%)	0.923
Female	8 (38.09%)	13 (39.4%)	
<b>Sides</b>			
Right	11 (52.38%)	15 (45.45%)	0.750
Left	9 (42.85%)	18 (54.54%)	
Bilateral	1 (4.76%)	0	
Pleural effusion amount ( ml )	1950	2300	-

Tab. 2. Post-operative follow-up and primary tumor

	G1	G2	P-value
<b>Complications</b>			
Chest pain	3 (14.28%)	2 (6.06%)	0.046
Fever	0	2 (6.06%)	
Recurrence	1 (4.76%)	7 (21.21%)	0.047
Death	1 (4.76%)	2 (6.06%)	0.839
<b>Success rate</b>			
	95.23%	78.78%	0.971
<b>Primary tumor</b>			
Lung	9 (42.85%)	14 (42.42%)	0.379
Breast	5 (23.8%)	7 (21.21%)	
Colon	3 (14.28%)	7 (21.21%)	
Thyroid	1 (4.76%)	0	
Prostate	2 (9.52%)	1 (3.03%)	
Lymphoma	1 (4.76%)	4 (12.12%)	

cases (42.42%), breast in 7 cases (21.21%), colon in 7 cases (21.21%), lymphoma in 4 cases (12.12%), and prostate in one case (3.03%).

Regarding the following three months, the recurrence is present in one case in G1 (4.76%) and 7 cases in G2 (21.21%). The death rate is present in one case in G1 (4.76%) and two cases in G2 (6.06%) as in Table 2.

## DISCUSSION

Malignant Pleural Effusion (MPE) accounts for about 15% of all patients with cancer especially lung cancer. The cause behind the development of MPE is mainly metastases to the pleural cavity [11]. The pleurodesis in these patients prevents recurrence of effusion, so improves the symptoms [12]. The patients were subdivided into two groups, G1 (21 patients) received povidone-iodine for pleurodesis, and G2 (33 patients) received Bleomycin for pleurodesis. The subdivision was random and did not depend on any criteria. This study includes only patients diagnosed with malignant exudative pleural effusion after specific investigations like a pleural aspiration for cytology, AFB and gram stain, culture, and sensitivity.

The mean age of patients in G1 is  $62 \pm 11.31$  years (range from 44-81), while in G2 is  $58 \pm 10.89$  years (range from 43-83). In Mohsen, et al. study, the mean age was  $50.2 \pm 7$  (range 32-62) years for the group treated with povidone-iodine [13]. The success rate means complete response without reaccumulation of fluid during the period of follow-up. The success rate in this study for G1 is 95.23% and in G2 is 78.78%. In Mohsen, et al. study, the success rate is 85% [13]. In El-Kolaly, et al. study, the success rate of iodine is 73.3% [14]. In Bakr, et al. study, the success rate was 70% and 60% in both iodine and bleomycin groups [15]. This difference is due to the low concentration of iodine that used in these studies in comparison to our study, in El-Kolaly, et al. study [14], instillation of 20 ml of 10% Betadine in 80 ml normal saline is used, while in Mohsen, et al. study, twenty milliliters of 10% povidone-iodine and 30 ml of normal saline was used. In Bakr, et al. study, 20 ml of 10% povidone-iodine with 50 ml of saline 0.9% and 10 ml of 2% xylocaine were used, and use 60 mg of bleomycin with 50 cc of saline 0.9%.

The most commonly reported adverse effects were chest and

fever [16]. In this study, there are 3 patients out of 21 (14.28%) who have postoperative chest pain in G1, while in G2, there are 2 patients out of 33 (6.06%) with postoperative chest pain and 2 patients (6.06%) with fever. In Bakr, et al. study, there are 50% of patients have postoperative chest pain and 50% of them have a fever with the iodine group, while in the Bleomycin group, there are 60% of patients have postoperative chest pain and 30% of them have fever [15]. In Carlos, et al. study, there are 3 patients (5.8%) who have pleuritic pain and systemic hypotension after the installation [7]. In Shouman, et al. study, there are 13% of patients with chest pain and 33% with fever in the iodine group, while in the Bleomycin group, there are 26% of patients have a fever and another 26% with chest pain [17]. These differences in postoperative complications may be due to the slow instillation of sclerosing agents in our study.

In this study, the recurrence is presented in one case in G1 (4.76%) and 7 cases in G2 (21.21%). In Godazandeh, et al. study, Recurrent effusion was presented in 10 patients (27.7%) [5]. In Ibrahim, et al. study, recurrence of effusion was noted in five patients out of 18 [18]. In Martinez-Moragon, et al. study, there are 20 patients out of 64 who have recurrence after instillation of Bleomycin [19]. This study has a limitation in sample size, which is small so, the possibility of error is high and a larger trial is required.

## CONCLUSION

The older age and male gender cancerous patients are the more complicated with MPE. Left sided MPE is the common observed. The most postoperative complications are chest pain and fever. Lung cancer is the major cause of MPE over other types of cancer.

Povidone-iodine is superior to Bleomycin as a sclerosing agent for pleurodesis because of its cheapness, high efficacy, availability, and least side effects.

## RECOMMENDATION

Conducting future studies on another different substance, that may be more safety and helpful to improve effusion. Careful management with those end stage diseases. Applying data of this study in the clinical situation.

## REFERENCES

- Chen H, Brahmer J. Management of malignant pleural effusion. *Curr Oncol Rep.* 2008; 10:287-293.
- Skok K, Hladnik G, Grm A, Crnjac A. Malignant Pleural Effusion and Its Current Management: A Review. *Medicina (Kaunas).* 2019; 55:490.
- Stokes LS. Percutaneous management of malignant fluid collections. *Semin Intervent Radiol.* 2007; 24:398-408.
- Lepus CM, Vivero M. Updates in Effusion Cytology. *Surg Pathol Clin.* 2018; 11:523-544.
- Godazandeh G, Qasemi NH, Saghafi M, Mortazian M, Tayebi P. Pleurodesis with povidone-iodine, as an effective procedure in management of patients with malignant pleural effusion. *J Thorac Dis.* 2013; 5:141-144.
- Sahn SA. Talc should be used for pleurodesis. *Am J Respir Crit Care Med.* 2000; 162:2023-2024.
- Olivares Torres CA, Laniado Laborín R, Chávez García C, Leon Gastelum C, Reyes Escamilla A, et al. Iodopovidone pleurodesis for recurrent pleural effusions. *Chest.* 2002; 122:581-583.
- Lachapelle JM, Castel O, Casado AF, Leroy B, Micali G, et al. Antiseptics in the era of bacterial resistance: a focus on povidone-iodine. *Clin Pract.* 2013;10:579-592.
- Pal GK. *Endocrine Physiology: Textbook of Medical Physiology.* India: Ahuja Publishing House. 2007; 346.
- Ahad F, Ganie SA. Iodine, Iodine metabolism, and Iodine deficiency disorders revisited. *Indian J Endocrinol Metab.* 2010; 14:13-17.
- Davies HE, Lee YC. Management of malignant pleural effusions: questions that need answers. *Curr Opin Pulm Med.* 2013; 19:374-379.
- Shaw P, Agarwal R. Pleurodesis for malignant pleural effusions. *Cochrane Database Syst Rev.* 2004:2916.

- |   |  |
|---|--|
| <p>13. Mohsen TA, Zeid AA, Meshref M, Tawfeek N, Redmond K, et al. Local iodine pleurodesis versus thorascopic talc insufflation in recurrent malignant pleural effusion: a prospective randomized control trial. <i>Eur J Cardiothorac Surg.</i> 2011; 40:282-286.</p> <p>14. El Kolaly RM, Abo Elnasr M, El Guindy D. Outcome of pleurodesis using different agents in management of malignant pleural effusion. <i>Egypt J Chest Dis Tuberc.</i>, 2016; 65:435-440.</p> <p>15. Bakr RM, El Mahalawy II, Abdel Aal GA, Mabrouk AA, Ali AA. Pleurodesis using different agents in malignant pleural effusion. <i>Egypt J Chest Dis Tuberc.</i> 2012;61(4):399-404.</p> | <p>16. Walker Renard PB, Vaughan LM, Sahn SA. Chemical pleurodesis for malignant pleural effusions. <i>Ann Intern Med.</i> 1994; 120:56-64.</p> <p>17. Shouman W, Elgazzar A, Hussien RM, ElShaaray M, Light RW. Chemical pleurodesis for malignant pleural effusion, Egyptian Egypt J Chest Dis Tuberc 2012;61:115-120.</p> <p>18. Ibrahim IM, Dokhan AL, El Sessy AA, Eltaweel MF. Povidone-iodine pleurodesis versus talc pleurodesis in preventing recurrence of malignant pleural effusion. <i>J Cardiothorac Surg,</i> 2015;10: 64.</p> <p>19. Martinez Moragon E, Aparicio J, Rogado MC, Sanchis J, Sanchis F, et al. Pleurodesis in malignant pleural effusions: a randomized study of tetracycline versus bleomycin. <i>Eur Respir J.</i> 1997; 10:2380-2383.</p> |
|---|--|
-