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Validity of pleurodesis with bleomycin by pigtail versus chest tube in malignant pleural effusion

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ABSTRACT

Background: Pleural drainage is the preferred treatment for patients with symptomatic malignant pleural effusion. Insertion of a large bore chest tube for drainage prior to chemical pleurodesis is a standard treatment procedure. Small sized catheters (pigtail) are another option. However, for use in pleural drainage and pleurodesis, the optimal size of chest drains is still debatable. *The aim of the study*: Comparing the consequences and efficacy of bleomycin in pleurodesis using small sized pigtail (10-12 Fr) versus chest tube (24-30 Fr) in malignant pleural effusion. *Patients and methods*: A total of 130 patients with malignant pleural effusion were enrolled in this study. The patients were divided into two categories, Group A: a small sized pigtail catheter (10-12 French) was used in 72 patients and group B: a chest tube (24-30 French) was used in 58 patients. Male patients were 19 in group A and 18 in group B, with nearly same age range (51-67) and (55-70) year, respectively. All patients with manifested coagulopathy, loculated effusion or serious comorbidity were excluded. *Results*: Comparative results found that lung cancer was the main cause in both groups: adenocarcinoma 38.9 % in group A and 37.9 % in group B, followed by squamous cell carcinoma 11.1 % versus 6.9 %, respectively. Most body cancers were presented in both groups except stomach cancer was 0 % in both groups. Total success was slightly higher in group A 75 % compared to 72.4 % in group B but not statistically significant. Total hospital stay, postoperative pain score and dyspnea incidence were significantly less in group A where small pigtails were inserted. *Conclusion*: The chemical pleurodesis with bleomycin using small pore catheter (Pigtail) in MPE management is more effective, more patient- tolerable, than chest tube method. It is recommended to use of the pigtail drainage system rather than a chest tube in the treatment of MPE.

Keywords: Pleurodesis, Bleomycin, pigtail, chest tube, malignant pleural effusion

1. INTRODUCTION

Malignant pleural effusion (MPE) is a common clinical issue in patients with low performance status and limited life expectancy associated with crippling breathlessness. It is also popular among patients who have primary pleuro-pulmonary or metastatic tumors. A pleural effusion might experience dyspnea, cough, or pleural chest pain that can negatively affect their quality of life (Firoozbakhsh et al., 2012; Ahmed et al. 2020). Breast cancers and lung cancers are the greatest commonly occurring metastatic pleural tumors among women and men, respectively. Together these malignancies account for about 50-65 percent of all malignancies. Another 25 percent of primary malignancies are lymphomas, genitourinary tract cancers, in addition to the GIT cancers as a group. 7 to15 percent of totally malignant pleural effusions are caused by pleural effusions of unknown origin (Psallidas et al., 2016).

As MPE affects patients with progressive neoplasm, its management stills a challenge. The main aim of MPE management is to prevent the return of tumor, improve symptoms and the quality of life with least hospitalization (Lee & Light, 2004). Several approaches can applied for effective managing of MPE. However, there is no consensus on the best MPE approach for palliative intervention. Some methods can be used at the same timeor successively (such as thoracocentesis and pleurodesis). A potential solution can be drainage of the effusion with the chest tube followed by chemical pleurodesis (Antony et al., 2001). Several drugs and methods have been used to manage pleurodesis by means of protection, effectiveness, availability and less complication. Bleomycin is one of those drugsused inchemical pleurodesis (Nikbakhsh et al., 2011; Bagheri et al., 2018). A traditional large-bore chest tube has been utilized forthoracostomy and chemical pleurodesis (Light, 2011). Pigtail catheter drainage is another popular simple method for drainage of fluids during pleurodesis (Bediwy & Amer, 2012; Chang et al., 2018).

Choosing the proper procedure for each patient should be selected according to the patient's clinical condition, under lying illnesses, state of performance, relatives and medical help in addition to passable access to medical facilities and tools (Dixit et al., 2017). So the aim of this study was to compare the outcome and efficacy of drainage of malignant pleural effusion and pleurodesis with bleomycin by small sized pigtail (10-12 Fr) versus chest tube (24-30 Fr).

2. METHODS

Study design and sampling

This study was carried out in Zagazig university hospitals from March 2018 to December 2019. Participants were chosen by systematic random sampling of patients admitted to cardiothoracic surgery and chest departments in hospitals at the Zagazig University. The study included 130 patients divided into two groups. Group A: included 72 patients who underwent pleurodesis with small sized pigtail catheter (10-12 French). Group B: included 58 patients who underwent chest tube (24-30 French).

Written informed consent was obtained from all participants for whom identifying information is included in this manuscript. Medical Ethics Committee of Faculty of Medicine's research ethics committee, Zagazig University, has approved the study. The work was carried out in accordance with World Medical Association's Code of Ethics (Helsinki Declaration) for human involvement studies. Ethical approval number is (ZU-IRB# 6587).

Inclusion criteria included adults willing patients confirmed that they had a malignant pleural effusion by cytological examination, recurrent malignant pleural effusion and patients with an estimated good performance status can live for several months. Exclusion criteria were patients with coagulopathy, loculated effusions, and patients with serious comorbid illness, and any patient who failed pleurodesis or on mechanical ventilation due to advanced malignancy.

Clinical and biochemical assessments

All patients underwent thorough medical history taking including patients' age, sex and type of primary tumor. Blood investigations including CBC, INR, Liver and renal function tests, CXR and cytological and biochemical examination of aspirated pleural fluid including (pH, LDH and Glucose) and the amount of drained pleural fluid.

Pleurodesis technique and evaluation

Group A: Under full aseptic technique, local anesthesia was achieved with 10 ml of 2% lidocaine. 10- 12 Fr catheter was inserted percutaneous intra-pleural using Seldinger catheter technique (Catheter over wire) inserted into the mid-axillary streak through the fifth or sixth intercostal space.

Group B: The blunt dissection technique was used and chest tube (24-30 Fr) was inserted and the patient was connected to an underwater seal drainage system. The safe triangle is identified, prepped, and draped. Generous local anesthesia is utilized in the skin, musculature, and pleura. Insertion of the chest tube was done through the 5th of 6th intercostal space along the anterior or mid-

axillary line. Clamp used to dissect tissues after doing small incision in the skin. The chest tube is positioned and guided towards the apex of the hemithorax, secured to the skin and connected to the underwater seal drain.

All patients had a plain chest x-ray taken after the procedure to evaluate the location of the pigtail catheter/chest tube and also to evaluate any immediate complications requiring intervention such as pneumothorax. Pleural fluid samples were collected and sent for biochemical and cytological analysis. The drainage of pleural fluids continued for two hours. Drainage was withheld if the amount reached 1.5 liters prior to the 2-hour period. Pleurodesis was done when the drainage was less than 150 ml/24 hours and CXR showing complete lung expansion. Before injection of bleomycin, lidocaine (3 mg / kg; max. 250 mg) was injected intra-pleural through the drainage catheter. Pethidine (50 mg IV /IM) was also considered a premedication to alleviate anxiety and pain. Sixty units of bleomycin (4 vials) in 50 cc saline solution were inculcated throughout the catheter into the pleural space. After sclerosant administration the intercostal tube was clamped for 2 hours. The catheter was then unclamped and the amount of catheter drainage was recorded on a daily basis. The pigtail/intercostal tube was removed when the daily drainage is less than 150 ml/day and lung is expanded in CXR. After 30 days of pleurodesis, x-ray repeated and compared to the one pre-pleurodesis and post-pleurodesis. Post catheter insertion variables including pain VAS score, total hospital stay (days), duration from catheter insertion till initiation of pleurodesis, duration from catheter insertion till removal of it, complications (Fever, Pneumothorax, Cellulitis, nausea or dyspnea) and/or death during hospital stay and within 3 months.

Pleurodesis success was evaluated as follows: CXR shows no re-accumulation was considered complete success, CXR shows small amount of PF re-accumulation but patient is asymptomatic and did not require pleural drainage was considered as partial success, and Re-accumulation with symptoms and need to repeat pleural drainage was considered as failed procedure.

3. RESULTS

Table 1 showed matched age and sex distribution in both groups 59 year and 61 year respectively, male was 38(52.8%) patients in group A versus 36(62.1%) patients in group B. The results represented most common type of malignant effusion was lung cancer with prevalence of adenocarcinoma 38.9% in pigtail and 37.9% in other group then rest of lung cancer, squamous cell carcinoma, small cell lung cancer then large undifferentiated carcinoma 8, 6, 4 patients in group A, and 4, 4, 2 patients in group B, respectively . Mesothelioma, breast cancer, ovarian cancer, lymphoma and cancer prostate were presented in the groups, no stomach cancer in our study and only 2cases (2.8%) of hematological malignancies and osteosarcoma included in group A. Four cases of cancer colon in group B.

Table 1 Demographic distribution and type of malignancy between both groups

	Group A N=72	Group B N=58
Age, mean (range)	59 (51-67) year	61 (55-70) year
Gender		
Male	38 (52.8%)	36 (62.1%)
Female	34 (47.2%)	22 (37.9%)
Diagnosis		
Cancer lung		
Pulmonary adenocarcinoma	28 (38.9%)	22 (37.9%)
Squamous cell carcinoma	8 (11.1%)	4 (6.9%)
Large undifferentiated carcinoma	4 (5.6%)	2 (3.4%)
Small cell lung cancer	6 (8.3%)	4 (6.9%)
Mesothelioma	10 (13.9%)	4 (6.9%)
Cancer breast	4 (5.6%)	6 (10.3%)
Ovarian cancer	4 (5.6%)	2 (3.4%)
Lymphoma	2 (2.8%)	4 (6.9%)
Cancer colon	0	4 (6.9%)
Osteosarcoma.	2 (2.8%)	0
Cancer prostate	2 (2.8%)	6 (10.3%)
Cancer stomach	0	0
Hematological malignancies	2 (2.8%)	0

In Table 2, as regard patients outcome, significant difference was found between both groups, total hospital stay was 7.9±1.94 day in group A and 8.9 ±1.86 day, also time from drainage to pleurodesis was 4.35±1.27 in group A, 5.05±1.15 in group B. Time from pleurodesis to removal of catheter were lower in pigtail group than chest tube but without significant difference (1.85±0.81 in group A and 2.1±1.07), Fig (1). In the current study, successful pleurodesis is found in group A complete success 44.5%, and partial success 30.5% compared to 37.9% and 34.5% for complete and partial success in group B, failed pleurodesis was 25% in group A and 27.6% in group B, Fig (2).

Table 2 Post pleurodesis variables

	Group A N=72	Group B N=58	*P*-value
Total hospital stays (days) mean ± SD Range	8.7±1.94 (5-12)	8.9±1.86 (4-13)	0.06
Time from drainage to pleurodesis (days) mean ± SD Range	4.2±2.15 (2-7)	5.2±1.75 (2-7)	0.27
Time from pleurodesis to removal (days) mean ± SD Range	1.85±0.81 (1-4)	2.1±1.07 (1-5)	0.132
Pleurodesis outcome Complete success Partial success Failed pleurodesis	32 (44.5%) 22 (30.5%) 18 (25%)	22 (37.9) 20 (34.5) 16 (27.6%)	0.75

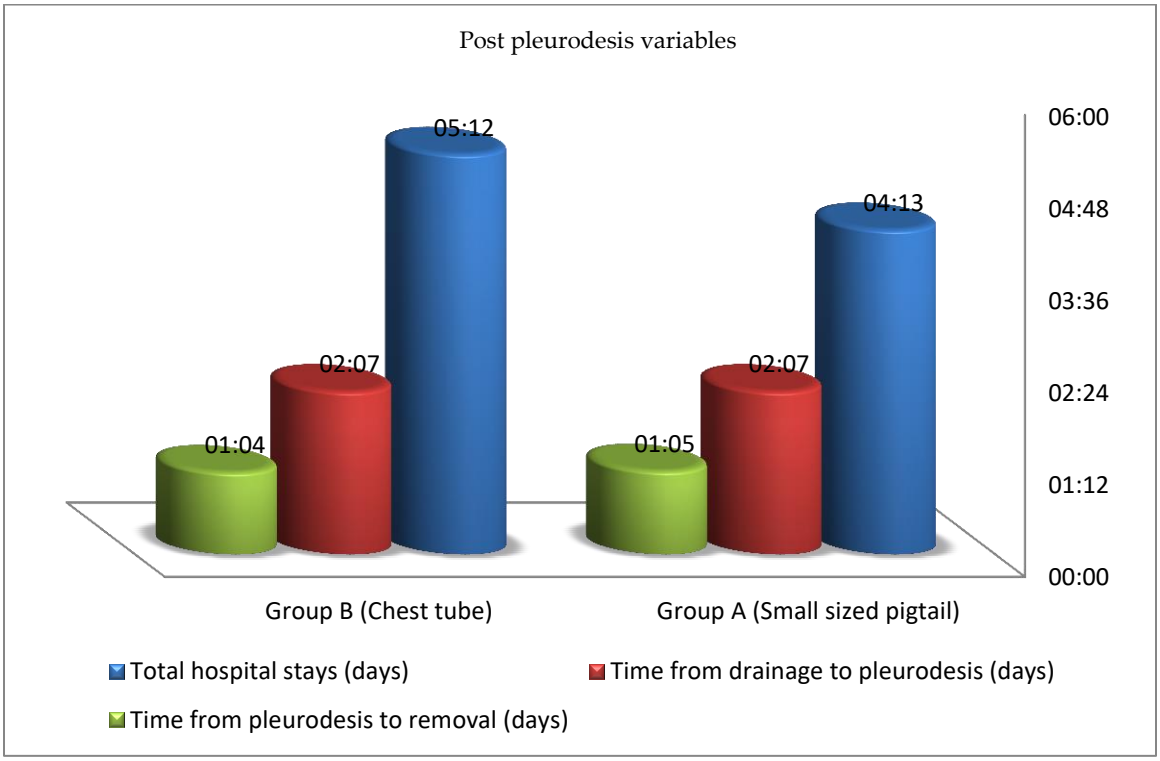

Figure 1 The post pleurodesis variables among Group A, and Group B.

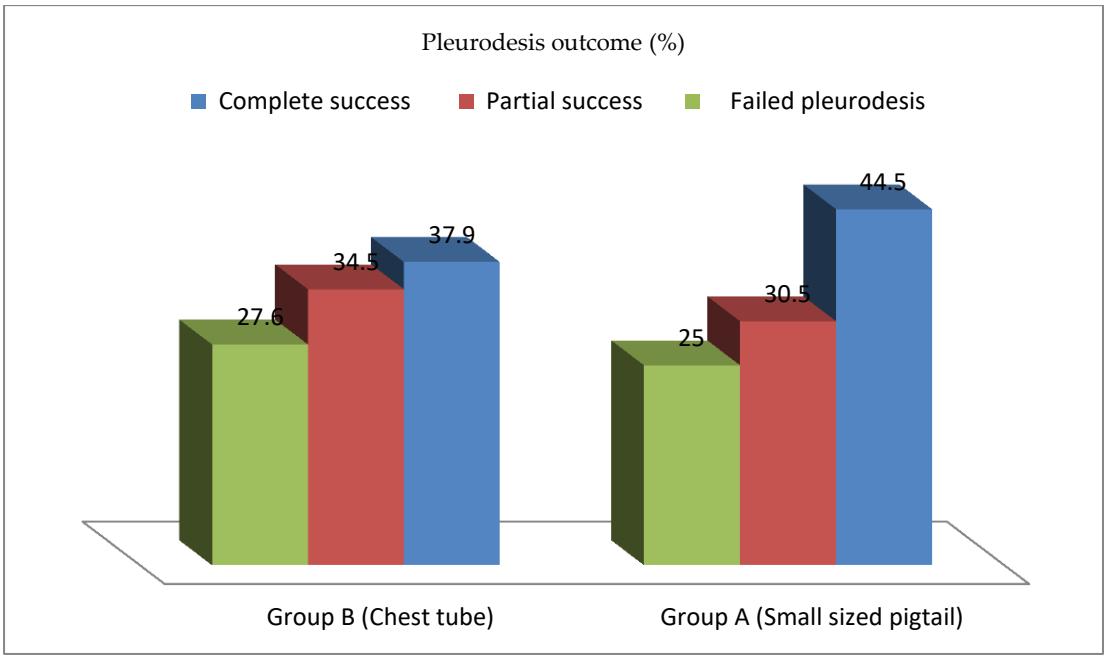

Figure 2 The pleurodesis outcomes among Group A, and Group B.

As shown in Table 3, complications of pleurodesis were less in pigtail group A, regarding dyspnea represented 11% in group A, and 24% in group B, also pain which assessed by visual analogue score (VAS) and it was 3.3 in group A and 5.1 in group B, (p value 0.02). Postoperative pain score and incidence of dyspnea were significantly less in group A than in group B. Table 4 explored pleural fluid analysis. It was comparable result without statistically significant difference; protein showed 3.5 ±1.3 g/dl and 3.6±1.4g/dl in group A and group B respectively, glucose 82 ±51mg/dl versus 88±49mg/dl, LDH was 1117±42 u/l in group A and 1112 ±48 u/l in group B, P value were >0.05 for all.

Table 3 Pleurodesis complications

	Group A N=72	Group B N=58	*P*-value
Visual Analogue Scale (VAS) score of pain	3.3± 1.02	5.1± 1.23	0.00*
Fever	20 (27%)	24 (41%)	0.1
Hypotension	4 (5%)	6 (10)	0.3
Pneumothorax	0	2(3%)	>0.99
Empyema	0	0	>0.99
Dyspnea	8 (11%)	14 (24%)	0.05*
Death	4 (5%)	6 (10%)	0.3

Table 4 Characters of pleural fluid effusion

	Group A	Group B	*P*-value
protein	3.5±1.3g/dl	3.6±1.4g/dl	0.67
glucose	82±51mg/dl	88±49mg/dl	0.49
LDH	1117±42 u/l	1112±48 u/l	0.75

4. DISCUSSION

The prognosis for a patient having malignant pleural effusion is fairly bad, with about ten to fifteen percent remaining alive after 1 year, and might be greatest within bronchial carcinoma as well as breast cancers (Dey et al., 2010). Chemical pleurodesis consider a comforting cure targeting obliteration of the pleural space. At a cellular level, mepacrine had an unknown influence, but it was found to induce a chemical pleuritis that results in adhesions and obliteration of the pleural space. On the other hand, bleomycin

was found to make inhibition to the synthesis of protein and DNA, nevertheless, pleurodesis is supposed to be caused by a distinct inflammatory reaction with secondary fibrosis. It was suggested that, a local cytotoxic influence might participate in the mechanism of action according to the fact that among patients who have primary tumors that respond to systemic bleomycin, effusion often responds to intra-pleural therapy by that medication (Rafei et al., 2015).

The demographic data of the current study revealed that malignant pleural effusion was more frequent in elder patients as the average age patients were around 60 years in both groups, and male patients were more than female patients in both groups. These results were in agreement with the results of Rafei et al., (2015) and Mendes et al., (2018) who revealed that the average age was 58.9 and 67 years, respectively, and this can be explained as malignant pleural effusion is age-related malignancy. In the current study, adenocarcinoma was the most common type of lung cancer of malignant effusion as it showed the highest prevalence in both patient groups but it was higher in group A (pigtail system) than group B (chest tube system) (38.9 % and 37.9 %, respectively), followed by mesothelioma and breast cancer in group A (13.9 % and 5.2 %), and breast cancer and prostate cancer in group B (10.3 % for both).

This was in agreement with several studies where lung cancer showed the uppermost percentage of affection. Likewise, a study in Iran in 2012 showed that lung cancer incidence was 55% followed by breast cancer 20% in the total number (Firoozbakhsh et al., 2012). Also, the study by Rafei et al., (2015) found that, the lung cancer prevalence was 41.9%, and adenocarcinoma was the most commonly occurred (30.6%) followed by breast cancer (17.7%). In addition, Mendes et al., (2018) revealed that pulmonary adenocarcinoma of lung cancer was of higher incidence in 31 (50.8 %) followed by breast cancer (8.2%).

In contrast, one study in our locality was conducted by Ghoneim et al., (2014) found that the incidence of breast cancer was higher (34%) than lung cancer (32 %), while the incidence of breast cancer in the current study was 5.6 % in group A and 10.3 % in group B, which may be explained by the fact that there are services in our locality for early diagnosis of breast cancer that could cause a decline in the number of cases of breast cancer. The patients' outcomes of pleurodesis in this study were better with the pigtail drainage system than the chest tube drainage system in spite of no statistical significance was found between the two groups in terms of total hospital stay, the time from drainage to pleurodesis, and the time from pleurodesis to removal of catheter that were lesser in pigtail group than chest tube, which is greatly beneficial as less days means less cost and less complication revealing the superiority for pigtail upon chest tube drainage system.

These findings were harmony with the findings of Aktürk et al., (2017) as the total hospital stay duration was lesser in small bore catheter drainage system thanin large bore catheter system with no statistical significant difference. In addition, the post catheterization stay length was significantly lower in small catheter group than large catheter group of pleurodesis (3.5 days vs. 5.4 days) respectively (Aktürk et al., 2017). Conversely, another study by Mendes et al., (2018) found that thetime of hospital stay as well as the time after drainage in chest tube drainage group was lesser than pigtail group with no statistical significance, but the limitation of that study was that the patients' number was not equal in both groups as chest tube group was 46 patients and small catheter group was 15 patients which could affect the results. Pleural fluid chemical analysis showed no significant difference in both groups as they have the same lesions, which represent exudative effusion not varied a lot. These results were in agreement with Ghoneim et al., (2014).

In terms of the current study's pleurodesis outcome, complete successful pleurodesis was higher in pigtail group than in chest tube group (44.5% vs. 37.9%) respectively, while partial success as well as failure in pleurodesis was lower in pigtail group than in chest tube group (30.5% vs. 35.5) and (25% vs. 27.6%) respectively but the difference was statistically insignificant. The study by Rafei et al., (2015) reported different results: 17.7% complete success, 12.9% partial success, and 40.3% failure in pleurodesis, this lower results of success refers to the loss of about a quarter of the patients in his study in the follow up, and thus the patients' number was greatly decreased and affected the end results. Also, by analyzing the success of pleurodesis by different sclerosing agents; bleomycin was 37.5% success and 12.5% for talc and tetracycline (Rafei et al., 2015). Likewise, an Egyptian study has reported a success rate, in the same locality, of 66% in pigtail group against 54% in chest tube group, and tetracycline was used in their study; however, the result of the current study was better (Firoozbakhsh et al., 2012).

Different results have been reported by Aktürk et al., (2017) where the success rate for small catheter drainage system was lower compare to large catheter drainage system (83% vs. 86%). This slight difference may be due to the number of cases involved in their study. Firoozbakhsh et al., (2012) also have informed 80% and 81% success rates for small and large catheter pleurodesis, respectively. In Tiwan, one study had a near number where the global success rate was 77% (Chen et al., 2000). Complications of the pleurodesis; Pain and Dyspnea in the current study were lower in pigtail group than chest tube group with significant difference. No empyema was reported between both groups. Chest pain score was measured by VAS, and it had a highly statistically significant lower value in pigtail group than chest tube group *(*p value=0.02*)*.

The results of the current study are in agreement with several studies (Sartori et al., 2004; Ghoneim et al., 2014; Rafei et al., 2015; Mendes et al., 2018; Chang et al., 2018) who showed lesser pain score in small-bore catheter group (pigtail) than large-bore catheter group. In their research, Hamad and Alfeky (2021) found also that small bore drainage catheter (pigtails) is an alternative to a traditional chest tube for pleural effusion drainage. It also has the benefits of mobility in terms of insertion site as well as suitability and protection in potentially risky conditions such as bleeding or damage to vascular systems, as well as a very thick chest wall.

5. CONCLUSION

The chemical bleomycin pleurodesis with small pore catheter (Pigtail) in malignant pleural effusion is effective, more patient-tolerable, and more advantageous than the use of large-bore catheters especially for pain tolerance and lower hospitalization time that reduces the hospitalization costs. We therefore consider the use of the pigtail drainage system rather than a chest tube in the treatment of malignant pleural effusion.

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This study has not received any funding.

Conflict of Interest

The authors declare that there are no conflicts of interests.

Informed consent

Written informed consent was obtained from all individual participants included in the study.

Ethical approval

The study was approved by the Faculty of Medicine's research ethics committee, Zagazig University (ZU-IRB# 6587).

Data and materials availability

All data associated with this study are present in the paper.

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