

The outcome of Pleurodesis in Malignant Pleural Effusion

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Abstract:

Background: Accumulation of fluid in the pleural space, which is malignant in nature, is secondary to lung, breast or ovarian tumors. Malignant effusion secondary to metastatic Adeno Ca is most commonly seen in males and breast Ca is most commonly seen in females. It indicates advanced disease and reduced survival.

Objectives: Is to study prospectively the outcome of pleurodesis in thirty patients with malignant pleural effusion by using two different agents Bleomycin and Talc.

Patient and methods: Data of thirty patients with malignant pleural effusion collected and analyzed using a form to categorize them according to their age, gender, presenting features, imaging studies and procedure performed to drain the fluid and to arrange chemical pleurodesis.

Results: Eighteen patients were male; twelve patients were female in a ratio of 1.5:1. The youngest was 52 years old while the oldest was 81 years old. The mean age was 65.8 ± 7.34 . Cough and dyspnea were the most frequent presenting features. Imaging studies showed that eleven patients had left sided effusion with an underlying mass. Eight patients had right sided effusion with an underlying mass while the remaining eleven patients had effusion only. Twenty patients received (Talc) and ten patients received (Bleomycin) with comparable recurrence rate of the effusion, in seven patients out of 20 in Talc (35%) and in three out of 10 patients receiving Bleomycin (30%).

Conclusion: Both (Talc and Bleomycin) can be used with comparable results and recurrence

Key words: pleurodesis, malignant effusion, Bleomycin, Talc

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Introduction:

Malignant pleural effusion (PE) is a condition in which cancer causes an abnormal amount of fluid to collect between the thin layers of tissue (pleura) covering the outside of the lung and the wall of the chest cavity. Lung cancer and breast cancer account for about 50-65% of malignant PE. Other common causes include pleural mesothelioma and lymphoma. [1] Neoplasms of the lung, breast, ovary, and lymphomas constitute more than 75% of cases of malignant PE [2]. Metastatic adenocarcinoma is the most common type. Lung cancer in male patients. Breast cancer in female are the most common underlying cause. A positive pleural effusion for malignant disease reflects an advanced

stage and in- operability for surgery. Involvement of the lymphatic drainage system by malignancy is the primary mechanism by which pleural metastases cause PE. This leads to the accumulation of the fluid which normally leaves the pleural space [3] Signs and symptoms of a PE vary depending on the underlying disease, but dyspnea, cough, and pleuritic chest pain are common. Chest X-ray usually confirms the presence of a PE, but if doubt exists, ultrasound or computed tomography (CT) scans are definitive for detecting small effusions and for differentiating pleural fluid from pleural thickening. [4] Except for patients with obvious heart failure, thoracentesis should be performed in all patients with more than a minimal PE of unknown origin (i.e., larger than 1 cm height on lateral decubitus radiograph, ultrasound, or CT). Analysis of the pleural fluid yields valuable diagnostic information or definitively establishes the cause of the PE. [5]. Cytology is positive in approximately 60 percent of malignant PE [6]. CT findings suggestive of malignant disease are the presence of pleural nodules or nodular

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pleural thickening, or infiltration of the chest wall or diaphragm. Positron emission tomography seems promising for differentiating between benign and malignant pleural diseases (sensitivity 97 % and specificity 88.5 % in one study) [7]. The process by which the pleural space is obliterated by inflammation induced through chemical or mechanical means, to achieve definitive and long-standing pleural apposition with fibrosis is name pleurodesis. Many agents have been described for chemical pleurodesis including Talc powder, Bleomycin, tetracycline, doxycycline, silver nitrate, iodopovidone, quinacrine, interferons, interleukin 2, and several chemotherapeutics [8] Bleomycin is the most widely administered antineoplastic agent with a success rate of 60–80%. Tetracycline and doxycycline are also commonly used for pleurodesis and have similar clinical success rates, although they are associated with intense pleuritic pain [9]. Talc, although talc is the most effective pleurodesant, it is not without complications with rare reports indicating that the incidence of acute respiratory distress syndrome (ARDS) can be as high as 1–9% due to intense pleuritis [10]

Patients and Methods:

Study type and setting: A prospective study of thirty patients who were referred to the Thoracic and Vascular Department of the Surgical Subspecialties Hospital (Ghazi Al-Hariri Hospital) with malignant PE, for chemical pleurodesis, or admitted to the Department with Pleural effusion, cytology of which turned to be malignant in nature so planned for pleurodesis.

Study design: the data were taken from the patients' files, and analyzed in relation to age, gender, presenting features, imaging (ultrasound, chest X-ray, and computerized tomography), procedure performed and the results of the obtained cytology.

Study period: the data were collected for a period of seven months, from the first of February 2019 until 31 August 2019.

Ethical considerations: The study was approved by the Iraqi Board for Medical

Specializations in Thoracic and Cardiovascular Surgery. All participants were informed about the study and a verbal consent was taken from each one of them or their families if they were unable to do it.

Interventional Methods: The pleural effusion was drained by tube thoracostomy under local anesthesia in the safety triangle, in the surgical ward or the theater, by aseptic condition by the senior residents or on call surgeon. The patients were kept in the ward until all the fluid was drained or were discharged with drain in place till full drainage. After total evacuation was achieved .The pleurodesis considered and usually done with sclerosant agents. We used Bleomycin (30mg in 50 cc normal saline) and talc (3g diluted in 50cc normal saline and xylocaine added for pain relief) .The tube was clamped for 4-6 hours , de-clamped for 4-6 hours under suction then the tube is removed, and patient is discharged home.

Statistical analysis:

Data management was done by the use of IBM© SPSS© (Statistical Package for the Social Sciences) Statistics Version 23.

The Chi-square was used for analyzing categorical data, and the independent samples T-test was used for numerical and normally distributed data. The Binary logistic regression model was used for predicting odd's ratio for recurrent PE. All analyses were done with 95% confidence intervals (CI). P-values less than 0.05 were considered statistically significant.

Results:

There were 18- males representing 60% of the study sample, 12 females (40%) were females. The youngest patient was 52 years old, the oldest patient was 82 years old, both were males .The mean age of the study sample was 65.8 ± 7.43 years. The distribution of the study sample according to age and gender is illustrated in Figure (1).

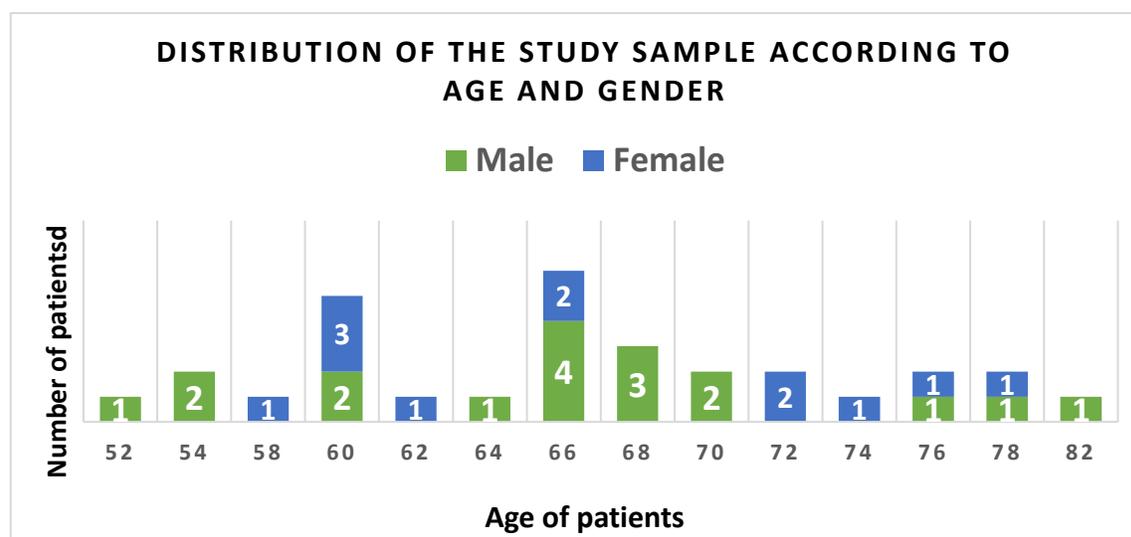


Figure 1: the study sample according to age and gender

Ten of our patients, (33.3%), were already diagnosed with malignant PE, while the remaining 20 were diagnosed through the course of the study. The most frequent presenting complaint was cough associated with dyspnea in 17 (56.7%) patients. Most of the patients were active or ex-smokers, as shown in Table (1)

Table (1): Distribution of the patients by presenting complaint and past medical history of the study group

Variables	Number	%	
Presenting complaint	Cough and Dyspnea	17	56.7
	Dyspnea	11	36.7
	Dyspnea and chest pain	2	6.7
Smoking	Current smoker	16	53.3
	Ex-smoker	9	30.0
	No	5	16.7

All patients were sent for chest X-ray, U/S, and CT scan, which revealed that 11 (36.7%) had left sided mass and effusion, eight (26.7%) had right sided mass and PE, while the remaining 11 (36.66%) patients showed effusions with no detectable mass by imaging. The ultrasound study revealed that males had slightly lower aspirated fluid compared to females, as males had a mean of 1611.1 ± 699.5 ml, compared to 1700 ± 555.9 ml in females. Lower values were observed in metastatic Adeno Ca (MAC), and the talc group as shown in table (2).

Table (2): distribution of the volume of the pleural fluid aspirated according selected variables

Gender	Mean \pm SD	
Female	1700 ± 555.9	0.715*
Male	1611.1 ± 699.5	
Histology	Mean \pm SD	P-value
SCC	1783.3 ± 767.9	0.329
MAC	1613.5 ± 628.3	
MM	1600**	
Type of drug used for pleurodesis	Mean \pm SD	P-value
Bleomycin	1810.0 ± 744.5	0.576
Talc	1565.0 ± 579.7	
Recurrence	Mean \pm SD	P-value
No	1650 ± 610.9	0.969
Yes	1640 ± 721.4	

*: Independent samples T-test, **: Chi-square test

Twenty -patients received talc injection 66.667% of the study group, while the remaining 10 patients received Bleomycin. The latter group was significantly older, but there was no gender or recurrence risk difference (Table 3)

Table (3): Age, gender and recurrence in relation to drug used for pleurodesis

Variables	Talc	Bleomycin	P-value
	Mean \pm SD	Mean \pm SD	
Age	63.65 ± 5.93	70.2 ± 8.47	0.020*
Gender	No. (%)	No. (%)	
Male	13(65.0)	5 (50.0)	0.774**
Female	7 (35.0)	5 (55.0)	
Recurrence	No. (%)	No. (%)	
No	13 (65)	7 (70)	0.999**
Yes	7 (35)	3 (30)	

Total No	20	10	-
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*:Independent samples T-test **: Chi-square test

Recurrence of effusion after pleurodesis in 10 patients (33.3 %)

Further analysis using binary logistic regression revealed that the recurrence was not related to gender, type of injection, smoking or alcohol consumption. It was inversely correlated with age, with younger patients being more likely to develop recurrence. As shown in Table (4), where the odd's ratio represents the increasing the risk of recurrence.

Table (4): risk stratification of recurrent pleural effusion after chemical pleurodesis

Variables	Odd's ratio	Lower 95% CI	Upper 95% CI	P-value
Age	0.775	0.646	0.930	0.006
Gender	3.408	0.458	25.366	0.231
Talc injection	1.034	0.129	8.312	0.975
Smoking/Alcohol*	0.301	0.071	1.285	0.105

Binary logistic regression, *: alcohol was combined with smoking due to small numbers

(46.7%) of our patients had lung cancer, (26.7%) had unknown primary tumor location, (16.7%) had breast Cancer, (6.7%) had colon Cancer and only one case (3.3%) had Malignant Pleural Mesothelioma.

Three patients (10%) developed local wound infection after thoracostomy tube insertion, were treated by daily dressing and anti-biotic based on culture results. No mortality was seen in our study.

Discussion:

The age distribution and the male: female ratio of the patient in the current study contradicts the results of Zakaria (2018) in Iraq who studied 30 cases of malignant PE admitted to Ibn Al- Nafees Teaching Hospital. He reported that most patients were between 50-60 years of age with 60% of them were females; which was attributed to the fact that AL-Amal Hospital(close to ibn al nafess hospital) which contributes to 53.3 % of the patients, referred the majority of advanced breast cancer cases (11). In a study by Nikbakhsh et al (2011), studied 51 cases of malignant PE in Iran, and reported that their mean age was 60.3 ± 15.8 years and 62% of them were females, and 40% of cases had breast cancer (12). The Iraqi Cancer Registry reported in 2009 that breast cancer was responsible for 19.6% of the cases of PE followed by bronchogenic cancer that was responsible for 10 % of cases (13). All of our patients suffered from dyspnea, which in 56.7% of the cases was associated with cough, and in 6.7% was associated with chest pain. This was comparable with results of Rafiei et al (2014) in Iran who studied 42 cases with malignant PE, and reported that 90.5% of patients presented with dyspnea (14). Some patients may initially be asymptomatic, but eventually the majority will develop dyspnea, that

requires treatment to alleviate symptoms (15). The mean volume of pleural fluid aspirate in our study was 1646.7 ± 637.2 ml, and the amount had no statistically significant differences between genders, histology of tumors, type of drug used for pleurodesis and recurrence. This amount was lower than results of Nikbakhsh et al (2011), in which the mean amount of pleural fluid was 2282 ± 848.69 ml, and was not related to outcome of pleurodesis [12]. In another study done by Lumachi et al in Italy (2012), who studied factors affecting the survival of patients having talc pleurodesis, reported the mean volume of PE was 2005.7 ± 1078.9 ml, and that it was not related to the survival of patient (16). Options to relieve dyspnea resulting from malignant PE may include, therapeutic pleural aspiration, drainage and injection of sclerosant agents or thoracotomy. If a sclerosing agent is too used, complete drainage of the PE is very important to increase success rate of the procedure, so the treatment should be tailored for each patient, and the amount is highly individualized, so it is quite difficult to compare between different study populations (17-18). The recurrence rate of malignant PE in our patients who treated with talc was 35%, while for those who treated with Bleomycin it was 30%. The recurrence rate from other studies is shown in the table 5:

Table (5): The recurrence rate in different studies

Author	Place/ date	Type of sclerosant	Recurrence Rate
Diacon et al (19)	Switzerland/ 2000	Talc vs bleomycin	Talc group (13%) after one month and (13%) after six months Bleomycin group (41%) after one month and (65%) after six months
Haddad et al (20)	Brazil/ 2004	Talc vs bleomycin	Talc group (9.8%) after one month and (27.8%) after six months Bleomycin group (12.4%) after one month and (32.2%) after six months
Saka et al (21)	Japan/ 2018	Talc vs bleomycin	Talc group (12%) Bleomycin group (16.7%)
Our study	Iraq/2020	Talc vs bleomycin	Talc group (35%) Bleomycin group (30%)

It can be seen from the table above that talc was superior to Bleomycin in reducing recurrence of PE, in the first three studies which was in contradiction to our results. The primary cause for this discordance was the use of Talc powder by video assisted thoracoscopic surgery (VATS) in most of the patients in the studies, which is not a routine procedure in our country. More than quarter of our patients had Ca lung, (26.66%) with unknown primary tumor location, while Zakaria M did not report any case with unknown primaries (11). This could be attributed to the fact that our patients with unknown primary tumor location, then had other

investigations to discover the primary tumor site, and this was comparable with the results of Ebata et al in Japan (2015) who investigated patients presenting with malignant PE as a first cancer diagnosis, and reported that 28.9% had unknown primary, and that malignancy of the lung was the most common primary tumor in those patients after further investigation/surgeries (22). In another study done by Clive et al (2014) multi-center study, the reported details for possible primaries causing malignant PE were breast and lung cancer (23). Post thoracostomy site wound infection, happened in 3 of our patients (10%), while the (Ebata T. et al 2015)(22) ,showed three patients out of 100 patients (3%) were treated for wound infection. No mortality was seen in our study which is similar to the results of (Clive AO. et al 2014) (23) .

Conclusion:

Both (Talc & Bleomycin) can be used with comparable results and recurrence rate.

Recommendations:

The future use of VATS with patients, who can tolerate the procedure (plurodesis), allows the increasing use of talc powder and decreases the recurrence rate.

Conflict of interest:

None

Author's contributions:

Waleed M. Hussien: contributed to study conception, study design, data analysis and interpretation, drafting of the manuscript.

Ali H. Said, Osama Elhassani: contributed to study conception, study design data analysis and interpretation,

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نتائج الالتصاق الجنبى في انصباب الجنب الخبيث

الاستاذ المتمرس الدكتور وليد مصطفى حسين كلية الطب / جامعة بغداد
الجراح الاختصاصى الدكتور علي هاشم سيد مستشفى بغداد التعليمي
المخدر الاستشاري الدكتور اسامه حيدر الحسني مستشفى بغداد التعليمي

المقدمة: تراكم السوائل في التجويف الجنبى، وهو خبيث في الطبيعة، ثانوي لأورام الرئة والثدي أو المبيض. ويعتبر الورم الغدي الثقيل الأكثر شيوعاً في الذكور وورم الثدي الأكثر شيوعاً في الإناث. إنه يشير إلى تقدم المرض وانخفاض نسبة النجاة.

الهدف: هو الدراسة المستقبلية لثلاثين مريضاً يعانون من الانصباب الجنبى الخبيث الذي تم اجراء لهم عملية التصاق جنبى كيميائى.

المرض والطرق: تم جمع وتحليل بيانات ثلاثين مريضاً يعانون من انصباب جنبى خبيث وتحليلهم باستخدام نموذج لتصنيفهم وفقاً لعمرهم ونوع الجنس والاعراض السريرية والتصوير الشعاعى والإجراءات التي تم إجراؤها لسحب السوائل وترتيب الالتصاق الجنبى الكيمايى

النتائج: ثمانية عشر مريضاً من الذكور. اثنا عشر مريضاً من الإناث بنسبة 1.5 : 1. كان أصغرهم يبلغ من العمر 52 عاماً وكان الأكبر عمره 81 عاماً. كان متوسط العمر 65.8 ± 7.34 . كانت أكثر الاعراض شيوعاً هي السعال وضيق التنفس. أظهرت دراسات التصوير الشعاعى أن أحد عشر مريضاً يعانون من انصباب جنبى أيسر مع ورم في الرئة. وكان ثمانية مريضاً يعانون من انصباب جنبى ايمن مع ورم في الرئة. بينما كان لدى المرضى المتبقين انصباب فقط. تم اجراء عملية الالتصاق الجنبى الكيمايى باستخدام (Talc) لعشرون مريضاً وتم اجراء عملية الالتصاق الجنبى الكيمايى باستخدام (Bleomycin) لعشرة مريضاً. بمعدل مقارب لتكرار الانصباب بينهما.

الخاتمة: ان معدلات التكرار بالانصباب كانت مقاربة في استخدام كل من (Talc & Bleomycin)

مفتاح الكلمات: الالتصاق الجنبى، الانصباب الخبيث، البليوميسين، التلك