Tetracycline Pleurodesis for Malignant Pleural Effusion- A Retrospective Review of 20 Cases

DR OGBUDU S O[1], ECHIEH C P[2], NWAGBOSO C I[3], EZE J N[4], DIEN E O[5], ETIUMA A U[6], OGBUDU H E[7]

[1, 2, 3, 4, 5, 6]*Division of Cardiothoracic/vascular Surgery, Department of surgery, University of Calabar Teaching Hospital. Calabar-CRS*

[7]*Department of Surgery, College of Medical Sciences, University of Calabar, Calabar, Nigeria*

Abstract- INTRODUCTION:

OBJECTIVE: Report our experience with the use of tetracycline for pleurodesis in the management of malignant pleural effusion and reasons for failed pleurodesis.

METHOD: All patients 18 years and above with malignant pleural effusion were all included in this prospective study except those with cardiac failure and malignant pleural effusion were excluded, Pre-treatment assessment was performed during admission and it include history and physical examination, full blood count, and a pre-drainage posterior anterior and lateral radiograph.

A thoracic catheter (sizes24f-32f) was inserted in the mid axillary line through the 5th or 6th intercostal space under local anaesthesia. In some cases, additional intravenous analgesics were administered. The pleural effusion was drained by gravity using under water sealed drainage. Massive pleural effusion was drained gradually. An initial drainage was a controlled drainage with a clamp until patient experience some chest discomfort. Subsequently 5mlskg^{-1}/hr and temporally suspended if patient experience chest discomfort, but not chest tightness nor difficulty in breathing and cough

Daily chest tube outputs were recorded and when drainage fell below 100mls/24hrs, posterior anterior/lateral radiographs were obtained to ensure that the fluid has been sufficiently evacuated, no loculated collections and the lung judged to be fully re-expanded then the patient were eligible for pleurodesis. Clinical response is evaluated according to Paladine's criteria (FIG 1):

Complete response (CR): fluid do not accumulate during the first 30days

Partial Response (PR): Recurrence of small amount of effusion which does not need tube drain

No response (NR): Recurrence of effusion which needs to be evacuated

In malignant empyema thoracis pus is drained till it is serous and culture negative for at least on two occasions. The same principle is applied to patients with Para malignant pleural effusion

The solution for pleurodesis consists of 3mg/kg of 2% lidocaine made up to 50mls with normal saline. Tetracycline powder is obtained from tetracycline capsules at 35mg/kg but not exceeding 2g and dissolve in this solution of lidocaine and normal saline, this solution will be drawn into a 50mls syringe and instil into the pleural cavity through the chest tube, the chest tube will be clamp for two hours and unclamp thereafter, If the post sclerotherapy drainage is below 100mls/24hours the chest tube is remove but if drainage is ≥5mls/kg pleurodesis is repeated

Complicated related to the procedure will be recorded. Posterior anterior and lateral chest radiographs will be done after removal of the chest tube in order to compare with the film that will be done in 30days time.

Clinical response will be evaluated according to Paladine's criteria and adverse reactions will be recorded.

RESULTS: Between 1st February 2020 and 28th February, 2023 20 cases of malignant pleural effusions were drained and pleurodeses with tetracycline.

The male female ratio was 1:10, the age ranges from 35-77years with an average age of 48.55years. Breast carcinoma account for 80% while ovarian carcinoma account for 10% while, liver cell carcinoma (PLCC), soft tissue sarcoma and thyroid carcinoma account for 5% each. Eighteen patients responded constituting 90% success while two patients had partial respond constituting 10%

failure. Right and left malignant effusion account for 50% each. All our patients presented with dyspnoea 100%, eighteen (90%) presented with chest pain and cough and 80% presented with generalised malaise and weight loss (Table 1). Two (10%) with ovarian carcinoma in addition to pleural effusion also presented with massive ascites. Carcinoma of the breast account for massive pleural effusion(2000mls-5000mls), followed by ovarian carcinoma and sarcoma(2600mls-4250mls). There are mostly serous effusions, while PLCC and Thyroid carcinoma account for mild to moderate pleural effusion and haemorrhagic and took longer time to drain(1200mls-3000mls). Dyspnoea was more severe in patients with Ovarian carcinoma may be from the ascites. The Numerical Rating scale for pain (NRS) post pleurodesis range from 5-8/10 and nearly all the patients require additional analgesics for pain management. Patient's performance status was accessed using Eastern Clinical Oncology Group (ECOG performance status). Two (10%) patients have an ECOG score of 1 while sixteen patients (80%) have an ECOG score of 3 and 2 (10%) with an ECOG score of 2. Metastases with pleural effusion is common in the age range 31-40years followed by 51-60years and same in the age range 41-50years and 71-80years, least in the age range 61-70years.

CONCLUSIONS: Tetracycline is effective in pleurodesis of malignant pleural effusion

Index Terms- Tetracycline, Pleurodesis, Malignant Pleural Effusion, Malignant Empyema Thoracis, Para Malignant Pleural Effusion, Evacuated and Lung Expansion.

Table 1: Distribution of symptoms of MPE

Symptom	*Number of Patient*	*Percentage %*
Dyspnoea	*20*	*100%*
Chest pain	*18*	*90%*
Cough	*18*	*90%*
Generalised malaise	*16*	*80%*
Weight loss	*16*	*80%*
Ascites	*2*	*10%*

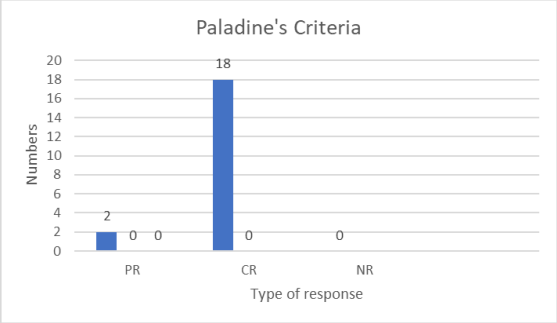


FIG 1 Paladine's Criteria

I. INTRODUCTION

Pleural effusion in the presence of malignancy may suggest malignant pleural effusion or Para malignant effusion, malignancy causes 13%-40% of all pleural effusions and responsible for 70% of all massive pleural effusions[1]. Pleural effusion develops in nearly half of all patients with metastatic cancer. Bronchogenic and breast carcinoma is responsible for 50-65% of malignant pleural effusions in both sexes with bronchogenic carcinoma as the most common metastatic tumour to the pleura in male and breast carcinoma in female. The remaining 25% representing a cross section of other neoplastic diseases while less than 15% of malignant pleural effusion are of unknown origin[1,2]. Only 40-80% of pleural fluid cytology is positive for malignancy[3]. The presence of malignant pleural effusion usually indicates metastatic or advanced disease with an uncertain life expectancy[1,4] majority of patients with malignant pleural effusion are symptomatic, up to 25% are asymptomatic with an incidental finding on clinical examination or on chest radiography[5] Dyspnoea is the most regular presenting symptoms, reflecting lung collapse with impair chest wall compliance and ventilation perfusion mismatch

Treatment options for malignant pleural effusion are tailored toward the primary cause of the effusion but are mainly palliative[6]. Malignant pleural effusions are effectively managed with complete drainage and fusion of the pleura with either observation, mechanical abrasion, therapeutic pleural aspiration, thoracoscopy drainage with abrasion or instillation of a sclerosant, placement of an indwelling thoracic catheter and intercostal tube drainage with instillation of a scleroscant[7]. Pleurodesis is achieve through

diffuse inflammatory reaction and local activation of the coagulation system with fibrin deposition. The most important requirement for successful fusion of the pleura is complete drainage, full lung re expansion and apposition of the pleura confirmed radiologically. Incomplete lung re expansion may be due a thickened visceral pleura, space occupying lesions such as loculation of effusion, persistent air leak and major airway obstruction[7,8.] An ideal sclerosing agent must possess several qualities such as high molecular weight and chemical polarity, low regional clearance, rapid systemic clearance, a steep dose response curve, and non-allergic agent but well tolerated with minimal or no side effects. The choice of a sclerosing agent will be determined by the efficacy of the agent, accessibility, affordability, safety, ease of administration and numbers of administration to achieve cure must be few but till date no ideal agent exist[4] Tetracycline, talc and bleomycin are considered as primary sclerosing agents[9]

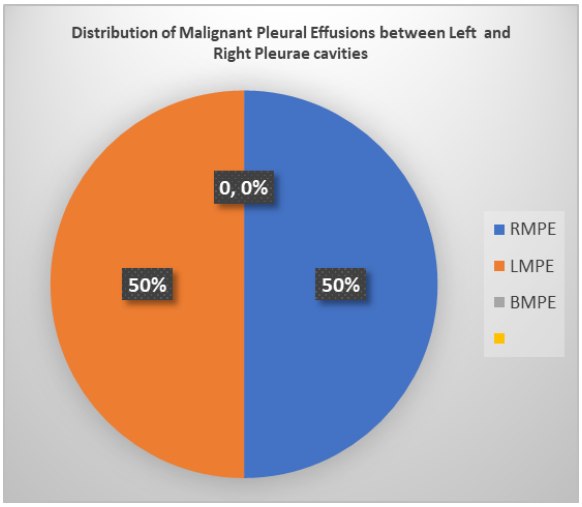
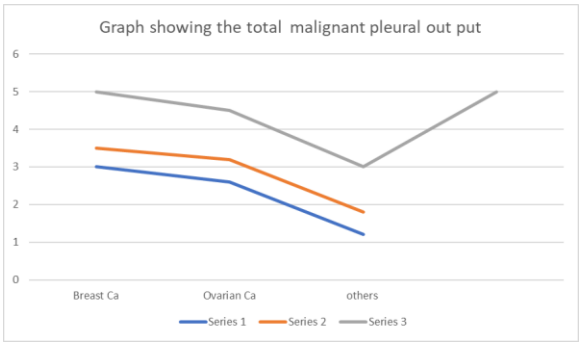
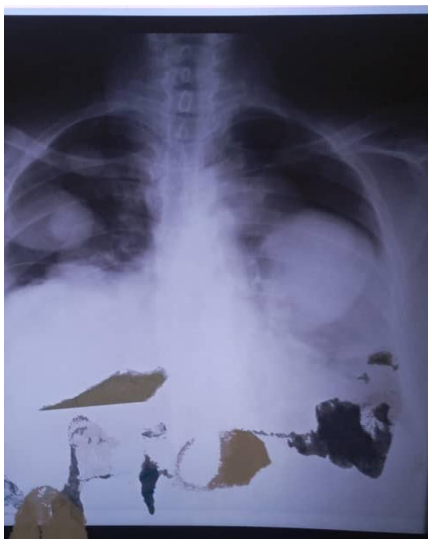
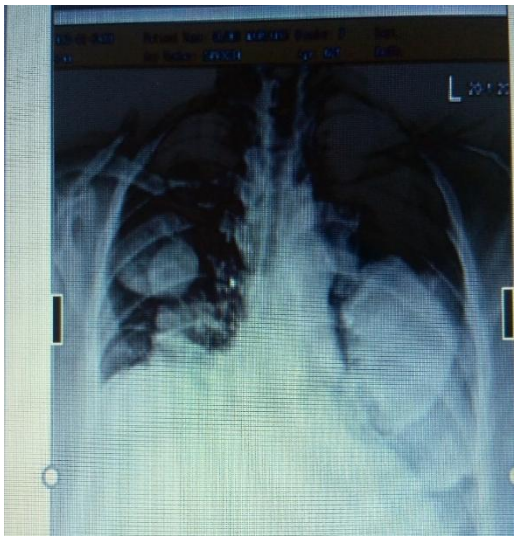


FIG 1: Distribution of Malignant Pleural effusion





Pre chest tube intubation



Post drainage /Post Pleurodesis

II. DISCUSSION

Malignant pleural effusion is a complication of end stage malignancy with a significant impact on the quality of life[1,2,3] the primary management of malignant pleural effusion is to give symptomatic relief, reduce reoccurrence of effusion and recurrent hospitalization. There are different treatment options for patients with malignant pleural effusions; including repeated Pleurocentesis, tube thoracostomy, long term indwelling catheter drainage, pleuroperitoneal shunt, pleurectomy, chemotherapy and radiotherapy or a combination of these. The choice of treatment

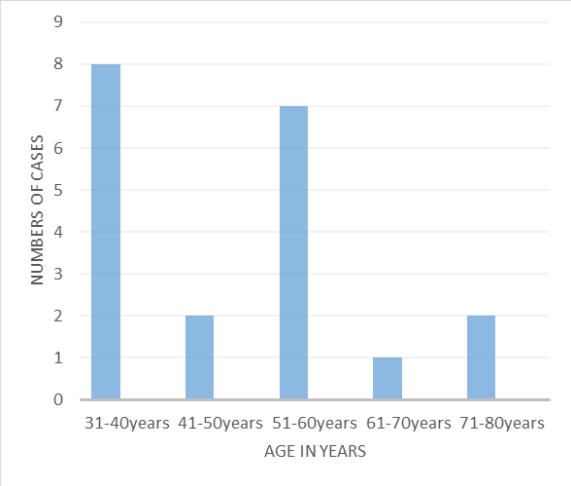


FIG 2 Age distribution of patients with malignant pleural effusion

is determined on the basis of patient's performance status (using ECOG performance status) and the state of the underlying lung[3,4] pleurodesis offers patients with malignant pleural effusion palliation of symptoms by fusion of the pleura that prevent re accumulation of the malignant pleural effusion[10]

The aim of this study is to report our experience with the use of solution of tetracycline for pleurodesis in the palliative management of malignant pleural effusion and reasons for failure. Dyspnoea was the regular presenting symptom in patients with malignant pleural effusions in this study. This is also reported in other studies[3,7,11-14] dyspnoea usually occurs because of a combination of impaired chest wall compliance, lung collapse/underlying lung condition, flattening of ipsilateral diaphragm and ventilation perfusion mismatch

Twenty patients participated and completed this study. The results showed that 18 of 20 patients (90%) had successful pleurodesis with tetracycline solution through indwelling chest tube after complete drainage. There was no need for further intervention during the six months follow up period. pleural instillation of tetracycline was used in all studies with success rate between 50-92% with a mean of 71%[7,11], Khalil M et al studied tetracycline in its powder form via medical thoracoscopy[7]. They achieved a success rate of 86.6% which is similar to the result of this present study. However, there is a difference in the methods for pleurodesis in the study by Khalil and colleagues[7].

While bronchogenic carcinoma and breast carcinoma are responsible for 50-60% of malignant pleural effusion in both sexes[1] in this study bronchogenic carcinoma was not seen. Studies[1,2,7,11-14] showed other carcinoma to account for 25% of malignant pleural effusion, this present study showed them to be responsible for 25% of malignant pleural effusion. Tetracycline is frequently used chemical pleurodesis agent, it directly stimulates mesothelial cells to release growth factors for fibroblast activites[7] Tetracycline has an excellent safety profile, and it is relatively cheap, it is well tolerated and side effects are infrequent, mild and transient[7,11] most studies[7,8,11-14] requires post procedure anti pyretic and analgesic our study was not an exception but mostly for analgesia but not antipyretic. The numerical pain score used post procedure to access these patients ranges from 5-8/10 managed with pentazocine as a stat dose and oral paracetamol.

The average duration post tetracycline instillation is 4±1 days, shorter than previous report by Khalil M et al 4.73±0.3 days, Hartman et al[7] reported 6.5±2.1 days. The result of this study showed no mortality related to procedure and significant complications. Eight (40%) of our patients developed mild to moderate chest pain which were managed with intramuscular pentazocine and paracetamol with good response. Khalil managed chest pain associated with his study with paracetamol[7].The commonly reported side effects of tetracycline pleurodesis in previous studies include fever (10%) and pleuritic chest pain (30%) which were usually transient and amenable to antipyretic and analgesia[7,11]

CONCLUSION

Malignant pleural effusion is a complication of metastatic malignancy. Management is palliative and chemical pleurodesis using tetracycline solution instal through an indwelling chest tube has shown to be safe and effective in this study.

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