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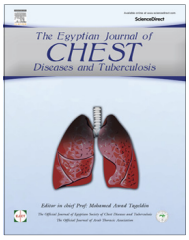

ORIGINAL ARTICLE

Pleural fluid CRP, LDH, and pH as predictors of successful pleurodesis in malignant pleural effusions

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KEYWORDS

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Abstract *Background:* Pleurodesis fails in 10–40% of patients with recurrent malignant pleural effusions (MPEs) and dyspnea. An accurate definition of the different characteristics of the patient would help to identify more precisely the population mostly benefiting from pleurodesis.

Aim: We aimed to assess the values of the initial pleural fluid LDH, CRP and pH characteristics on pleurodesis outcome for MPEs.

Methods: Between April 2013 and December 2014, 40 patients with MPE were subjected to pleurodesis with doxycycline and were divided into two groups, successful pleurodesis (group I) and failed pleurodesis (group II) according to their radiographic response at the end of the 4 weeks follow-up period. Before pleurodesis, pleural tapping and the initial pleural fluid biochemical parameters (Total protein, glucose, PH, LDH and CRP levels) were measured.

Results: After 4 weeks follow up, the success rate of pleurodesis was 62.5%. In successful pleurodesis, the initial total pleural fluid proteins, pleural fluid LDH and pleural fluid CRP were significantly lower than unsuccessful pleurodesis, with *P*-values <0.05, <0.001, <0.05 respectively while, pleural fluid glucose was statistically very highly significantly lower at the unsuccessful pleurodesis group ($P < 0.001$). Both groups together revealed positive correlation between pleural fluid LDH at one side and (pleural fluid CRP and proteins) at the other side (*P*-value < 0.01 and <0.05) respectively, while, there was a negative correlation between pleural fluid LDH and pleural fluid glucose (*P*-value < 0.01). The complications of tube thoracotomy and pleurodesis in both successful and failed pleurodesis were higher in unsuccessful pleurodesis than in successful pleurodesis.

Conclusion: High CRP, high LDH and low PH in MPEs have a poorer outcome of pleurodesis. So, it may be advantageous when selecting patients for pleurodesis to include in their routine tests, the initial pleural fluid CRP, LDH and PH levels.

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Introduction

Most of the malignant pleural effusions are the result of metastases to the pleura from other sites. The primary tumors were, in the decreasing order of frequency: lung (37%), breast (17%), unknown site (10%), lymphoma (9%), gastrointestinal (8%), ovary (7%) and mesothelioma (3%) [1]. Management of malignant effusions depends on palliation of dyspnea and prevention of the reaccumulation of pleural fluid to provide the highest possible quality of life, regardless of the need for other treatment modalities [2].

Pleurodesis is defined as the symphysis between the visceral and parietal pleural surfaces, its function is to prevent accumulation of either air or fluid into the pleural space. Effusions of malignant origin are the most common indication for pleurodesis [3].

Unfortunately, pleurodesis fails in 10–40% of patients with recurrence of pleural fluid and dyspnea. Because pleurodesis is associated with considerable cost and morbidity, the identification of patients who will experience an unsuccessful pleurodesis would be desirable [4].

The utility of various clinical and biochemical parameters in predicting pleurodesis outcome is still controversial. A better definition of the different characteristics of the patient would help to identify more precisely the population mostly benefiting from pleurodesis. These factors may allow clinicians to make better treatment decisions in a patient with recurrent MPE [5].

Aim of the study

We aimed to assess the values of the initial pleural fluid LDH, CRP and pH characteristics on pleurodesis outcome for malignant pleural effusions (MPEs).

Patients and methods

Study population

- Over the period from April 2013 to December 2014, a prospective study was conducted in which 40 consecutive patients with malignancy and recurrent symptomatic malignant pleural effusion (MPE) were found eligible to participate. Patients were admitted at Chest and Cardiothoracic Surgery Departments, Zagazig University Hospitals, Egypt.
- They were diagnosed finally by pleural fluid cytology and/or CT-guided biopsy or tissue biopsy (Abrams or thoracoscopic biopsy).
- Informed consent was obtained from all patients enrolled in the study. This consent was approved by the Institutional Review Board at Zagazig Faculty of medicine
- *Inclusion criteria*
  - Massive or rapidly reaccumulating pleural effusion after drainage, which requires frequent thoracentesis (< 3 days).
  - Subjective improvement of dyspnea following thoracentesis.
  - Re-expansion of the lung after drainage.
  - Life expectancy > 6 months, Karnofsky scale score $\geqslant 60$.
  - Pleural fluid pH > 7.2.
- *Exclusion criteria*
  - Atelectasis due to endobronchial obstruction.
  - Pleural fluid pH < 7.2.
  - Prior intrapleural therapy in the previous two weeks.
  - Significant irradiation to the affected hemithorax.
  - Patient receiving systemic corticosteroids or a non-steroid anti-inflammatory drug including pure analgesic medication during the study.

The following data were collected from all the patients

(1) Thorough medical history.
(2) Full clinical examination of both general and local (chest) examinations.
(3) Assessment of Karnofsky performance status (KPS).
(4) Routine investigations to evaluate the patient general condition (complete blood count, erythrocyte sedimentation rate, and liver and kidney function tests).
(5) Plain chest X-ray (CXR) (postero-anterior and lateral views).
(6) Before pleurodesis, pleural tapping and the aspirated fluid were analyzed for the following biochemical parameters (Total protein, glucose, lactate dehydrogenase (LDH) and CRP levels).
(7) A 2-ml pleural fluid sample was collected in a heparinized syringe and the pleural fluid pH was measured within 30 min after thoracentesis, before pleurodesis. The blood pH/gas analyzer, Rapid lab 1265 (Bayer, USA), was used for these measurements.

Procedures

Tube thoracostomy insertion

- Conventional large-bore chest tubes (24–28 F; Pleurocan, Braun, Germany) were inserted in all cases.
- Patients were premedicated with 0.6 ml atropine sulfate given intramuscularly 30 min prior to the procedure.
- Proper position with the patient supine, skin disinfection and anesthesia was infiltrated with 10 CC xylocaine 2% followed by aspiration to confirm the presence of the fluid.
- An incision about 2 cm was done in the fifth or sixth intercostal space in the midaxillary line. The incision was made at the upper border of the rib below and parallel to the rib. A large bore chest tube (24–28 F) was used to allow adequate drainage. After appropriate positioning, fixation of the tube was done by the suture. The chest tube was connected to underwater seal to allow slow drainage of the effusion.
- When the amount of effusion became less than 100 ml/24 h and chest X-ray showed complete lung expansion and there was no evidence of bronchopleural fistula, pleurodesis was carried out.

Pleurodesis [1,6]

- Premedication with 20 cc xylocaine 2% (Astra Zeneca, London, UK) was installed intrapleurally 30 min before chemical agent was injected.

- Inject 500 mg of doxycycline (Vibramycin, Pfizer company, 100 mg capsules, costing 20 LE for the pack) diluted in100 ml of normal saline 0.09% into the pleural space, Clamp chest catheter for 2 h, all patients underwent rotational maneuvers during the time that the chest tube was clamped. After 2 h, the tube was opened.
- The chest tube was removed when the drainage fell below 150 ml/24 h, and a chest X-ray was obtained to confirm complete lung expansion. All complications from the pleurodesis were recorded.
- Each patient had a pre-drainage baseline posteroanterior (PA) radiograph. Post-pleurodesis PA radiographs were obtained at the following time: (1) after removal of the chest tube, (2) 3 days after removal (early response), and (3) 4 weeks (late response) following the procedure.

Assessment of the response was based on radiologic appearance [5]

(1) At the end of the 4 weeks follow-up period, the radiographic response was classified as follows: (1) complete response (CR; no re-accumulation of pleural fluid after post-pleurodesis radiography), (2) partial response (PR; re-accumulation above the post-pleurodesis level, but below the pre-pleurodesis level), and (3) no response (NR; re-accumulation or above the pre-pleurodesis level).
(2) Global response refers to the sum of the complete and partial responses [7].
(3) The patients who died or who were lost to follow-up within the first month of chest tube removal were excluded from the study.

Statistical methods

Data were statistically described in terms of mean ± standard deviation (±S.D.), or frequencies (number of cases) and percentages when appropriate. Comparison of numerical variables between the study groups was done using Student's *t* test for independent samples in comparison with normally distributed data. For comparing categorical data, Chi square (χ^2) test was performed. The correlation of two continuous variables was measured with Pearson's correlation coefficient (*r*).

For all the above-mentioned statistical tests, the threshold of significance is fixed at the 5% level (*P*-value), a *P*-value $\geqslant 0.05$ indicates non-significant results, a *P*-value < 0.05 indicates significant results, a *P*-value < 0.01 indicates high significant results, and a *P*-value < 0.001 indicates very high significant results.

All statistical calculations were done using computer program SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) version 15 for Microsoft Windows.

Results

Of the 40 patients who completed the study, 25 (62.5%) patients showed successful pleurodesis (group I), while 15 (37.5%) patients showed failed pleurodesis (group II). The mean age of the patients included in our study was 53.7 ± 26.3 and 48.2 ± 30.1 years in groups I and II respectively.18 patients were males and 7 were females, in group I, while 9 patients were males and 6 were females, in group II. The malignant pleural effusions were either of primary pleural origins (malignant mesothelioma) in 10 patients or of metastatic etiology in 30 patients, of which 15 cases were due to bronchogenic carcinoma, 12 cases were due to metastasis from [Breast (9 patients), colon (2 patients) and ovary (one patient)] and lastly 3 lymphoma patients The mean KPS was comparable in the 2 studied groups. In addition, there was no statistically significant difference in the mean duration of pleural fluid drainage after pleurodesis in both groups (Table 1).

There was statistically significant difference between the studied groups regarding the initial pleural fluid values of (proteins, glucose, LDH, and CRP) (Table 2).

Table 3 revealed that in both studied groups together, there were positive correlations between the initial pleural fluid LDH at one side and (initial pleural fluid CRP and proteins) at the other side with statistically significant difference (*P*-value < 0.01 and < 0.05) respectively. While, there was negative correlation between the initial pleural fluid LDH and pleural fluid glucose with statistically significant difference (*P*-value < 0.01). Other parameters (mean ages, KPS, pleural fluid PH and the mean duration of pleural fluid drainage after pleurodesis) showed no statistically significant difference (*P*-value > 0.05) in correlation with pleural fluid LDH.

Table 4 shows that in the successful pleurodesis group (group I), only the initial pleural fluid proteins is significantly negative correlated with pleural fluid LDH (*P*-value < 0.05).

Table 5 shows that in the failed pleurodesis group (group II), the pleural fluid PH was very highly significantly negatively correlated with the initial pleural fluid LDH (*P*-value < 0.001), while the initial pleural fluid CRP and

Table 1 Characteristics of the study population with successful and failed pleurodesis descriptive data.

Patient characteristics	Successful pleurodesis (group I) (25 patients)	Failed pleurodesis (group II) (15 patients)	*P*-value
Success rate % (No. of patients in each group/total number of studied patients)	25/40 (62.5%)	15/40 (37.5%)	0.046
Age (mean ± S.D.) (years)	53.7 ± 26.3	48.2 ± 30.1	0.09
Gender No (%)			
Female	7 (28%)	6 (40%)	0.66
Male	18 (72%)	9 (60%)	0.66
Tumor type No (%)			
• Bronchogenic	9 (36%)	6 (40%)	0.8
• Mesothelioma	6 (24%)	4 (26.7%)	0.85
• Metastasis	8 (32%)	4 (26.7%)	1.00
• Hematologic malignancy	2 (8%)	1 (6.6%)	0.64
Karnofsky performance scale (KPS), mean ± S.D.	76.9 ± 10.9	68.7 ± 8.3	0.31
Duration of drainage after pleurodesis (days), mean ± S.D.	3.7 ± 1.2	4.1 ± 1.1	0.26

Table 2 Comparison of the initial pleural fluid glucose level, protein level, LDH, pH, and CRP between successful and failed pleurodesis.

Variables	Successful pleurodesis (25 patients)	Failed pleurodesis (15 patients)	*P*-value
Total pleural fluid proteins (g/dl)	4.54 ± 0.68	5.16 ± 0.79	<0.05
Pleural fluid glucose (mg/dl)	106.8 ± 10.5	53.7 ± 8.3	<0.001
Pleural fluid LDH (IU/l)	867 ± 130	1814 ± 691	<0.001
Pleural fluid CRP (mg/l)	2.62 ± 0.57	4.73 ± 1.63	<0.05
Pleural fluid PH	7.47 ± 0.46	7.26 ± 0.04	0.23

Table 3 Correlation between all parameters and the initial pleural fluid LDH by Pearson correlation coefficient in both successful and failed pleurodesis groups together.

Variables (mean ± S.D.)	*r* value	*P* value
Age (years)	−0.07	>0.05
Karnofsky performance scale (KPS)	−0.02	>0.05
Pleural fluid CRP (mg/l)	0.67	<0.01
Pleural fluid pH	−0.22	>0.05
Pleural fluid proteins	0.36	<0.05
Pleural fluid glucose	−0.61	<0.01
Duration of drainage	0.02	>0.05

Table 4 Correlation between all parameters and the initial pleural fluid LDH by Pearson correlation coefficient in the successful pleurodesis group only.

Variables	*r* value	*P* value
Age (±S.D.) (years)	0.29	>0.05
Karnofsky performance scale (KPS)	0.1	>0.05
Pleural fluid CRP (mg/l)	0.1	>0.05
Pleural fluid PH	0.01	>0.05
Pleural fluid proteins	−0.43	<0.05
Pleural fluid glucose	0.25	>0.05
Duration of drainage	0.05	>0.05

proteins were significantly positive correlated with the initial pleural fluid LDH (*P*-value < 0.05).

As regards the complications of the tube thoracotomy and pleurodesis, Table 6 reveals that in group I, chest pain, fever and superficial chest wall infection were 16%, 16% and 0% respectively, while in group II, chest pain, fever and superficial chest wall infection were 26.7%, 20% and 6.6% respectively, but with no statistically significant difference between both groups as regards these complications.

Table 7 demonstrates the radiologic response after 3 days of tube thoracotomy and pleurodesis in which the (complete, partial and no) response in both successful and failed pleurodesis groups were 80%, 20% and 0% and 30%, 50% and 20% respectively, with statistically significant difference between both groups *P*-value < 0.05).

Table 5 Correlation between all parameters and the initial pleural fluid LDH by Pearson correlation coefficient in the failed pleurodesis group only.

Variables	*r* value	*P* value
Age (±S.D.) (years)	0.1	>0.05
Karnofsky performance scale (KPS)	0.22	>0.05
Pleural fluid CRP (mg/l)	0.38	<0.05
Pleural fluid pH	−0.70	<0.001
Pleural fluid proteins	0.30	<0.05
Pleural fluid glucose	0.25	>0.05
Duration of drainage	−0.14	>0.05

Table 6 Complications of tube thoracotomy and pleurodesis in both successful and failed pleurodesis by chi square.

Complications	Successful pleurodesis (25 patients)	Failed pleurodesis (15 patients)	*P*-value
Chest pain, No (%)	4 (16%)	4 (26.7%)	>0.05
Fever, No (%)	4 (16%)	3 (20%)	>0.05
Superficial chest wall infection, No (%)	0 (0%)	1 (6.6%)	>0.05

Table 7 Radiological response after 3 days of tube thoracotomy and pleurodesis in both successful and failed pleurodesis by chi square.

Radiological response after 3 days	Successful pleurodesis (25 patients)	Failed pleurodesis (15 patients)	*P*-value
Complete response, *N* (%)	20 (80%)	5 (30%)	<0.05
Partial response, *N* (%)	5 (20%)	7 (50%)	<0.05
No response, *N* (%)	0 (0%)	3 (20%)	<0.05

Table 8 demonstrates the radiologic response after 4 weeks of tube thoracotomy and pleurodesis in which the (complete, partial and no) response in both successful and failed pleurodesis groups were 68%, 32% and 0% and 0%, 0% and 100% respectively, with statistically significant difference between both groups *P*-value (<0.05).

Discussion

We aimed to assess the values of the initial pleural fluid LDH, CRP and pH characteristics on pleurodesis outcome for malignant pleural effusion (MPE).

Over the period from April 2013 to December 2014, a prospective study was conducted that included 40 consecutive patients with recurrent symptomatic malignant pleural effusion (MPE) who were eligible to participate.

Patients were admitted at Chest and Cardiothoracic Surgery Departments, Zagazig University Hospitals. They were diagnosed finally by pleural fluid cytology and/or CT-

Table 8 Radiological response after 4 weeks of tube thoracotomy and pleurodesis in both successful and failed pleurodesis by chi-square.

Response after 4 weeks	Successful pleurodesis (25 patients)	Failed pleurodesis (15 patients)	*P*-value
Complete response, *N* (%)	17 (68%)	0 (0%)	< 0.05
Partial response, *N* (%)	8 (32%)	0 (0%)	< 0.05
No response, *N* (%)	0 (0%)	15 (100%)	< 0.05

guided biopsy or tissue biopsy (Abrams or thoracoscopic biopsy). Pleurodesis was done by injection of 500 mg of doxycycline diluted in100 ml of normal saline 0.09% into the pleural space.

In our study, after 4 weeks follow up, the success rate of pleurodesis was 62.5% (Table 1). The current study results on doxycycline pleurodesis agreed with a study done by Costa et al. [8] who treated 41 malignant pleural effusion patients with doxycycline pleurodesis. A successful pleurodesis (complete or partial) was accomplished in 25 (61%). Our results were less than the following studies: Mohamed and Hassan [9] who reported that the oral forms of doxycycline pleurodesis (using 1000 mg of doxycycline and mixed in 50 ml physiological saline) in 22 patients with malignant pleural effusions were successful in sixteen patients (72.7%) at 1 month. Also, Herrington [10], who evaluated doxycycline (1 g) as a pleurodetic agent in the treatment of malignant and nonmalignant pleural effusions and refractory pneumothoraces, Out of 12 patients with malignant pleural effusion, 8 (67%), achieved a complete response, 2 had a partial response, and 2 had no response. Our results were less than the previous 2 studies because they used a higher dose and concentration of doxycycline and a smaller number of patients than our study.

Elnady and Sakr [11], performed pleurodesis in twenty-seven patients with malignant pleural effusion. (thoracoscopic doxycycline poudrage ''TDP'') where about 500–1000 mg of doxycycline was taken and prepared as a powder from the oral preparation (Vibramycin 100 mg/capsule), 74.1% had a successful pleurodesis, 18.5% had partial response and 7.4% had failed pleurodesis at 1 month. This study used thoracoscopic pleurodesis, not tube thoracotomy as our study so the former study results were better than our results.

The following 2 studies showed also better results than our study may be due to larger number of patients, different techniques or different pathological types of MPE used in our study, Heffner et al. [12] examined the outcome in 31 patients receiving doxycycline through a chest tube for malignant pleural effusions or persistent bronchopleural fistulae, Of the 27 patients with malignant pleural effusions, 21 patients had successful pleurodesis (77.8%) at 1 month. Porcel et al. [13] conducted a prospective study of 36 rapid pleurodesis procedures in 34 patients with malignant pleural effusions. Patients received 500 mg of intrapleural doxycycline, complete success of pleurodesis was achieved in (55%), partial success in (26%), and failure in (19%). Thus, the overall success rate of pleurodesis was 81%.

We observed in successful pleurodesis, the initial total pleural fluid proteins, pleural fluid LDH and pleural fluid CRP were significantly lower than unsuccessful pleurodesis with *P*-value < 0.05, < 0.001, < 0.05 respectively while, pleural fluid glucose was statistically very highly significantly lower at the unsuccessful pleurodesis group ($P < 0.001$). The initial pleural fluid PH was lower in the unsuccessful group, but statistically insignificant (Table 2). These results can be explained as the unsuccessful pleurodesis is due to extensive intrapleural tumor deposits that prevent the apposition of visceral to parietal pleural surfaces [14]. This abnormal pleural membrane appears primarily responsible for low glucose [15]. The high level of CRP is an indication of the inflammatory response within the pleural cavity induced by neoplastic progression [16]. Also, high pleural fluid LDH levels (reflecting localized, acute inflammation, necrosis and cell death within the pleural cavity) are indicative of a poor prognosis in MPE [17]. Alsayed et al. [18] indicate that pleurodesis success is much more liable if pleural fluid pH is > 7.30 and pleural glucose levels are > 60 mg/dl. Below these values, pleurodesis failure is common. Several studies reported conforming results such as Rodriguez-Panadero and Mejias [19] who attempted pleurodesis in 62 patients having MPEs evaluated after a month. They stated that there was a close relationship found between low pleural glucose and pH levels and the extension of lesions observed during follow-up and Heffner et al. [4] reported that the clinical features of pleural fluid pH (*P*-value 0.0001), pleural fluid glucose (*P*-value 0.0002), and %LDH (*P*-value 0.0005) were associated with the failure of pleurodesis. Lapidot et al. [20] stated that pleural fluid CRP levels may reliably predict pleurodesis success and symptomatic failure among MPE patients. So, it may be advantageous when selecting patients for pleurodesis to incorporate in the routine tests, the pleural fluid CRP levels.

We choose the pleural LDH for comparison with the initial pleural fluid glucose level, protein level, pH, and CRP in both successful and unsuccessful pleurodesis groups because LDH elevation is an indicator of pleural inflammation and cell damage. A significant elevation is observed in pleural fluid LDH levels and pleural fluid/serum LDH ratios in cases with malignant effusions. Its measurement is highly sensitive and routinely done for the diagnosis of pleural effusion and for predicting MPE prognosis [21] (Tables 3–5).

In our study, both groups together revealed a positive correlation between pleural fluid LDH on one side and (pleural fluid CRP and proteins) on the other side with statistically significant difference (*P*-value < 0.01 and < 0.05) respectively. While, there was negative correlation between pleural fluid LDH and pleural fluid glucose with statistically significant difference (*P*-value < 0.01). This result was agreed with Alsayed et al. [18] who stated that there was a significant negative correlation between glucose levels and LDH value in pleural fluid i.e. as glucose levels increased, LDH values decreased. This meant that the malignant infiltration process of the pleura was less severe (less LDH) resulting in better glucose transfer into the pleural cavity (more glucose in pleural fluid). In our study, there was a positive correlation between both pleural fluid CRP and LDH as both were sensitive markers of pleural inflammation and their levels increased and directly related to the neoplastic progression. Other parameters (mean ages, KPS, pleural fluid PH and the mean duration of pleural fluid drainage after pleurodesis) showed no statistically significant difference (*P*-value > 0.05) in correlation with pleural fluid LDH, this may be due to small number of patients in the present study (Table 3).

The correlation between all parameters and pleural fluid LDH in successful pleurodesis group revealed that only initial total pleural fluid proteins were significantly negative correlated with initial pleural fluid LDH levels (P-value < 0.05). While, there was positive correlation between pleural fluid CRP and pleural fluid LDH, but statistically insignificant (Table 4). More studies with larger number of patients will be needed to achieve significant results.

The correlation between all parameters and pleural fluid LDH in the unsuccessful pleurodesis group revealed that the pleural fluid PH was very highly significant negative correlated with the initial pleural fluid LDH (P-value < 0.001), while the initial pleural fluid CRP and proteins were significantly positive correlated with the initial pleural fluid LDH (P-value < 0.05) (Table 5). Our results agreed with Alsayed et al. [18] who reported that there was also a significant negative correlation between glucose, LDH and pH values in pleural fluid i.e. as glucose levels decreased, LDH values increased. This meant that the malignant infiltration process of the pleura was more severe (more LDH) resulting in less glucose transfer from blood into the pleural cavity (less glucose in pleural fluid) and slow transport of its metabolic products (CO2 and Lactic acid) out of pleural space thus resulting in low pH values of pleural fluid. Also, Shoukry [22] showed similar results. He reported that pleural fluid levels of pH and LDH were the most sensitive markers that discriminated those with failed pleurodesis from those with successful pleurodesis, where the cut-off points that discriminated success from failure were pH < 7.33 and LDH > 1023 IU/l and with decreasing pH < 7.33 and increasing LDH > 1023 IU/l, there were increased probabilities of pleurodesis failure.

The complications of tube thoracotomy and pleurodesis (Chest pain, fever and infection) in both successful and failed pleurodesis were higher in unsuccessful pleurodesis than successful pleurodesis, this reflects that the pleurodesis is safe and successful one, but there was no statistically significant difference between both groups as regards the previous complications. Mohamed and Hassan [9] reported that the pain observed in 10 cases (45.5%) was due to chest tubing or the tumor itself rather than doxycycline powder. Analgesics, prescribed in general for 24 h, easily overcame this problem. A fever greater than 38.5 °C lasting for about 24 h was a recorded complication in 2 cases (9.1%) but it was easily controlled with paracetamol. Bakr et al. [6] and Herrington [10] found twenty-two (81%) of 27 patients in their studies experienced adverse effects with pleurodesis, with pain (81%) and fever (11%) being the most prevalent. As pain is the most common complication associated with doxycycline pleurodesis, narcotic analgesic and/or conscious sedation is often recommended or the solution may be mixed with 10 ml of lignocaine to reduce pain. Also, Elnady and Sakr [11], concluded that doxycycline is inexpensive, well tolerated, reasonably effective, comparatively simple, safe, and capable of alleviating respiratory symptoms.

Table 7 shows the response after 3 days of tube thoracotomy and pleurodesis in both successful and failed pleurodesis, in which the (complete, partial and no) response in all 40 patients together was 62.5%, 30% and 7.5% respectively. Bakr et al. [6] reported that The immediate follow up results (24–72 h of pleurodesis) showed that in group II (pleurodesis with doxycycline), 8 patients had CR (80%) while partial response (PR) was recorded in 1 case (10%) and failure in 1 case (10%).

Table 8 shows the response after 4 weeks of tube thoracotomy and pleurodesis in both successful and failed pleurodesis, in which the (complete, partial and no) response in all 40 patients together were (42.5%, 20% and 37.5%) respectively. While, Bakr et al. [6] reported that after two and three months follow up of the patients in group II (pleurodesis with doxycycline), 8 patients had CR (80%), while failure was found in 2 cases (20%), the later results were better than our results which may be due to smaller number of patients (10) included in the later study, also they used more concentrated doxycycline for pleurodesis (Seven milligram per kilogram of doxycycline diluted in 50 ml of saline 0.9%).

Conclusion

Success of pleurodesis is decided by observing whether or not symptomatic fluid occurs 4 weeks after sclerosing agent application. When we predict the outcome of the pleurodesis procedure, it might allow us to avoid performing this invasive procedure with its side effects or might allow the re-application of sclerosing agent within the first two or three days before the chest tube is withdrawn.

The initial pleural fluid CRP, LDH and PH levels may reliably predict pleurodesis success and symptomatic failure among MPE patients. As, high CRP, high LDH and low PH in MPEs have a poorer outcome of pleurodesis. So, it may be advantageous when selecting patients for pleurodesis to incorporate in their routine tests, the initial pleural fluid CRP, LDH and PH levels.

Conflict of interest

Authors have no conflict of interest to declare.

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