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Thoracoscopic Talc Insufflation Versus Doxycycline Pleurodesis For The Management Of Malignant Pleural Effusion.

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Abstract

Background: Malignant pleural effusions (MPEs) can be a complication of virtually any malignancy. Quality of life with MPE is often compromised due to debilitating symptoms like dyspnea, cough, orthopnea,chest pain or pressure. There are several approaches to MPE management, with the objective of each procedure to drain the pleural space and to relieve respiratory symptoms. If the MPE recurs after initial thoracentesis, several approaches can be taken for further control: repeat thoracentesis, placement of tunneled pleural catheter (TPC), tube thoracostomy with pleurodesis, or medical pleuroscopy with pleurodesis. Wide spread practice variation in performing pleurodesis would underscore the importance of appropriate clinical trials to determine the best clinical practices in performing pleurodesis.

Objective of study: This study was performed to compare 2 widely used pleurodesis techniques, tube thoracostomy doxycycline pleurodesis and thoracoscopic talc insufflation, aiming to explore the effectiveness and safety of both procedures.

Patients and methods: Thirty patients with documented MPE were selected and divided into 2 groups, subjects of group1 (20 patients) were managed by thoracoscopic talc insufflation and subjects of group 2 (10 patients) were managed by tube thoracostomy doxycycline pleurodesis.

This study was conducted at Cairo University Hospitals. Approval of the Ethical Committee and written informed consent from all participants were obtained. Study period: January 2011 to May 2014.

Results: Results of study showed that:

- Both thoracoscopic talc insufflation and tube thoracostomy doxycycline pleurodesis achieved satisfactory success rates in controlling malignant pleural effusions with slightly higher success rate with talc insufflation.
- Both techniques were not associated with major complications but frequency of complications was higher with doxycycline.

Conclusion:

- Thoracoscopic talc insufflation should be offered as the treatment of choice in controlling malignant pleural effusions provided that the required resources are available (sterile talc, thoracoscopes, skilled operators).
- Tube thoracostomy doxycycline pleurodesis is a valuable alternative when thoracoscopic talc insufflation can not be done.

Key Words: Thoracoscopic, talc, insufflation, doxycycline, pleurodesis, malignant, pleural, effusion.

Introduction

Malignant pleural effusions (MPEs) are a common problem in cancer patients with advanced disease. Approximately 50% of patients with breast carcinoma, 25% of patients with lung carcinoma, and 35% of patients with lymphoma develop a malignant effusion during the course of their disease [1].

Patients usually present with symptoms that compromise their quality of life, including progressive dyspnea, cough, and/or chest pain [2].

Treatment options for (MPEs) depend on the extent of disease, effectiveness of systemic therapy, and patient performance status.

Pleural effusions in patients with lymphoma, small cell lung cancer, or germ cell cancer, may be controlled by systemic treatment [3].

Therapeutic thoracentesis may serve as the primary therapeutic modality in some patients. In patients with far advanced disease, poor performance status, and low pleural fluid pH (pH $\leq$ 7.2) relief can be provided by periodic outpatient therapeutic thoracenteses [4].

Chemical pleurodesis is accepted palliative therapy for patients with recurrent, symptomatic malignant pleural effusions. Patients selected for pleurodesis should have significant symptoms that are

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relieved when pleural fluid is evacuated. Also there should be evidence of complete re-expansion of the lung following the initial thoracentesis [4].

Various chemicals have been used in an attempt to produce pleurodesis. For many years, tetracycline was the sclerosing agent of choice. However, when it became commercially unavailable, alternative agents were investigated. Doxycycline, a tetracycline analogue, has been recommended as a replacement for tetracycline with a success rate of up to 80–85% in carefully selected patients [5].

Another agent frequently recommended for pleurodesis is bleomycin. Many studies demonstrated similar or higher success rates when utilizing bleomycin as a sclerosing agent, compared with tetracycline [6].

Talc is an inexpensive and highly effective pleurodesis agent when administered by either poudrage or slurry in patients with malignant pleural effusions [4].

The most widely reported method of talc instillation into the pleural space for malignant effusion is talc poudrage, which is usually performed under thoracoscopic guidance. On average, reported success with talc poudrage is > 90% [7].

Talc slurry is also an effective pleurodesis agent in malignant effusions. Potential disadvantages of slurry include lack of uniform distribution and accumulation in dependent areas of the pleural space possibly leading to incomplete pleurodesis and loculations [8].

Major surgical procedures, such as parietal pleurectomy, decortication, or pleuropneumonectomy have proved to provide neither superior palliation nor prospects for cure, compared with pleurodesis alone [4].

Wide spread practice variation in performing pleurodesis would underscore the importance of appropriate clinical trials to determine the best clinical practices in performing pleurodesis [9].

Aim of the work

This study aimed to assess the effectiveness and safety of thoracoscopic talc insufflation compared to doxycycline pleurodesis in controlling recurrent malignant pleural effusion.

Patients and methods

Type of the study: It was a prospective randomized study, carried on 30 subjects suffering from recurrent malignant pleural effusion and who fulfilled the inclusion criteria of this study.

Study period: January 2011 to May 2014.

Inclusion criteria:

1- Documented recurrent symptomatic malignant pleural effusion. Documentation of malignant pleural effusion was by either **cytology** of pleural fluid showing malignant cells or **histopathology** of pleural biopsy showing malignancy.

2- Subjects should have a good performance status graded by Karnofsky's performance score.

3- Subjects should show relief of symptoms after the initial therapeutic thoracentesis with evidence of complete lung re-expansion and without evidence of neither bronchial obstruction nor trapped lung.

Exclusion criteria:

1- Poor performance status graded by Karnofsky's performance score.

2- Failure of initial therapeutic thoracentesis to achieve relief of symptoms or failure of complete re-expansion of lung with evidence of bronchial obstruction or trapped lung.

Subjects were divided into 2 groups:

Group 1: included 20 subjects managed by thoracoscopic talc insufflation under local anesthesia and conscious sedation. Two to four grams of sterile asbestos-free talc were sprayed into the pleura under thoracoscopic guidance.

Group 2: included 10 subjects managed by doxycycline pleurodesis. A dose of 500-1000 mg (10mg/kg) doxycycline was added to 20-30 ml of sterile normotonic saline and mixed with 20

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ml of 2% lidocaine and then injected into the pleural space through a standard thoracostomy tube. Repeated doses of doxycycline at 1 week interval were used if output from chest tube remained > 200 ml /24 hour.

After taking a detailed informed consent, all subjects were subjected to:

1- Thorough history taking.

2- General and local clinical examination.

3- Plain Chest x-ray.

4- Chest C.T scan.

5- Routine labs including hemoglobin, leucocytic count,ALT, AST, serum proteins, serum albumin, urea, creatinine,prothrombin activity%, INR and serum LDH.

6- At least one therapeutic thoracentesis with a post-procedure radiological examination.

7- Analysis of pleural effusion for protein content, effusion proteins/serum proteins ratio, total and differential leucocytic count and LDH.

8- Subjects of group 1were subjected to **talc insufflation pleurodesis** as follows:

- The procedure was performed in thoracoscopy room under aseptic conditions.

- Patients were pre-medicated with atropine intramuscularly (0.5 mg atropine sulphate).

- Patients were carefully monitored throughout the procedure for: heart rate, blood pressure, oxygen saturation. Patients breathed spontaneously and supplemental oxygen was given when needed.

- Patients were positioned in a lateral decubitus with the diseased hemi-thorax up.

- Under local anesthesia using lidocaine 2% solution, an incision was made in the 5th or 6th intercostal space mid-axillary line, then subcutaneous tissues and intercostal muscle layer were dissected down to the parietal pleura.

- A 10 mm trocar was then introduced (through the incision) into the pleural cavity and the pleural fluid was totally aspirated by a suction device.

- A rigid thoracoscope was then inserted through the obturator, the pleural cavity was thoroughly examined for detection of any abnormalities like adhesions, nodules and visceral pleural thickening. Any adhesions were severed mechanically by biopsy forceps to free the pleural space.

- Using an insufflator, 2-4 grams of sterile asbestos-free talc (Luzenac talc, Canada) were sprayed on the parietal and visceral pleural surfaces under thoracoscopic guidance.

- Thoracoscope was then removed and a 24-28 F chest tube was inserted, secured in place by sutures and connected to underwater seal.

- Patients were observed for side effects of procedure and daily output of chest tube.

- When output from chest tube was 150-200 ml/24 hour, tube was removed and a chest radiograph was taken as a base line.

9- Subjects of group 2 were subjected to **tube thoracostomydoxycycline pleurodesis** as follows:

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- Under local anesthesia using lidocaine 2% solution and with aspeptic precautions, a 24-28 F chest tube was introduced into the pleural space through the 5th or 6th intercostal space mid-axillary line. Patients were pre-medicated by atropine intramuscularly (0.5mg atropine sulphate).

- The daily output from the chest tube was observed until it drained < 100 ml/24h.

- To prepare doxycycline as a chemical sclerosant,oral form of doxycycline (**doxycycline hyclate** capsules; **VIBRAMYCIN ®**) was used with each capsule containing 100 mg. A dose of 10 mg/kg doxycycline was prepared by dissolving doxycycline in 80 ml sterile normotonic saline mixed with 20 ml of lidocaine 2% solution. The mixture was then injected through the chest tube into the pleural cavity and the tube was clamped for 2 hours following the procedure.

- Following intrapleural injection of doxcycyline, patients were observed for **side effects** and total **daily output** from chest tube.

- When output from chest tube became 150-200 ml/24h, chest tube was removed and a chest radiograph was taken as a base line.

- Repeated doses of doxycycline at 1 week interval were used if output from chest tube kept > 200 ml /24 hour.

- A narcotic analgesic (Nalbuphine ;Nubain®) was used occasionally to control severe pain.

10- All patients were followed up for 3 months following the procedure and chest radiographs were taken at 4 weeks interval to assess success of pleurodesis.

Success of pleurodesis was graded as follows:

Complete success: no pleural fluid re-accumulation greater than that observed on the baseline radiograph, taken immediately after the procedure.

Partial success: pleural fluid re-accumulation which did not require further thoracenteces or remained asymptomatic.

Failure: any results other than the previous descriptions.

Handling and analysis of data: The collected raw data were coded and transformed into coding sheets. Data were entered into SPSS system files (SPSS package version 18) and analysis & interpretation of data were conducted.

The following statistical measures were used:

- Descriptive statistics including frequency, mean, and standard deviation.

- Univariate analysis including t-test and Mann Whitney test were used to test the significance of results of quantitative variables. Moreover, Chi-Square test, Monte Carlo test and Yates corrected Chi-Square test, were used to test for significance among qualitative variables.

- Analysis of variance (ANOVA) was used when tests of univariate analysis were not applicable.

-The significance of the results was at the 5% level of significance.

The obtained results were presented as tables and graphs then discussed to explore effectiveness and safety of both talc poudrage and doxycycline pleurodesis.

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Personal characteristics	Doxycycline pleurodesis (n=10)		Talc Insufflation pleurodesis (n=20)		Significance
	No.	%	No.	%	
Sex					
Male	4	40	9	45	P=0.767
Female	6	60	11	55	
Age					
Min-Max	39 - 63		39 - 66		P=0.388
Mean ± SD	50.27 ± 8.86		52.8 ± 8.2		
Smoking habit					
Non-smoker	6	60	9	45	P=0.519
Ex-smoker	0	0	1	5	
Smoker	4	40	10	50	
Smoking index					
Min-Max	0 - 700		0 - 900		P=0.392
Mean ±S D	181.33 ± 249.6		262.5 ± 290.59		

Results

Table (1): Personal characteristics of the studied cases.

*** significant at P≤0.05.**

This table shows a comparison between the personal characteristics of cases of group I (those managed by doxycycline pleurodesis) and cases of group II (those managed by talc insufflation pleurodesis).

There was no significant difference between the 2 groups regarding the demographic data.

Table (2): Medical characteristics of the studied cases.

Medical characteristics	Doxycycline pleurodesis (n=10)		Talc insufflation pleurodesis (n=20)		Significance
	No.	%	No.	%	
History of malignancy					
	3	**30**	**6**	**30**	
non small cell carcinoma	**1**	**10**	**2**	**10**	
Hepatocellular carcinoma	**1**	**10**	**2**	**10**	……
Mesothelioma	**4**	**40**	**7**	**35**	
Breast cancer	**0**	**0**	**1**	**5**	
Ovarian cancer	**1**	**10**	**2**	**10**	
Prostatic cancer					
History of chronic disease					
None			**7**	**35**	**P=0.463**
Hypertension	**4**	**40**	**8**	**40**	**P=0.686**
Diabetes Mellitus	**3**	**30**	**6**	**30**	**P=0.833**
Renal impairment	**3**	**30**	**5**	**25**	**P=0.066**
Hepatic impairment	**0**	**0**	**2**	**10**	**P=0.088**
	2	**20**			
Miscellaneous	**Mean**	**SD**	**Mean**	**SD**	
					P=0.898
Karnofsky's performance score	**70.76**	**8.84**	**71**	**6.41**	**P=0.368**
*Number of thoracenteces	**4.93**	**1.22**	**4.6**	**0.94**	**P=0.398**

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**Duration of malignanc	**12.8**	**14.14**	**9.5**	**8.61**

*** significant at P≤0.05**

* Thoracenteces done before pleurodesis.

** Time elapsed in months since documentation of malignancy.

This table shows a comparison between the medical characteristics of cases of group I (doxycycline pleurodesis) and cases of group II (talc insufflation pleurodesis).

There was no significant difference between the 2 groups regarding the medical characteristics of studied cases.

Table (3): Laboratory findings of the studied cases.

Laboratory findings	Doxycycline pleurodesis(n=10)	Talc insufflation pleurodesis (n=20)	Significance
Hemoglobin (gm/dl)			
Min-Max	8.5 - 11	8.7 - 12	**P=0.028***
Mean±SD	9.61 ± 0.74	10.33 ± 1.02	
WBC count			
Min-Max	3900 - 6500	4000 - 9300	**P=0.004***
Mean±SD	5100 ± 897.62	6573 ± 1694	
ALT			
Min-Max	25 - 85	24 - 90	**P=0.713**
Mean±SD	42.73 ± 17.7	40.55 ± 16.88	
AST			
Min-Max	27 - 90	28 - 86	**P=0.441**
Mean±SD	43.33 ± 20.01	38.7 ± 15.2	
Urea			
Min-Max	24 - 46	27 - 88	**P=0.007***
Mean±SD	33 ± 6.45	48.3 ± 19.76	
Creatinine			
Min-Max	0.7 - 1.1	0.7 - 2.2	**P=0.169**
Mean±SD	0.9533 ± .141	1.16 ± 0.54	
Prothrombin activity %			
Min-Max	64 - 73	70 - 75	**P=0.05**
Mean±SD	70.4 ± 2.67	72 ± 1.97	
INR			
Min-Max	1 - 1.3	1 - 1.2	**P=0.764**
Mean±SD	1.11 ± 0.11	1.06 ± 0.068	
Serum protein (gm/dl)			
Min-Max	5.2 - 7.3	5.5 - 7.2	**P=0.755**
Mean±SD	6.25 ± 0.58	6.3 ± 0.515	
Serum albumin (gm/dl)			
Min-Max	2. 6 - 3.5	2.7 – 4.2	**P=0.474**
Mean±SD	3.16 ± 0.25	3.26 ± 0.46	
Serum LDH (unit/l)			
Min-Max	390 - 2340	370 – 2032	**P=0.717**
Mean±SD	709.6 ± 526.03	767.25 ± 408.69	

*** significant at P≤0.05.**

This table shows a comparison between laboratory findings found in cases of group I (doxycycline pleurodesis) and those found in cases of group II (talc insufflation pleurodesis).

There was a significant difference between the 2 groups regarding serum level of haemoglobin as P=0.028, white blood cells count as P=0.004 and the blood urea level as P=0.007.

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Table (4): Findings of pleural fluid analysis of the studied cases.

Findings of pleural fluid analysis	Doxycycline group (n=10)		Talc group (n=20)		T-test	
	Mean	SD	Mean	SD	t	P-value
Total proteins in pleural fluid (g/dl)	4.25	0.48	3.96	0.41	1.905	0.066
Albumin in pleural fluid (g/dl)	3.23	0.35	2.56	0.33	5.805	<0.001*
LDH in pleural fluid	358.4	155.56	380.6	190.08	0.369	0.715
Effusion proteins/Serum proteins	0.61	0.07	0.63	0.04	0.802	0.428
Leucocytic count in pleural fluid	2767	1574	1508	794	3.101	0.004*
Percentage of lymphocyes in pleural fluid leucocytes	52.07	18.22	64.05	13.85	2.214	0.034*

*** significant at P≤0.05.**

This table shows a comparison between findings of pleural fluid analysis observed in cases of group 1 (doxycycline pleurodesis) and those observed in cases of group 2 (talc insufflation pleurodesis).

There was a significant difference between the 2 groups regarding albumin in pleural fluid as P<.001, leucocytic count in pleural fluid as P=0.004 and percentage of lymphocytes in pleural fluid leucocytes as P=0.034.

Table (5): Side effects associated with pleurodesis procedure in cases of the studied groups.

Side effects of pleurodesis procedure		Doxycycline group		Talc group		Chi-square	
		N	%	N	%	X^2	P-value
Empyema after procedure	absent	6	60	17	85	2.804	**0.094**
	present	4	40	3	15		
Persistent lung collapse after procedure	absent	9	90	18	90	0.094	**0.759**
	present	1	10	2	10		
Fever after procedure	absent	6	60	15	75	0.895	**0.344**
	present	4	40	5	25		
Vomiting after procedure	absent	4	40	18	90	9.943	**0.002***
	present	6	60	2	10		
Pain after procedure	mild	4	40	14	70	3.15	**0.076**
	moderate	6	60	6	30		

This table shows a comparison between side effects of pleurodesis procedure observed in cases of group 1 (doxycycline pleurodesis) and those observed in cases of group 2 (talc insufflation pleurodesis).

There was a significant difference between the 2 groups as regarding occurrence of vomiting after procedure as P=0.002.

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Table (6): X-ray findings in the follow up period following pleurodesis procedures in cases of studied groups.

Follow up X-ray findings	Doxycycline pleurodesis (n=10)		Talc pleurodesiss (n=20)	
	N	%	N	%
After 1 month				
Effusion				
No effusion	**6**	**60**	**12**	**60**
Mild non-symptomatic effusion	**1**	**10**	**1**	**5**
Moderate effusion	**2**	**20**	**6**	**30**
Massive effusion	**1**	**10**	**1**	**5**
Persistent lung collapse				
absent	**9**	**9**	**18**	**90**
present	**1**	**10**	**2**	**10**
After 2 months				
Effusion				
No effusion	**4**	**40**	**10**	**50**
Mild non-symptomatic effusion	**2**	**20**	**3**	**15**
Moderate effusion	**3**	**30**	**6**	**30**
Massive effusion	**1**	**10**	**1**	**5**
Persistent lung collapse				
absent	**9**	**90**	**18**	**90**
present	**1**	**10**	**2**	**10**
After 3 months				
Effusion				
No effusion			**9**	**45**
Mild non-symptomatic effusion	**4**	**40**	**4**	**20**
Moderate effusion	**2**	**20**	**6**	**30**
Massive effusion	**3**	**30**	**1**	**5**
Persistent lung collapse	**1**	**10**		
absent	**9**	**90**		
present	**1**	**10**	**18**	**90**
			2	**10**

This table shows follow up x-ray findings observed in cases of group 1 (doxycycline pleurodesis) and in cases of group 2 (talc insufflation pleurodesis) during a period of 3 months following the procedures.

Table (7): Outcome of pleurodesis procedures in cases of the studied groups.

Outcome of procedure	Doxycycline group (n=10)		Talc group (n=20)		Chi-square	
	N	%	N	%	X^2	P-value
Success	**4**	**40**	**9**	**45**	**0.516**	**0.773**

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Partial success	**2**	**20**	**4**	**20**		
Overall success	**6**	**60**	**13**	**65**		
Failure	**4**	**40**	**7**	**35**		

This table shows outcome of pleurodesis procedures in cases of group 1 (doxycycline pleurodesis) and cases of group 2 (talc insufflation pleurodesis).

Table (8): Correlation between personal,medical,laboratory,radiological characteristics of cases and outcome of pleurodesis in doxycycline group.

Characteristics	Outcome of procedure in doxycycline group						**Significance**	
	Failure		**Partial success**		**Success**		x^2/t	P
Gender	N	%	N	%	N	%	1.250	0.535
male	2	20	1	10	1	10		
female	2	20	1	10	3	30		
Age	Mean	SD	Mean	SD	Mean	SD	0.304	0.743
	48.00	6.54	52.25	10.24	51.40	11.37		
Smoking Index	Mean	SD	Mean	SD	Mean	SD	0.099	0.906
	211.67	254.59	187.50	217.47	140	313.05		
Hypertension	N	%	N	%	N	%	0.900	0.638
present	1	10	1	10	1	10		
absent	3	30	1	10	3	30		
Diabetes Mellitus	N	%	N	%	N	%	0.900	0.638
present	1	10	1	10	1	10		
absent	3	30	1	10	3	30		
Duration of malignancy (months)	Mean	SD	Mean	SD	Mean	SD	1.097	0.365
	19.2	7.3	10.5	3.7	7	4.12		
Karnofsky's score	Mean	SD	Mean	SD	Mean	SD	1.249	0.322
	75	5.5	67.5	5	68	13		
Weight loss	N	%	N	%	N	%	0.225	0.894
present	3	30	2	20	3	30		
absent	1	10	0	0	1	10		
Amount of effus.	N	%	N	%	N	%	1.275	0.529
moderate	2	20	2	20	3	30		
massive	2	20	0	0	1	10		
Pleural thickening in CT	N	%	N	%	N	%	6.830	0.033*
present	3	30	0	0	1	10		
absent	1	10	2	20	3	30		
Total proteins in pleural fluid	Mean	SD	Mean	SD	Mean	SD	ANOVA	
	4.23	0.47	4.53	0.58	4.04	0.36	0.339	
Leucocytic count in pleural fluid	Mean	SD	Mean	SD	Mean	SD	ANOVA	
	3334	2134	2197	792	2544	1278	0.531	

This table shows correlations between personal, medical, laboratory, radiological characteristics of cases and outcome of pleurodesis in doxycycline group.
Pleural thickening in CT had significant correlation with outcome of procedure in doxycycline group as P=0.033.*

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Table (9): Correlation between personal, medical, laboratory, radiological characteristics of cases and outcome of pleurodesis in talc group.

Characteristics	Outcome of procedure in talc group						Significance	
	Failure		Partial success		Success		x^2/t	P
Gender	N	%	N	%	N	%	4.416	0.110
male	1	5	2	10	6	30		
female	6	30	2	10	3	15		
Age	Mean	SD	Mean	SD	Mean	SD	0.623	0.548
	50	8.33	55	11.40	55	6.93		
Smoking Index	Mean	SD	Mean	SD	Mean	SD	1.155	0.339
	150	259.8	225	229.8	366.7	317.2		
Hypertension	N	%	N	%	N	%	3.003	0.223
present	1	5	2	10	5	25		
absent	6	30	2	10	4	20		
Diabetes Mellitus	N	%	N	%	N	%	1.028	0.598
present	2	10	2	10	2	10		
absent	5	25	2	10	7	35		
Duration of malignancy	Mean	SD	Mean	SD	Mean	SD	0.772	0.478
	12.7	5.7	6.8	2.2	8.2	3.2		
Karnofsky's score	Mean	SD	Mean	SD	Mean	SD	0.425	0.661
	72.9	4.9	70	0	70	8.7		
Weight loss	N	%	N	%	N	%	1.065	0.587
present	4	20	1	5	4	20		
absent	3	15	3	15	5	25		
Amount of effus.	N	%	N	%	N	%	1.028	0.598
moderate	5	25	2	10	7	35		
massive	2	10	2	10	2	10		
Pleural thickening in CT	N	%	N	%	N	%	6.028	0.049*
present	4	20	3	15	1	5		
absent	3	15	1	5	8	40		
Total proteins in pleural fluid	Mean	SD	Mean	SD	Mean	SD	ANOVA	
	4.01	0.30	4.1	0.62	3.87	0.39	0.617	
Leucocytic count in pleural fluid	Mean	SD	Mean	SD	Mean	SD	ANOVA	
	1621	945	1622	769	1369	752	0.796	

This table shows correlations between personal, medical, laboratory, radiological characteristics of cases and outcome of pleurodesis in talc group.

Pleural thickening in CT had significant correlation with outcome of procedure in talc group as P=0.049*. Neither protein content nor total leucocytic count of pleural fluid had any correlation with outcome of pleurodesis in both studied groups.

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Discussion

*** Thoracoscopic talc insufflation pleurodesis**

In this study, overall success rate for thoracoscopic talc insufflation pleurodesis was 65% with (complete success rate 40% and partial success rate 25%).

In agreement with success rates of talc insufflation pleurodesis achieved in the present study, **Y. C. Gary Lee et al in 2003** reported in an international survey a clinical success rate of 73 ± 17% [9]. Success was defined as satisfactory improvement of dyspnea and no re-accumulation of pleural fluid to a degree that requires additional pleural fluid drainage. The survey did not explain the observation period following the procedure.

On the other hand, and in contradiction with results of the present study, **A. Stefani et al in 2006** performed thoracoscopic talc insufflation pleurodesis in 72 patients having MPE with overall success rate of 88.3% after an observation period of 90 days and using definitions of success and failure similar to those used in the present study [10]. Similarly,**S. Kolschmann et al** reported success rate of 82.6 % by the end of 180 days of observation, the study included 46 patients, performed between 1999 and 2001, and successful pleurodesis was described as an absence of fluid re-accumulation with long-term symptom relief [11].

The lower success rate achieved in the present study compared to higher rates in the above mentioned studies might be attributed to:

- The present study was performed in a tertiary referral center where most of the patients seen in advanced stages.
-The possible different impact of malignancy type and stage on the outcome of procedure.

***Tube thoracostomy doxycycline pleurodesis**

In the present study, overall success rate for tube thoracostomy doxycycline pleurodesis was 60% (with complete success rate 40% and partial success rate 20%).

Pamela B. Walker-Renard et al [12]reported 72% success rate of doxycycline pleurodesis in a survey that collected all published doxycycline pleurodesis trials between 1966 and 1992.

J. M. Porcel et al [13]in a study published in 2006,reported success rate of 81% using doxycycline administered by small-bore catheter. They had the same definitions of success and failure as the present study with observation period > 30 days. Similarly, **Muir JF and colleagues** [14]ina study published in 1987, demonstrated 85% success rate with 2 or more administrations of the drug.

The most commonly encountered **complications** were empyema, lung collapse, fever and vomiting. **Empyema** occurred in 3/20 patients of talc poudrage group (15%) compared to 4/10 patients of doxycycline group (40%). Incidence of empyema was much lower with talc poudrage. Occurrence of empyema with talc poudrage in MPE had been reported by **Jean-Regis Viallat et al** (2.5%) [15]and**A. Stefani et al** [192,10] (1.4%). For doxycycline pleurodesis, empyema was reported by **Ramadan M. Bakr et al** [16](10%).**Persistent lung collapse** occurred in 2/20 patients of talc poudrage group (10%) compared to 1/10 patients of doxycycline group (10%). Results showed equal incidence of lung collapse following both procedures. Search in literature for comparative reports regarding collapse returned very few data. **Fever** occurred in 5/20 patients of talc poudrage group (25%) compared to 4/10 patients of doxycycline group (40%). Incidence of fever was much lower with talc poudrage.**Takeo Inoue et al** [17] reported 10 % incidence of mild fever with talc poudrage pleurodesis, while **Ramadan M. Bakr et al** 16]reported 30% incidence of fever in doxycycline pleurodesis. **Y. C. Gary Lee, R.W. Light et al**[9] reported that fever was significantly more common with talc poudrage than with tetracycline derivatives. **Vomiting** occurred in 2/20 patients of talc poudrage group (20%) compared to 6/10 patients of doxycycline group (60%).Incidence of vomiting was far much lower with talc poudrage. Search in literature for comparative reports regarding vomiting returned no results. Mild pain was perceived by 14/20 patients of talc poudrage group (70%) and moderate pain in 6/20 (30%). While in doxycycline group, mild pain was perceived by 4/10 patients (40%) and moderated pain in 6/10 (60%), **Pamela B. Walker-Renard et al** [12] and **Ramadan M. Bakr et al** [16] reported incidence of pain with doxycycline pleurodesis of 40 % and 60% respectively compared to much lower incidence in talc poudrage reported by **Takeo Inoue et al** [17](14%).

Statistical analysis of personal, medical, radiological and laboratory characteristics of patients was done to explore any possible correlation between any of these characteristics and outcome of procedure. Result of analysis showed that the presence of **visceral pleural thickening in CT** correlated significantly with failure in both talc poudrage and doxycycline pleurodesis. Neither duration of malignancy, amount of effusion, Karnofsky's score, protein content of pleural fluid, nor total leucocytic count of pleural fluid had any correlation with outcome of pleurodesis in both studied

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groups. Accordingly, it might be suggested that patients with marked pleural thickening would be better managed by other modalities rather than pleurodesis.

There is still much controversy among investigators who tried to identify reliable predictors of success and failure of pleurodesis.

E. Martínez-Moragón et al [18] reported that pH <7.2 , Glucose < 60 mg/dl, LDH < 600 u/l, Karnofsky's score < 70 , massive effusions and presence of additional radiographic abnormalities, all these factors were negative predictors of success of pleurodesis and survival as well.

A study by **J. E. Heffner et al** [19] showed that pleural fluid pH has only modest predictive value for predicting failure and should be used with caution, if at all, in selecting patients for pleurodesis.

In a study of talc pleurodesis by **J.A. Burgers et al** [20] in 2008, they reported that predictors of success were receiving anti-tumor therapy following pleurodesis procedure and good apposition of pleural surfaces during drainage while neither pH nor LDH level had any predictive values.

SomcharoenSaeteng et al [21] reported that short time interval between onset of effusion and performance of talc poudrage had good prognostic value.

Patients who failed pleurodesis were managed by repeated thoracenteces. Only 2 patients with rapid re-accumulation were managed by tunneled pleural catheter (TPC).

Conclusion

Results of the present study showed that:

- Both thoracoscopic talc insufflation and tube thoracostomy doxycycline pleurodesis achieved satisfactory success rates in controlling malignant pleural effusions with slightly higher success rate with talc insufflation.

- Both techniques were not associated with major complications but frequency of complications was higher with doxycycline.

- Failure correlated with the presence of visceral pleural thickening and this suggests using it as a possible predictor of failure.

- With higher success rates and fewer complications, thoracoscopic talc poudrage could be suggested as the procedure of choice to control recurrent MPEs.

- Multiple doses doxycycline is a valuable alternative for controlling malignant pleural effusions.

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