

Efficacy of short term versus long term tube thoracostomy drainage before tetracycline pleurodesis in the treatment of malignant pleural effusions

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Abstract

Background – A study was undertaken to compare the efficacy of short term tube thoracostomy drainage with standard tube thoracostomy drainage before instillation of tetracycline for sclerotherapy of malignant pleural effusions.

Methods – The study consisted of a randomised clinical trial in a sequential sample of 25 patients with malignant pleural effusions documented cytopathologically. Fifteen patients were randomly assigned to group 1 (standard protocol) and 10 to group 2 (short term protocol). Patients in group 1 had tube thoracostomy suction drainage until radiological evidence of lung re-expansion was obtained and the amount of fluid drained was < 150 ml/day, before tetracycline (1.5 g) was instilled. The chest tube was removed when the amount of fluid drained after instillation was < 150 ml/day. Patients in group 2 also had suction drainage, but the tetracycline (1.5 g) was instilled when the chest radiograph showed the lung to be re-expanded and the effusion drained, which was usually within 24 hours. The chest tube was removed the next day.

Results – The response to tetracycline sclerotherapy in the two groups was the same (80%) but the duration of chest tube drainage was significantly shorter for patients in group 2 (median two days) than for those in group 1 (median seven days).

Conclusions – The duration of chest tube drainage before sclerotherapy for malignant pleural effusions need not be influenced by the amount of fluid drained daily but by radiographic evidence of fluid evacuation and lung re-expansion. Shorter duration of drainage will reduce the length of hospital stay without sacrificing the efficacy of pleurodesis.

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Malignant pleural effusions are associated with a poor prognosis and often cause distressing symptoms such as dyspnoea and cough. Although the underlying malignant lesion is usually incurable, evacuation of the effusion can provide considerable relief of symptoms. Such palliative treatment is commonly accomplished with tube thoracostomy drainage and

the instillation of a sclerosing agent to induce a chemical pleuritis and obliterate the pleural space. Apposition of the visceral and parietal pleura before instillation of the sclerosing agent is necessary to achieve successful pleurodesis,^{1,2} but it is not clear what the optimal duration of tube thoracostomy drainage should be before and after instillation. Several studies have examined the efficacy of different sclerosing agents such as tetracycline,³⁻¹⁶ talc,¹⁷⁻²³ quinacrine,^{6,24-29} and bleomycin.^{14,16,23,30-33} Some authors^{34,35} have stated that the daily amount of fluid drained should be minimal – that is, less than 150 ml/day before instillation of sclerosant, and some^{16,36} have used this criterion for their study protocol. We found no data to support or refute this practice. We prospectively compared the efficacy of a protocol in which tetracycline was instilled when fluid drainage was less than 150 ml/day with a short term drainage protocol in which tetracycline was instilled within 24 hours of insertion of the chest tube, provided there was radiological evidence of full lung re-expansion, irrespective of the amount of fluid draining.

Methods

DESIGN OF STUDY

This study was prospective and randomised; tetracycline was used because of its proven efficacy, good safety record, and low cost.³⁻¹⁶ The protocol was approved by the Research Committee/Institutional Review Board of the Lahey Clinic Medical Center.

Eligibility

Patients eligible for the study were those with a moderate to large malignant pleural effusion, proved by cytological examination or pleural biopsy, causing respiratory symptoms, and an expected survival of at least one month with a Karnofsky score³⁷ of at least 40% (disabled, requires special care and assistance). Patients were excluded if a previous chemical pleurodesis had been undertaken on the same effusion, or if ipsilateral atelectasis due to complete airway obstruction by endobronchial tumour was present.

Treatment

After giving informed consent patients were randomly assigned by computer to one of two

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Table 1 Demographic and primary disease characteristics

Characteristics	Group 1 standard protocol (n=15)	Group 2 short term protocol (n=10)
Median (range) age (years)	67.5 (41-81)	70.5 (43-79)
Sex		
Male	5	4
Female	10	6
Primary site of tumour		
Breast	5	3
Lung	5	6
Prostate	0	1
Ovarian	3	0
Rectal	1	0
Unknown	1	0

groups. Patients in group 1 (standard protocol described by Sahn³⁴) underwent tube thoracostomy suction drainage until re-expansion of the lung and until the amount of fluid drained was less than 150 ml/day. Tetracycline (1.5 g diluted in 100-150 ml normal saline solution plus 20 ml 1% lignocaine) was then instilled intrapleurally. The chest tube was removed when the amount of fluid drained after instillation was less than 150 ml/day. Patients in group 2 (short term protocol) also had tube thoracostomy suction drainage, but the tetracycline (1.5 g diluted in the same manner) was instilled as soon as full re-expansion of the lung was radiologically documented, which was usually within 24 hours. The chest tube was removed the day after instillation of tetracycline. Other aspects of the pleurodesis technique were similar in the two groups. For pleural drainage a 28-French intercostal drainage catheter was inserted by the standard technique. After instillation of the tetracycline the tube was clamped and the position of the patient was rotated by the method described by Wallach.⁴³⁸ The tube was unclamped and suction drainage was resumed until the chest tube was removed.

A follow up chest radiograph was obtained after 30 days to determine the response to sclerotherapy. Subsequent follow up was provided by the patient's primary care physician.

STATISTICAL ANALYSIS

The two groups were compared with respect to demographic characteristics, site of primary tumour, duration of chest tube drainage, response to sclerotherapy, length of follow up study, and patient outcome. The response to sclerotherapy was determined by criteria described by Hausheer and Yarbo.³⁵ A response was defined as having no fluid reaccumulation for at least one month as determined by chest

radiography, or no further requirement for fluid drainage within one month of treatment, or both. Non-response was defined as recurrence of greater than 50% of the original volume of effusion, or the requirement for fluid drainage within one month of treatment.

Continuous variables were analysed with the Mann-Whitney test. Contingency tables were analysed by Miettinen's modification of the Fisher exact test. Statistical significance of differences between distributions were analysed by the Tarone-Ware method.³⁹ Probabilities are two-tailed with $p < 0.05$ being regarded as significant.

Results

Between May 1989 and August 1991 25 patients entered the study. Fifteen were randomly assigned to group 1 (standard protocol) and 10 to group 2 (short term protocol). The asymmetry between the size of the two groups was a result of the randomisation process. The demographic and primary disease characteristics are summarised in table 1. No significant difference existed between the two groups with regard to age or sex distribution. The frequency of carcinoma of the breast or lung, the most common primary tumour sites, was similar for both groups.

The data on duration of chest tube drainage, response to sclerotherapy, length of follow up study, and patient outcome are summarised in table 2. As expected, the duration of chest tube drainage was significantly shorter for patients in group 2 (median two days) than for those in group 1 (median seven days). Two patients in group 2 required a relatively long period of drainage; one had slow re-expansion of the lung because of partial airway obstruction by tumour, and one had a prolonged bronchopleural fistula as a result of carcinoma of the lung.

The response to sclerotherapy was similar in the two groups, both having about an 80% response rate. The two patients in group 2 whose treatment failed had subsequent tube thoracostomy drainage and instillation of tetracycline by the standard protocol. Repeated attempts at sclerotherapy failed in both patients.

Discussion

Despite the poor prognosis associated with malignant pleural effusions,⁴⁰⁻⁴² investigation into palliative treatment has been extensive. Treatments have included repeated thoracentesis,⁴³ tube thoracostomy alone,^{43,44} pleuroctomy,^{43,45,46} and placement of a pleuroperitoneal shunt,^{47,48} but the most commonly used method has been closed tube thoracostomy with instillation of a sclerosing agent. Much research has focused on the efficacy of sclerosing agents^{3-18,25-28} but not on the duration of chest tube drainage required.

With the use of tetracycline as the sclerosing agent, no difference in efficacy was found whether we waited until the daily chest tube drainage was less than 150 ml/day, as recommended by some authors,^{16,34-36} or whether

Table 2 Duration of chest tube drainage, response to sclerotherapy, length of follow up, and eventual patient outcome

	Group 1 standard protocol (n=15)	Group 2 short term protocol (n=9)*	p
Median (range) duration of chest tube drainage (days)	7.0 (3-19)	2.0 (2-9)	<0.01
Response to sclerotherapy			
Response	12 (80%)	7 (78%)	NS
Non-response	3	2	
Median (range) length of follow up (months)	3.0 (1-26)	1.0 (1-9)	NS
Patient outcome			
Alive	2	0	NS
Dead	13	9	

* Data were incomplete in one patient.

tetracycline was instilled as soon as the chest radiograph showed lung re-expansion which was usually within 24 hours. Both groups had an 80% response rate to tetracycline sclerotherapy, similar to published results.³⁻¹⁶ The duration of chest tube drainage, however, differed greatly. The median duration for patients in group 1 (seven days) was significantly longer than that for patients in group 2 (two days).

Two studies have been reported in which the authors stated that the duration of pleural drainage before instillation of the sclerosing agent was less than 24 hours; both reported successful pleurodesis.^{6,43} One study¹⁵ used intrapleural suction "until roentgenograms confirmed complete evacuation of the pleural space and complete lung expansion" before successful tetracycline pleurodesis, but did not report the duration of drainage. McAlpine *et al*⁴⁹ surveyed chest physicians in the United Kingdom and found that "those using intercostal tube drainage tended to remove the drain either immediately or within 24 hours". They found that only 13% of respiratory physicians and 23% of thoracic surgeons varied the duration of drainage according to the volume of fluid drained each day. Our study is the first to show in a prospective randomised trial that short term drainage before sclerotherapy is, indeed, effective.

We feel that, regardless of the sclerosing agent used, the duration of chest tube drainage need not be guided by the amount of fluid drained but by radiological evidence of fluid evacuation and lung re-expansion. This can result in a shorter duration of drainage, thus reducing the number of days in hospital and improving patient comfort without sacrificing efficacy of pleurodesis.

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