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

Andrew G Villanueva, Anthony W Gray Jr, David M Shahian, Warren A Williamson, John F Beamis Jr

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.**

(*Thorax* 1994;49:23–25)

Section of Pulmonary and Critical Care Medicine
A G Villanueva
A W Gray Jr
J F Beamis Jr

Department of Thoracic and Cardiovascular Surgery
D M Shahian
W A Williamson

Lahey Clinic, Burlington, Massachusetts 01805, USA

Reprint requests to: Dr AG Villanueva.

Received 22 February 1993
Returned to authors 27 April 1993
Revised version received 16 September 1993
Accepted for publication 11 October 1993

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 score[37] 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

Thorax: first published as 10.1136/thx.49.1.23 on 1 January 1994. Downloaded from http://thorax.bmj.com/ on April 23, 2024 by guest. Protected by copyright.

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 Sahn[34]) 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.[4 38] 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.

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.

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] pleurectomy,[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

Thorax: first published as 10.1136/thx.49.1.23 on 1 January 1994. Downloaded from http://thorax.bmj.com/ on April 23, 2024 by guest. Protected by copyright.

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 study[15] 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.

1 Malden LT, Tattersall MHN. Malignant effusions. *Q J Med* 1986;**58**:221–39.
2 Tattersall MHN, Boyer MJ. Management of malignant pleural effusions. *Thorax* 1990;**45**:81–2.
3 Rubinson RM, Bolooki H. Intrapleural tetracycline for control of malignant pleural effusion: a preliminary report. *South Med J* 1972;**65**:847–9.
4 Wallach HW. Intrapleural tetracycline for malignant pleural effusions. *Chest* 1975;**68**:510–2.
5 Sarma PR, Moore MR. Approach to the management of pleural effusion in malignancy. *South Med J* 1978;**71**:133–6.
6 Bayly TC, Kisner DL, Sybert A, MacDonald JS, Tsou E, Schein PS. Tetracycline and quinacrine in the control of malignant pleural effusions: a randomized trial. *Cancer* 1978;**41**:1188–92.
7 O'Neill W, Spurr C, Moss H, Richards R, White D, Cooper MR. A prospective study of chest tube drainage and tetracycline sclerosis versus chest tube drainage alone in the treatment of malignant pleural effusions (Abstract). *Proc AACR and ASCO* 1980;**21**:349.
8 Gupta N, Opfell RW, Padova J, Margileta D, Soudjian J. Intrapleural bleomycin versus tetracycline for control of malignant pleural effusion: a randomized study (Abstract). *Proc AACR and ASCO* 1980;**21**:366.
9 Zaloznik AJ, Oswald SG, Langin M. Intrapleural tetracycline in malignant pleural effusions: a randomized study. *Cancer* 1983;**51**:752–5.
10 Leahy BC, Honeybourne D, Brear SG, Carroll KB, Thatcher N, Stretton TB. Treatment of malignant pleural effusions with intrapleural *Corynebacterium parvum* or tetracycline. *Eur J Respir Dis* 1985;**66**:50–4.
11 Fentiman IS, Rubens RD, Hayward JL. A comparison of intracavitary talc and tetracycline for the control of pleural effusions secondary to breast cancer. *Eur J Cancer Clin Oncol* 1986;**22**:1079–81.
12 Kefford RF, Woods RL, Fox RM, Tattersall MHN. Intracavitary adriamycin, nitrogen mustard and tetracycline in the control of malignant effusions. A randomised study. *Med J Aust* 1986;**2**:447–8.
13 Gravelyn TR, Michelson MK, Gross BH, Sitrin RG. Tetracycline pleurodesis for malignant pleural effusions: a 10-year retrospective study. *Cancer* 1987;**59**:1973–7.
14 Kessinger A, Wigton RS. Intracavitary bleomycin and tetracycline in the management of malignant pleural effusions: a randomized study. *J Surg Oncol* 1987;**36**:81–3.
15 Sherman S, Grady KJ, Seidman JC. Clinical experience with tetracycline pleurodesis of malignant pleural effusions. *South Med J* 1987;**80**:716–9.
16 Ruckdeschel JC, Moores D, Lee JY, Einhorn LH, Mandelbaum I, Koeller J, *et al*. Intrapleural therapy for malignant pleural effusions: a randomized comparison of bleomycin and tetracycline. *Chest* 1991;**100**:1528–35.
17 Haupt GJ, Camishion RC, Templeton JY III, Gibbon JH Jr. Treatment of malignant pleural effusion by talc poudrage. *JAMA* 1960;**172**:918–21.
18 Camishion RC, Gibbon JH, Nealon TF. Talc poudrage in the treatment of pleural effusion due to cancer. *Surg Clin North Am* 1962;**42**:1521–6.
19 Starkey GW. Recurrent malignant pleural effusions. *N Engl J Med* 1964;**270**:436–8.
20 Pearson FG, MacGregor DC. Talc poudrage for malignant pleural effusion. *J Thorac Cardiovasc Surg* 1966;**51**:732–8.
21 Adler RH, Rappole BW. Recurrent malignant pleural effusions and talc powder aerosol treatment. *Surgery* 1967;**62**:1000–6.
22 Adler RH, Sayek I. Treatment of malignant pleural effusion: a method using tube thoracostomy and talc. *Ann Thorac Surg* 1976;**22**:8–16.
23 Hamed H, Fentiman IS, Chaudary MA, Rubens RD. Comparison of intracavitary bleomycin and talc for control of pleural effusions secondary to carcinoma of the breast. *Br J Surg* 1989;**76**:1265–7.
24 Gellhorn A, Zaidenweber J. Ultmann J, Hirschberg E. The use of Atabrine (quinacrine) in the control of recurrent neoplastic effusions: a preliminary report. *Dis Chest* 1961;**39**:165–76.
25 Ultmann JE, Gellhorn A, Osnos M, Hirschberg E. The effect of quinacrine on neoplastic effusions and certain of their enzymes. *Cancer* 1963;**16**:283–8.
26 Rochlin DB, Smart CR, Wagner DE, Silva ARM. The control of recurrent malignant effusions using quinacrine hydrochloride. *Surg Gynecol Obstet* 1964;**118**:991–4.
27 Dollinger MR, Krakoff IH, Karnofsky DA. Quinacrine (Atabrine) in the treatment of neoplastic effusions. *Ann Intern Med* 1967;**66**:249–57.
28 Hickman JA, Jones MC. Treatment of neoplastic pleural effusions with local instillation of quinacrine (mepacrine) hydrochloride. *Thorax* 1970;**25**:226–9.
29 Taylor SA, Hooton NS, MacArthur AM. Quinacrine in the management of malignant pleural effusion. *Br J Surg* 1977;**64**:52–3.
30 Paladine W, Cunningham TJ, Sponzo R, Donavan M, Olson K, Horton J. Intracavitary bleomycin in the management of malignant effusions. *Cancer* 1976;**38**:1903–8.
31 Bitran JD, Brown C, Desser RK, Kozloff MF, Shapiro C, Billings AA. Intracavitary bleomycin for the control of malignant effusions. *J Surg Oncol* 1981;**16**:273–7.
32 Ostrowski MJ. An assessment of the long-term results of controlling the reaccumulation of malignant effusions using intracavity bleomycin. *Cancer* 1986;**57**:721–7.
33 Ostrowski MJ, Priestman TJ, Houston RF, Martin WMC. A randomized trial of intracavitary bleomycin and *Corynebacterium parvum* in the control of malignant pleural effusions. *Radiother Oncol* 1989;**14**:19–26.
34 Sahn SA. Pleural effusion in lung cancer. *Clin Chest Med* 1982;**3**:443–52.
35 Hausheer FH, Yarbo JW. Diagnosis and treatment of malignant pleural effusion. *Semin Oncol* 1985;**12**:54–75.
36 Walsh FW, Alberts M, Solomon DA, Goldman AL. Malignant pleural effusions: pleurodesis using a small-bore percutaneous catheter. *South Med J* 1989;**82**:963–72.
37 Karnofsky DA. Cited by Haskell CM, ed. *Cancer treatment*. 2nd edn. Philadelphia: Saunders, 1985:190.
38 Wallach HW. Intrapleural therapy with tetracycline and lidocaine for malignant pleural effusions (Letter). *Chest* 1978;**73**:246.
39 Tarone RE, Ware J. On distribution-free tests for equality of survival distributions. *Biometrika* 1977;**64**:156–60.
40 Light RW. Malignant pleural effusions. In: Light RW, ed. *Pleural diseases*. 2nd edn. Philadelphia: Lea and Febiger, 1990:97–115.
41 Fentiman IS. Diagnosis and treatment of malignant pleural effusions. *Cancer Treat Rev* 1987;**14**:107–18.
42 Chernow B, Sahn SA. Carcinomatous involvement of the pleura: an analysis of 96 patients. *Am J Med* 1977;**63**:695–702.
43 Anderson CB, Philpott GW, Ferguson TB. The treatment of malignant pleural effusions. *Cancer* 1974;**33**:916–22.
44 Lambert CJ, Shah HH, Urschel HC Jr, Paulson DL. The treatment of malignant pleural effusions by closed trocar tube drainage. *Ann Thorac Surg* 1967;**3**:1–5.
45 Jensik R, Cagle JE, Milloy F, Perlia C, Taylor S, Kofman S, *et al*. Pleurectomy in the treatment of pleural effusion due to metastatic malignancy. *J Thorac Cardiovasc Surg* 1963;**46**:322–30.
46 Martini N, Bains MS, Beattie EJ Jr. Indications for pleurectomy in malignant effusion. *Cancer* 1975;**35**:734–8.
47 Little AG, Kadowski MH, Ferguson MK, Staszek VM, Skinner DB. Pleuro-peritoneal shunting: alternative therapy for pleural effusions. *Ann Surg* 1988;**208**:443–50.
48 Tsang V, Fernando HG, Goldstraw P. Pleuro-peritoneal shunting for recurrent malignant pleural effusions. *Thorax* 1990;**45**:369–72.
49 McAlpine LG, Hulks G, Thomson NC. Management of recurrent malignant pleural effusion in the United Kingdom: survey of clinical practice. *Thorax* 1990;**45**:699–701.

Thorax: first published as 10.1136/thx.49.1.23 on 1 January 1994. Downloaded from http://thorax.bmj.com/ on April 23, 2024 by guest. Protected by copyright.