

A Comparison of Intracavitary Talc and Tetracycline for the Control of Pleural Effusions Secondary to Breast Cancer

I.S. FENTIMAN, R.D. RUBENS and J.L. HAYWARD

ICRF Clinical Oncology Unit, Guy's Hospital, London SE1 9RT, U.K.

Abstract—Forty-one patients with malignant pleural effusions secondary to breast cancer were randomly allocated to treatment with either intracavitary talc or intracavitary tetracycline. Of 33 evaluable patients, radiological control was achieved in 11/12 (92%) of the talc group compared with 10/21 (48%) of the tetracycline group ($P = 0.022$). Intracavitary talc provides effective palliation of metastatic pleural effusions secondary to breast cancer.

INTRODUCTION

PATIENTS with metastatic breast cancer often develop symptomatic pleural effusions, either as a first manifestation of recurrence, or during the course of advanced disease. For patients without other detectable metastatic disease a local treatment may be preferable to systemic therapy. Furthermore, even those with evidence of metastases at other sites may better be palliated with intracavitary therapy in addition to systemic treatment. In a review of patients treated in this Unit it was found that control of effusions was achieved only in approximately one third of patients treated systemically [1]. Most patients with pleural effusions secondary to breast cancer are not in a preterminal state and the median survival is 13 months [1]. Therefore effective palliation of the effusion can relieve months of potential dyspnoea. Many agents have been recommended for instillation into the pleural cavity in order to produce pleurodesis, and include radioactive phosphorus [2], gold [3], thiotepa [4], mustine [5], quinacrine [6], tetracycline [7] and talc [8]. In a recent controlled trial, in which patients were randomly treated by either intracavitary talc or intracavitary mustine the former treatment was found to be superior [9]. Because talc produced the best control of effusions with no recurrence in 90% of patients, this method of treatment was adopted as the routine management on this unit. However, intra-cavitary tetracycline was becoming more widely used elsewhere as an intrapleural sclerosant and had the

potential advantage over talc that it can be instilled without the need for a general anaesthetic. For these reasons the present controlled trial has been conducted, in which patients with symptomatic pleural effusions secondary to breast cancer have been randomly allocated to treatment with either intracavitary talc or intracavitary tetracycline.

PATIENTS AND METHODS

Forty-one patients were entered into the trial. To be eligible, each had histologically confirmed breast cancer, together with a symptomatic pleural effusion which had been verified radiologically. None had received any previous treatment other than simple needle aspiration without indwelling tube drainage. Furthermore, none had evidence of non-malignant causes for the pleural effusion. All patients had to be suitable for general anaesthesia and either form of treatment, with no history of sensitivity to tetracycline. Patients were stratified according to the presence or absence of other metastatic lesions requiring treatment and were then randomly allocated to one of the two treatment arms.

Talc pleurodesis

The detailed technique of talc pleurodesis has been described previously [9]. In summary under a general anaesthetic, the pleural cavity was drained to dryness and inspected thoracoscopically. Simple talc was then insufflated, intercostal drains were inserted and remained in place for 5 days.

Tetracycline pleurodesis

These patients were also examined thoracoscopically under general anaesthesia after drainage of the effusion. One intercostal drain was inserted. After recovery from anaesthesia, 16–24 hr later, once radiological confirmation of lung re-expansion had been obtained, tetracycline 500 mg in 50 ml normal saline was instilled and the patient postured to ensure widespread distribution of the sclerosant. After the first two cases developed severe pain on instillation of tetracycline, despite being given opiates, lignocaine 500 mg was added to the instilled solution and this prevented this symptom. The drains were left in place for 3–5 days.

Assessment of response

The method of assessing response has been previously described [9]. To be assessable patients had to survive for more than 1 month after pleurodesis so that the chest radiograph at this time could be compared with the baseline film taken immediately after aspiration. A continued absence of fluid on all follow up films was deemed a success. Any reaccumulation was a treatment failure. The minimum period of follow up was 12 months.

RESULTS

Of the 41 cases, 23 were treated with intracavitary tetracycline and 18 with intracavitary talc. This inequality was due to randomisation being non-balanced. The features of the patients in the two groups were given in Table 1. There were more patients in the talc group with Stage III TNM tumours and more in the tetracycline group with Stage II TNM tumours. However, there was no significant difference in the distribution. Similar proportions of both groups had malignant cells in the effusion and there was no difference between the mean volumes aspirated.

Table 1. Comparison of the features of the patients in the study

	Talc(n=18)	Tetracycline(n=23)
Age at cancer diagnosis (mean \pm S.E.)	50.6 \pm 2.6	54.2 \pm 2.2
Disease-free interval in months (mean \pm S.E.)	53.7 \pm 10.9	84.4 \pm 14.6
TNM stage		
1	1	1
2	4	11
3	7	4
4	2	1
7	4	6
Cytology positive	13 (72%)	18 (78%)
Volume aspirated (mean \pm S.E.)	1630 ml \pm 218	1470 ml \pm 143

Complications

Surgical emphysema occurred in five cases (two talc, three tetracycline) and in one case this was of moderate severity. Two patients in the talc group developed wound infections at the drain site but in neither case did this cause any serious problems and no case of empyema occurred. One patient in the tetracycline group died 2 days postoperatively and autopsy showed that the patient had suffered a brain stem haemorrhage. Two patients in the talc group had asystolic arrest under general anaesthesia while being turned from the supine to the lateral position. Both patients were successfully resuscitated and neither suffered any neurological, cardiovascular or renal sequelae.

Assessment

Of the entire series eight patients (six talc, two tetracycline) died within 1 month of pleurodesis. Since the object of the study was to compare two forms of palliative treatment, and follow-up radiographs were necessary for assessment, the cases were not evaluable. These deaths were due to progression of metastatic disease and were not attributable to pleurodesis and so these cases were excluded from the analysis. There were therefore 12 assessable talc patients and 21 assessable tetracycline patients. The results are given in Table 2 which shows that successful palliation was achieved in 11 (92%) of the talc as compared with 10 (48%) of the tetracycline group (Fisher's exact test $P = 0.022$). Of the 11 patients in the tetracycline group with recurrence of effusion four were subsequently treated with intracavitary talc which produced effective control in all cases.

Table 2. Results of treatment

	Talc group n=18	Tetracycline group n=23
Not evaluable	6	2
Failure	1 (8%)	11 (52%)
Success	11 (92%)	10 (48%)

$P = 0.022$.

DISCUSSION

This study has shown that talc is superior to tetracycline in preventing recurrence of pleural effusion secondary to breast cancer. This can be achieved without major side effects, but because instillation of talc does produce immediate parietal pleural pain it is necessary to perform the procedure under a general anaesthesia and for this an experienced anaesthetist is required. Severe prolonged post-operative pleuritic pain has not been

a problem. Patients were given opiate analgesics for the first 24 hr postoperatively and thereafter usually only required mild analgesics. In this series empyema did not occur but this had been a complication in one patient who was treated before this trial started. In that case the drains were left in for more than 5 days because of a persistent pneumothorax. It is therefore recommended that whenever possible the intercostal drains should be

removed after no more than 5 days. With these provisions intracavitary talc provides an effective method of achieving successful pleurodesis which is suitable for the majority of patients with this complication of metastatic breast carcinoma. What still has to be achieved is a more accurate identification of those patients with poor prognosis who will die within one month and therefore will not benefit from aggressive local therapy.

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