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Medical Talc Pleurodesis: Which Patient with Cancer Benefits Least?

Aldona Wajda, MD, Helena Engström, MD, and H. Lennart Persson, MD, PhD

Abstract

Background and Objective: Successful talc pleurodesis (TP) for malignant pleural effusion (MPE) gives symptom relief, but may be too exhaustive in cases with poor performance status. The selection of eligible patients is therefore a challenging task. The study was undertaken to evaluate frequency of successful TPs, side effects, complications, performance status, hospitalization time, remaining time alive, and the responsible physician's prediction of a successful TP judged by radiologic findings prior to TP.

Methods: Side effects of TPs performed during a 1-year period were consecutively recorded and the TP outcomes were retrospectively evaluated 6 years later.

Results: TP success rate was 56% and 79% among best support of care subjects (BSC; $n=10$) and subjects eligible for cancer therapy (non-BSC; $n=19$), respectively, while side effects did not differ. Performance status was poorer and survival shorter among BSC subjects. Time spent in hospital of the remaining time alive for BSC and non-BSC subjects was $42\% \pm 27\%$ and $4\% \pm 4\%$, respectively. Poor performance status of subjects with lung cancer correlated with short survival time, which in turn correlated with many days at hospital for TP. The physician's prediction of a successful TP was correct in 50% of all cases.

Conclusions: Performance status of BSC subjects are probably too poor for TP and these subjects have to spend too much time at hospital during the procedure. The responsible physician is able to correctly predict a successful TP outcome in only every second case, supporting the need of additional predictive analysis.

Introduction

MALIGNANT PLEURAL EFFUSION (MPE) often causes disabling breathlessness.¹⁻⁶ Pleurodesis, using talc administered bedside as a slurry (TP), is the first-line therapeutic approach for patients presenting with symptomatic MPE.^{1-3,7-9} MPE may be a sign of advanced end-stage disease associated with a poor prognosis (expected survival less than 3 months).^{2,10} Such patients account for more than one-third of all MPE cases.¹¹ For these patients TP is used as a part of the best support of care (BSC) management.^{1,2} However, many TP-treated patients have longer life expectancy (3 months or more) because of treatments that still are available.^{2,6,10-14} In these cases TP is performed to improve conditions prior to planned cancer therapy, i.e., chemotherapy and/or radiation.

The estimated chance for successful TP should be accounted for before a decision is made to proceed to TP. Some researchers favor a variety of analyses on the pleural fluid,^{15,16} but in clinical practice expected TP success is usually based

solely upon clinical and radiologic findings presented to an experienced pulmonologist. Thus, TP is not suitable in cases of very poor performance status (performance status 4 according to WHO¹⁷), i.e., patients completely disabled and therefore confined to bed or chair,^{2,6,10,15} and cases of trapped lung, thus, when the visceral and parietal pleural layers are apart after the fluid is evacuated.^{1,2} In these cases an indwelling pleural catheter is probably a better treatment alternative.^{1,2}

Considering this, the aim of the present study was to compare the outcome of subjects with symptomatic MPE treated with TP, either as a procedure of BSC management (subjects no longer eligible for cancer therapy) or in addition to planned or ongoing cancer therapy (hereafter called non-BSC). TP success rate, side effects (i.e., chest pain/dyscomfort, desaturation, and fever), complications, hospital days due to TP, remaining time alive (from chest tube insertion to death), and performance status were recorded. Based on the radiologic findings presented prior to TP, the pulmonologist in charge was also asked for a prognosis regarding the chance of successful TP.

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Materials and Methods

Ethical considerations

The study protocol was approved by the local Ethical Committee (Linköping, Sweden; 2011/266-31) according to the guidelines of the Helsinki Declaration.

Study population

Patients admitted for TP at the Department of Pulmonary Medicine, University Hospital in Linköping, Sweden, were consecutively included during a 1-year period. After obtained consent, TP was performed on 30 Caucasians. Approximately 6 years after the last included subject the outcome was evaluated retrospectively using patient medical records. One patient was later diagnosed with pleural effusion of benign etiology and was therefore excluded. The remaining 29 subjects had histocytologically proven MPE.

All TPs were performed in hospital according to local routines using either small-bore (6–16F; mainly pig-tail catheters) or large-bore (20–28F) tubes (Portex-Smiths Medical, Dublin, OH). Timing of talc insertion (as a bedside slurry of 5 grams of talc per 200 mL of sterile 0.9% NaCl) was determined by the attending pulmonologist, when the lung was fully or nearly fully reexpanded and drainage volume was less than 150 mL per 24 hours. Unless there was any other reason for further inpatient care, patients were discharged following a satisfactory post-TP chest radiograph.

Assessment of outcomes

Chest pain/discomfort (assessed using a visual analogue scale [VAS] scale scoring from 0 to 10), saturation (SAT%), and body temperature (°C) during chest drainage post-talc instillation, complications during hospitalization, the number of days in hospital (i.e., days with chest tube and days after TP required for recovery), and the remaining time alive after talc instillation were recorded. When it was considered possible to predict, the physician in charge of the TP was also asked for a prognosis regarding the chance for a successful TP before TP was performed. Successful TP was defined as not needing another ipsilateral TP at any time. Based on presented radiology (chest X-ray findings prior to TP (after evacuation of pleural fluid), i.e., whether or not the lung was fully expanded, a thickened visceral pleura and/or organized fluid were present) the predicted outcome of the planned TP for each subject was scored as either “excellent,” “fair,” or “poor.” Functional and physical performance was assessed using the WHO score¹⁷: 0=able to carry out all normal activity without restriction; 1=restricted in physically strenuous activity but ambulatory and able to carry out light work; 2=ambulatory and capable of all self-care but unable to carry out any work, up and about more than 50% of waking hours; 3=capable of only limited self-care, confined to bed or chair more than 50% of waking hours; and 4=completely disabled, cannot carry out any self-care, totally confined to bed or chair. TP was not performed unless performance status was 3 or less.

Statistical analysis

The results are the means $\pm$ 1 standard deviation (SD). STATISTICA (version 10; StatSoft, Tulsa, OK) was used for

comparison (the *t* test; $p < 0.05$ [*], $p < 0.01$ [**], and $p < 0.001$ [***]) of groups and correlations between variables. The χ^2 test and Kolmogorov-Smirnov test were used for assessment of normal distribution.

Results

Advanced lung cancer was the main cause behind TP-treated MPE

Population characteristics are summarized in Table 1. Subjects were divided into two groups; the BSC group (no further cancer therapy planned and therefore expected survival less than 90 days) and the non-BSC group (planned or ongoing cancer therapy and therefore expected survival 90 days or more). There was no significant difference regarding age (70 ± 13 years versus 70 ± 9 years). The BSC group comprised 10 subjects (5 males and 5 females); 7 subjects with lung cancer, 2 subjects with breast cancer, and 1 subject with tongue cancer. The non-BSC group comprised 19 subjects (4 males and 15 females); 10 subjects with lung cancer, 2 subjects with gynecologic cancer, 3 subjects with cancer in

TABLE 1. CHARACTERISTICS OF THE POPULATION STUDIED

No.	Gender	Age	Type of cancer	Tube/size
BSC management (expected survival <90 days)				
1	M	86	Lung	Pig/12
2	M	77	Lung	Port/28
3	M	63	Lung	Pig/12
4	F	70	Tongue	Port/20
5	F	50	Lung	Port/20
6	F	61	Breast	Port/20
7	F	52	Breast	Port/22
8	M	81	Lung	Pig/14
9	M	75	Lung	Port/20
10	F	82	Lung	Pig/6
	50% females	70 $\pm$ 13	70% lung cancer	60% large-bore
Non-BSC (planned or ongoing cancer therapy; expected survival $\geq$ 90 days)				
1	M	65	Lung	Port/20
2	F	64	Lung	Port/16
3	F	64	Lung	Port/20
4	F	80	Lung	Port/20
5	F	66	Lung	Pig/8
6	M	65	Lung	Port/22
7	F	66	Lung	Port/20
8	F	62	Lung	Port/20
9	F	65	Lung	Port/14
10	M	53	Mesothelioma	Port/20
11	F	84	Unknown primary	Port/20
12	F	80	Urinary tract	Port/20
13	F	80	Urinary tract	Port/16
14	F	74	Gynecologic	Port/20
15	F	70	Gynecologic	Port/20
16	F	70	Kidney	Port/20
17	M	81	Lung	Port/16
18	F	79	Breast	Port/20
19	F	57	Breast	Port/20
	79% females	70 $\pm$ 9 (0.99)	53% lung cancer	74% large-bore

Data are presented as the means $\pm$ 1 standard deviation (SD). BSC, best support of care.

the urinary tract (including kidney cancer), 1 subject with mesothelioma, and 1 subject with an unknown primary tumor. Large-bore tube sizes ($\geq 20F$) were more frequent in the non-BSC group.

TP success and complications

Success rate was 79% (15/19 cases) in the non-BSC group, but only 56% (5/9 evaluable cases) in the BSC group (Table 2). Overall success rate of TPs was 71% (20/28 evaluable cases). Talc pleurodesis performed with small-bore tube sizes (i.e., $< 20F$) were successful in 5 of 9 cases (56%), while TPs performed using large-bore tube sizes were successful in 15 of 19 evaluable cases (79%). One patient in the BSC group died during hospitalization as a result of the TP performed

(Table 2). Three subjects were infected and another subject had a stroke, but all 4 subjects recovered and were eventually discharged (Table 2). Complication frequency was 17% (5/29 subjects).

Poorer performance status and shorter survival characterized the BSC group

The performance status of subjects in the BSC group was significantly poorer (2.5 ± 0.5) than the performance status of non-BSC subjects (1.5 ± 0.7 ; $p=0.0006$; Table 2). Survival time in the BSC group after TP was significantly shorter than in the non-BSC group; 44 ± 26 days and 410 ± 455 days, respectively ($p=0.003$; Table 2). The survival time agreed well with life expectancy, thus, 8 of 9 evaluable BSC subjects

TABLE 2. THE OUTCOME OF THE PLEURODESIS PERFORMED

No.	Successful pleurodesis	Performance status	Survival (days)	Days in hospital (days)	Days in hospital/survival (%)	Physician's assessment
BSC management (expected survival < 90 days)						
1	No	3	25	16	64	Not predictable
2	No	3	51	14	27	Not predictable
3	No ^{a,b}	3	16	16	100	Not predictable
4	Yes	3	39	14	36	Excellent
5	Yes	2	36	14	39	Not predictable
6	No	2	17	9	53	Fair
7	Unknown	2	Unknown	7	Unknown	Excellent
8	Yes ^c	2	63	14	22	Not predictable
9	Yes	2	97	7	7	Not predictable
10	Yes ^d	3	52	19	32	Excellent
	56% successful	2.5 ± 0.5	44 ± 26	13 ± 4	42 ± 27	40% Fair/excellent
Non-BSC (planned or ongoing cancer therapy; expected survival ≥ 90 days)						
1	Yes ^e	1	Unknown	9	Unknown	Excellent
2	Yes ^c	2	153	10	6	Excellent
3	Yes	0	388	16	4	Excellent
4	Yes	1	453	2	0.4	Excellent
5	No ^f	1	93	11	12	Not predictable
6	Yes ^f	2	122	11	9	Fair
7	Yes	1	298	7	2	Not predictable
8	Yes	2	400	7	2	Not predictable
9	Yes ^g	2	151	7	5	Excellent
10	No	2	936	3	0.3	Excellent
11	Yes	1	632	8	1	Excellent
12	No	2	384	15	4	Not predictable
13	Yes ^b	2	321	7	2	Fair
14	Yes	2	362	6	2	Fair
15	Yes	3	102	17	17	Not predictable
16	Yes	1	149	6	4	Excellent
17	No	1	115	6	5	Excellent
18	Yes	2	2021	7	0.3	Excellent
19	Yes	1	Unknown	8	3	Excellent
	79% successful	1.5 ± 0.7 (0.0006)	410 ± 455 (0.003)	9 ± 4 (0.009)	4 ± 4 (0.003)	74% Fair/excellent

Data are presented as the means ± 1 SD.

^aThis patient died during hospitalization (pleurodesis performed with reduced amount of talc).

^bOnly 3 g talc was given.

^cThese two patients displayed a typical clinic for pneumonia and responded well to antibiotic treatment but the diagnosis were not microbiologically or radiologically verified.

^dMepacrine chloride was used because of a very thin pleural catheter.

^eThis patient was diagnosed and treated successfully for empyema, which was microbiologically not verified.

^fPartly trapped lung.

^gThis patient was diagnosed with a stroke the day after performed procedure, but recovered without significant sequel.

SD, standard deviation; MPE, malignant pleural effusion; PS, performance status; BSC, best support of care management; TP, talc pleurodesis.

were dead within 90 days and all eligible non-BSC subjects ($n=18$) were alive after 90 days or more.

BSC subjects spent more time at hospital due to TP

Subjects in the non-BSC group spent 9 ± 4 days in the hospital, corresponding to $4\% \pm 4\%$ of their remaining time alive (Table 2). In contrast, subjects scheduled for BSC spent 13 ± 4 days ($p=0.009$) in hospital, and hospitalization time constituted a major part of their remaining time alive ($42\% \pm 27\%$; $p=0.003$; Table 2). Accounting only for lung cancer subjects, the same comparisons were significantly different as well ($p<0.01$ and $p<0.03$).

The pulmonologist's assessment of radiology was a poor predictor of successful TP

The TP outcome was known in 28 of 29 cases. Only 18 of these (64%) were regarded as possible to predict (Table 2). Notably, 67% of the TPs of the BSC group were categorized as "not predictable" (6/9 subjects).

Correspondingly, only 26% (5/19 subjects) of the non-BSC subjects was "not predictable." Overall, in 11 of 28 planned TPs (39%) the physician considered the TP as not possible to predict. All predictable TPs ($n=17$) were expected to have a good chance for a success ("excellent" or "fair"). Of these the clinician's assessment of successful TP was correct in 14 cases (2 BSC subjects and 12 non-BSC subjects) of 17 cases (82%). However, for all eligible cases the clinician was correct about a successful TP only in 14 of 28 subjects (50%).

Poor performance status and short survival of lung cancer subjects were associated with a long hospitalization for TP

Correlation studies of groups (i.e., type of cancer [all cancer types, lung cancer only and cancer of other origin than the lung] and planned management in these groups [BSC and non-BSC]) were performed comparing subjects regarding the following variables: age, performance status, number of hospitalization days, and survival. Performance status and days of hospitalization ($r=0.4345$, $p=0.024$) and survival time and number of hospitalizations days ($r=-0.4163$, $p=0.031$) correlated for all included subjects. Similarly, survival time and length of hospitalization ($r=-0.6407$, $p=0.007$) and performance status and survival time ($r=-0.6011$, $p=0.014$) correlated for lung cancer subjects. A significant correlation was also observed in the BSC group between performance status and number of hospitalization days ($r=0.6950$, $p=0.038$).

Lung cancer subjects desaturated more than non-lung cancer subjects did after TP

Side effects of TP (chest pain, desaturation, and a rise of body temperature) of all subjects included are shown in Figure 1. All variables were significantly changed versus the initial assessment at day 2, and were normalized within a couple of days. No difference was found between BSC versus non-BSC and small-bore tube size versus large-bore tube size. However, subjects with lung cancer, compared to those

with cancer of other origin, displayed significantly lower saturation before and after TP (data not presented).

Discussion

The aim of the present study was to compare the outcome of subjects with symptomatic MPE treated with TP, either as a procedure of BSC management (subjects no longer eligible for cancer therapy) or in addition to planned or ongoing cancer therapy (non-BSC). The present study defines a group of MPE subjects not suitable for TP in terms of poor chance for successful TP and long time spent at hospital as days and hospitalization time relative to survival post-TP. These subjects had poor performance status, making them no longer eligible for chemotherapy, and, as a consequence, scheduled for TP as part of BSC management. According to previous reports, time spent at hospital during TP is usually 4–6 days.^{4,5} In the present study BSC subjects stayed 13 ± 4 days in the hospital and non-BSC subjects 9 ± 4 days ($p<0.01$). Due to very short survival, hospitalization time became a major part of the remaining time alive of BSC subjects, $42\% \pm 27\%$, compared to $4\% \pm 4\%$ for non-BSC subjects ($p<0.01$). Unlike many other studies, which assess TP success at approximately 30 days post-TP, in the present study a successful TP success was defined more correctly as not needing another ipsilateral TP at any time after the TP performed. According to this definition, overall success rate of TPs in the present study was well in line with previous reports (approximately 70%–80%).^{9,10,18} In contrast, TPs performed on BSC subjects was successful in every second case. Considering the very long time spent in the hospital by many of the BSC subjects, such a low success rate is unsatisfactory.

Performance status was significantly poorer in the BSC group, but most subjects (6/9 subjects) lived more than 30 days post-TP, which is a life expectancy considered as appropriate to perform TP.^{2,9,14} The outcome of TP depends very much on the aggressiveness of the tumor causing MPE and the intention to treat, BSC or cancer therapy. One might therefore question whether this relatively small cohort of MPE subjects at a single center is representative. However, similar to larger cohort studies,^{1,2,9–11} the proportions of subjects with lung cancer and BSC subjects were two thirds and one third, respectively. In recent studies improvement of quality of life is an important outcome of TP.^{5,19,20} This variable of TP success was not assessed in the present study, which is a weakness.

Complication frequency in the present study was higher than what is previously reported in the literature (1%–10%).^{17,18} This observation may indicate that the subjects included were less suitable for TP than those participating in similar studies. It should be pointed out however that MPE/TP studies define and describe the complication rate very differently, making comparisons of studies rather difficult. As in the present study, some researchers choose to distinguish serious complications from the more common and expected side effects. Regarding the latter, lung cancer subjects exhibited significantly lower saturation pre- and post-TP than non-lung cancer subjects did, which most likely is because of concomitant lung disease (lung tumor and chronic obstructive pulmonary disease) involving the lung parenchyma.

In the present study the ability of the responsible pulmonologist to assess the chance for successful TP was studied, as

FIG. 1. Side effects during chest drainage post-TP, i.e., chest pain (A), fever (B), and desaturation (C) for the total number of patients evaluated. Values are the means $\pm$ 1 SD. Significant differences versus the initial assessment are indicated as follows: * $p < 0.05$, ** $p < 0.01$, and *** $p < 0.001$. TP, talc pleurodesis; SD, standard deviation; SAT, saturation; VAS, visual analogue scale.

far as we know, for the first time. Naturally, none of the TPs performed was defined as having a “poor” chance for success (in such a case TP should never be considered). Notably, more than two-thirds of planned TPs were considered by the physician in charge as not possible to predict. This issue was a dominating feature of the BSC group, which might suggest that the physician in charge, indeed, had some doubts regarding the value of the TP planned. The decision to proceed to TP was in all cases made by an experienced senior pulmonologist and in most cases also preceded by a consensus statement of two or more senior consultants. In other studies attempts have been made to predict TP outcome on the basis of analysis of different pleural fluid parameters.^{10,15,16} Since only every second TP were correctly predicted as successful, it seems that even experienced pulmonologists would need the support of reliable predictive tests.

The present study is relatively small and done at only one center. Thus, local treatment customs and the opinions of individual physicians when to proceed to TP (or not) might have some impact on the results presented. Even though TP seems less favorable among BSC subjects, suggesting that repeated thoracentesis or indwelling pleural catheters would be better treatment options, such comparison of different therapies was beyond the scope of the present study. TP is generally considered as a cost-effective procedure, but naturally, this is only if time of hospitalization is kept short.^{9,14,21}

Conclusions

Lessons learned from the present study are that TP should probably not be considered as a first choice of treatment for MPE patients planned for BSC management. The present study also supports the concept that the physician's assessment of clinic and radiology is inadequate in most cases for the prediction of the TP outcome.

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A.W. collected some data, analyzed all data, and wrote the manuscript. H.E. planned and conducted the study, collected most data, and analyzed some data, while H.L.P. analyzed all data and wrote the manuscript. All authors have given their final approval of the version submitted. This study was performed at the Divisions of Pulmonary Medicine, Linköping University, Sweden.

Author Disclosure Statement

No competing financial interests exist.

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