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ORIGINAL ARTICLE

Effect of Betadine in chemical pleurodesis in patients with recurrent malignant pleural effusion between 2013 and 2015

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Abstract

Introduction: Application of Talc powder, Bleomycin and Tetracycline is among conventional treatments in recurrent malignant pleural effusion caused by malignant pleurodesis. The aim of this research is to estimate the effect and safety in application of betadine as a cheap and available chemical factor in treatment of pleurodesis.

Methods: In this quasi-experimental study, all patients suffering from recurrent pleural effusion, who were admitted in the thoracic surgery department because of malignant nature of the diseases in a period of one year, were incorporated in the study. To perform pleurodesis, chest tube was initially inserted in the duration of 24-48 hours. Thereafter, 20 ml iodopovidon, 10 ml lidocaine, 80 ml normal saline of liquids were injected into the pleural cavity by a chest tube. All the patients were examined for the pleural effusion and pleurodesis recurrence monthly for 6 months. Chi-square and Fisher exact test were used as the qualitative and independent parameters in the quantitative comparison in this study.

Results: In this study, a total number of patients was 50 among whom 23 were male (46%) and 27 were female (54%). The mean age of the patients was 53.25±12.49 years. In the six months follow-up, 40 patients (80%) were completely recovered and the recurrence of the pleural effusion was noticed in 10 patients (20%). Comparison of the success rate of recovery in terms of the gender of the patients showed no significant relation between gender and response to the recovery process (P=0.219). Of the total of 32 patients (64%) with chest pain after pleurodesis, 23 patients had complete recovery, and the incidence of chest pain in patients with no improvement was significantly higher (P=0.018). However, there was no significant relationship between the severity of pain and the success of the treatment (P=0.92).

Conclusions: Compared with other sclerosant chemical substances, Iodopovidone is more cheaply available, is of high efficacy, and can be a good choice in treatment of malignant pleural effusion.

Key Words: Neoplasm; Metastasis; Pleurodesis; Pleural Effusion

Introduction

Pleuraisserosal membrane covers lung parenchyma, mediastinum, diaphragm, and the ribs (1). A liquid layer is normally present between visceral and thoracic wall of pleura and acts as a lubricant. The liquid is always being secreted from the pleural capillary net and being absorbed by most of the lymphatic system (1-3). The interaction with the normal system of secretion or absorption will cause pleural effusion, and the involved malignancy of pleura can be the third etiologic

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factor for pleural effusion (4, 5).

About 50% of the patients suffering from a metastatic cancer usually have pleural effusion (6, 7). This finding classifies these patients as untreatable with surgical methods for whom there is a low survival rate (5).

The quality of life in these patients significantly reduces as their life is associated with dyspnea and cough with injecting sclerosant substance into the pleural cavity (8).

Chemical pleurodesis is a process of injecting a sclerosant substance into the pleural space and is typically used in recurrent malignant pleural effusion.

Clinical manifestations depend on the amount of liquid and the severity of lung compression. If the volume of the pleural effusion liquid is less than 150-200 ml, diagnosis is easily possible with simple chest x-ray (5, 8). In case of more fluid, lung expansion gets limited whereby patients manifest some clinical symptoms such as dyspnea and dry cough as a result of bronchial irritation or mediastinal replacement (2, 7, 9).

Conventional treatments of recurrent or malignant pleural effusion involve pleurodesis with chemical substances such as talc powder, nitrogen mustard, bleomycine, tetracycline, betadine solution, and some surgical techniques like pleurectomy, pleuroperitoneal shunt, or application of pleural catheter. Nonetheless, common therapies not fail to improve patients' diseases but also impose extraordinary costs to the patients; meanwhile, surgical procedures are not welcome by most patients because of their invasive nature (4, 8, 9).

There are multiple treatment alternatives for the recurrent malignant pleural effusion; the proper treatment will be selected with consideration of general conditions of patients, primary malignant tumor and its response to the systemic treatment and re-expansion of lungs after evacuation of the pleural fluids, (5, 12, 13). Even the therapeutic thoracosynthesis, as a first step, is inevitable but studies have shown that pleurodesis is the best reliving treatment in a malignant recurrent pleural effusion (3, 4, 9).

Multiplesclerosant substances are being applied in pleurodesis among which Talc powder, tetracycline, and bleomycine can be mentioned (5, 6, 14). Lately, iodopovidone has been frequently used as a selected sclerosant substance especially because of the effect of iodine as an antiseptic liquid, the availability of this substance, and its cheap price. According to studies, in about 80-90% of patients with malignant pleural effusion, the substance has been accompanied by a good response to the treatment (1, 6). Unfortunately, in pleurodesis, different sclerosant substances have been applied, and in these studies, we could not find any preference of these materials to each other. In total, studies in this field are not completely clear.

The purpose of this research is to assess the effectiveness and safety of betadine as a chemical factor in pleurodesis. The reason of applying betadine as a chemical factor in treatment of pleurodesis is acceptability, ease of use, and its low price.

Methods

In this quasi-experimental study, after approval by the regional ethics committee of the faculty of medicine, affiliated with Tabriz University of Medical Sciences (registration number TBZMED.REC.1392.104), all admitted patients in the thoracic surgery department were investigated based on inclusion and exclusion criteria. Inclusion criteria comprised of patients with malignancy and approved diagnosis of recurrence and malignancy according to cytology findings of pleural effusion fluids. On the other hand, the patients who had allergy to iodine, those who had leucopenia and kidney failure, patients without recovery after thoracosynthesis, those who had obstructed bronchi's, lung expansion fibrosis, patients with history of kidney diseases, and thyroid were excluded from the study. All the participants in this study signed the consent form.

At the beginning of the study, medical history was taken, and full examination including chest auscultation (heart and chest) was performed. Routine lab investigations such as the CBC (complete blood count) kidney test and thyroid function test were performed. Chest x-ray and chest CT scan with the aim of checking the site and intensity of pleural effusion were performed. According to the fact that many of these patients had undergone chemotherapy, CBC, T3-T4-TSH-BUN, and Creatinine were necessary so that the patients with Hb< 9, platelets less than 50 thousand /ml, TSH less than 0.32 m.uni/ml, FT4 <0.7, Nano gram/deciliter and GFR (Glomerular Filtration Rate) less than 90 were excluded from this study. After the patients were included in the study, they underwent pleurodesis with Betadine.

To perform pleurodesis, a chest tube number F28 was inserted, in a sterile condition and in an operation theatre, parallel with the medial auxiliary line and in the fifth or sixth intercostal space. After 24 up to 48 hours of insertion, a chest tube lateral view and AP profile of chest x-ray was

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taken. After assurance of lung expansion, pleurodesis in the following way was performed: a fluid content 20 ml iodopovidone 10%, 10 ml lidocaine, and 80 ml normal saline by chest tube were injected in the pleural cavity, and the chest tube was clamped. In case the chest x-ray showed complete expansion of the lung and the chest tube drainage was less than 100 ml without air leak and in a duration of 24 hours, the tube was clamped and extracted.

All patients were followed up by checking them in terms of the intensity of the pain after pleurodesis, dyspnea, fever (body temperature higher than 38 ℃ in the first 48 hours after surgery), and hypotension (BP systolic less than 90 mmHg, and diastolic less than 60 mmHg). On the other hand, the pain intensity a day after pleurodesis was checked by using Visual Analogue Scale (VAS) where grade 0 meant no pain, 1-3 mild pain, 4-6 moderate, and 7-10 showed severe pain. During the morning round, pain was checked. Vital signs were examined every 6 hours by staff nurses and recorded on a special form. In case of pain and according to the patients' request, opioid was indicated and applied.

Patients with extracted chest tube were discharged, and if because of some clinical reasons, the chest tube was not extracted, the patient had to remain in the hospital up until the chest tube was extracted. In case there was no response to the therapy and based on the doctor's decision, these patients had to go through more advanced treatments like thoracoscopy.

Recovered and admitted patients undering chest tube insertion were followed up once a month for a length of 6 months, and in each visit of these patients, clinical manifestations of pleural effusion like dyspnea, cough, chest pain, and respiratory auscultation were checked. Subsequently, radiologic examination like chest x-ray was performed and their recovery was estimated. After evaluation, the efficacy of pleurodesis was classified in three categories:

1- Patients without recollection of fluid and total recovery
2- Patients with a reminded fluid in pleural cavity or recollection, without symptoms and not in need of any special procedure
3- Patients requiring thoracosynthesis and reinsertion of chest tube, classified as failed treated patients

After collecting all the data of the patients, they were analyzed by the SPSS software version18. Quantitative data presentation was through mean and standard deviation and qualitative data were shown as frequency and percentage.

To compare qualitative and quantitative data, student and Chi-square tests were used, and to compare prevalence of malignancies and pain severity in both groups, Fisher exact test was used. To review the relationship between response to the treatment and the pain after pleurodesis, odds ratio was used and the P-value less than 0.05 was considered as statistically significant.

Results

In this study, the efficacy of pleurodesis with iodopovidone was evaluated on 50 patients with recurrent malignant pleural effusion.

The participating patients included 23 males (46%) and 27 females (54%). The mean age of these patients was 36.26±12.49 years in the age range of 33 to 90 years.

Recurrent malignant pleural effusion was detected in 19 patients with lung cancer, 12 patients with unknown origin of primary cancer, 10 patients with breast cancer, 5 patients with mesothelioma, and 4 patients with lymphoma. Evaluating these patients as an affected hemi thorax showed that all the patients had unilateral pleural effusion where in 26 patients (52%), the right hemi thorax was involved, while in 24 (48%) patients, the left hemi thorax was involved.

Following pleurodesis with iodopovidone, a number of symptoms were reported in 32 patients: chest pain in 32 patients (64%), fever in 7 patients (14%), and hypotension in 3 patients (6%).

During the 6-month follow-up, 40 patients (80%) were totally cured and no patient with remained fluid or recollected fluid in pleural effusion had asymptomatic manifestation of diseases. Only 10 patients (20%) were affected by symptomatic pleural effusion, and no death case was reported.

The therapeutic success showed that there is no connection between the gender of the patients and adequate response to the therapy (P=0.219). The results also showed that there is no relation between the involved hemi thorax, the gender of patients, and the response to the treatment in recurrent pleural infusion (P=0.179).

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Table 1: Comparison of demographic data and patient findings by type of response to treatment

Variables		Recovery	Recurrence of pleural effusion	P-value
Age, mean±SD		54.46±18.84	49.82±14.27	0.042
Gender, n (%)	Male	20 (86.9%)	3 (13.1%)	0.219
	Female	20 (74%)	7 (26%)	
Hemi thorax, n (%)	Right	18 (75%)	6 (25%)	0.179
	Left	22 (84.6%)	4 (15.4%)	
Malignancy, n (%)	Lungs	14 (73.7%)	5 (26.3%)	0.73
	Breast	9 (90%)	1 (10%)	
	Lymphoma	3 (75%)	1 (25%)	
	Mesothelioma	5 (100%)	0	
	Metastasis	10 (83.3%)	2 (16.7%)	

Table 2: Comparison of pain severity in patients according to response to treatment

Variable		Pain severity		
		I	II	III
Response to treatment	Failure	3 (33.3%)	5 (55.5%)	1 (11.2%)
	Complete recovery	8 (19.5%)	10 (24.4%)	5 (12.2%)
Fisher's exact test		P=0.92		

Results indicate that there is no significant relationship between the type of malignancy and recurrent pleural effusion (P=0.179) (Table 1).

Also, from among the 32 patients with chest pain after pleurodesis, 23 patients (71.8%) had good and complete response to the therapy (Table 2).

Comparing the appearance of pain after surgery using the Fisher test showed that after insertion of the chest tube in these patients, the number of cases with no response to therapy after pleurodesis was significantly high (P=0.018). In the end, comparing the pain severity with good response to therapy or failure of the treatment, the study did not show a significant relationship between the severity of pain in these patients and success of the therapy (P=0.092).

Discussion

Recurrent and symptomatic pleural effusion is the most common complication in patients with malignant conditions, and according to studies, 25% of patients with lung cancer and 50% with breast cancer suffer from pleural effusion (10-12). In general, lung and breast cancers are the most etiologic factors for symptomatic pleural effusion.

Considering the need for repeated aspirations to relieve symptoms caused by recurrent pleural effusion, the quality of life of these patients is significantly reduced (5, 9). Therefore, along with effective treatment, it is of crucial importance to both manage the primary disease and to prevent from intensification of the symptoms.

The results of this study showed that after six months of follow-up, 80% of the participants had complete therapeutic response, so that none of them had a fluid collection in their pleural cavity as confirmed by the chest x-rays.

However, the most common complication of pleurodesis, i.e., chest pain was found in 64% of the patients (n=32). It was also found that lung cancer was one of the most etiologic factors for pleural effusion.

Dey and colleagues examined the role of pleurodesis with iodopovidone in the treatment of symptomatic malignant pleural effusion, reporting that 85% of patients with pleurodesis treated by iodopovidone had complete recovery which is higher than the success rate in patients treated by talc powder (79%).

In this study, chest pain was reported in 18% of the patients. Moreover, the level of complete recovery was similar to previous studies which can be the result of compliance with the inclusion and exclusion criteria in such studies and the style of patient selection.

However, in our study, 64% of our patients had chest pain followed by pleurodesis which is

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significant as compared with previous studies. This difference can be attributed to the qualitative approach to the study of the severity of pain in patients based on the pain score in our study.

Mohsen and colleagues compared the efficacy of two sclerosant substances, talc and iodopovidone, that were used in the treatment of recurrent malignant pleural effusion. Over the course of six months, treatment failure was reported in 15% of the patients. However, in our study, the failure rate was 20% during follow-up. Similar to the results of this study, in our study, there was no significant relationship between demographic factors and response to pleurodesis treatment with iodopovidone.

Moreover, in the study of Mohsen et al, only patients with breast cancer were studied, while in our study, all patients with recurrent malignant pleural effusion were examined. However, the comparison of the results of both studies shows that the type of malignancy has no effect on the response to the treatment.

In another trial, the efficacy of iodopovidone in the treatment of recurrent malignant pleural effusion was 72% (16). In our study, the prevalence of pleurodesis complications was reported in 64% of the patients, which is significantly higher than the rates in other studies.

However, the most common complication in these patients was chest pain, and all patients with complications of the operation had the above complaint

Chest pain prevalence in patients with poor recovery after pleurodesis treated by betadine was more than patients with good recovery; nevertheless, there was no significant difference in terms of severity of pain between patients with good recovery and those without good recovery.

Therefore, it is likely that the application of the pain scoring method in our study caused a significant false increase in chest pain complaints as well as the overall prevalence of post-pleurodesis complications with iodopovidone in patients.

However, comparing the results of this study with previous studies, the percentage of complete patient recovery is different where in a few of reports, complications associated with the use of iodopovidone have been published.

However, all studies, especially clinical trials show that the success rate of treatment of pleurodesis with iodopovidone has been reported equal or greater than that of other substances such as talc, which is making a good reason of improvement of patient's life quality (2, 6, 17, 18).

Therefore, considering the cheap price, availability, and acceptable efficiencies in treatment of recurrent malignant pleural effusion, iodopovidone can be a good alternative to other existing treatments and the sclerosant substances used earlier.

Our study had a few limitations in some ways. For instance, the low prevalence of recurrent malignant pleural effusion prevented the clinical trial from being performed with a large sample size. On the other hand, the census sampling method adopted in this study did not take into consideration the previous measures taken by patients for the treatment of pleural effusion.

It was not possible to follow up the patients with the history of previous interventions for the treatment of pleural effusion.

Conclusions

Considering the reasonable cost, availability, and acceptable efficacy in the treatment of recurrent malignant pleural effusion, iodopovidone is a proper substance and a good alternative for other existing treatments and previously used sclerosant substances and that because comparing this substance with other applied substances in treatment of pleurodesis, iodopovidone has significantly improved the quality of life of patients.

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Conflict of interest: None

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