

Povidone-Iodine and Bleomycin in the Management of Malignant Pleural Effusion

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Abstract- Malignant pleural effusion is a common complication in certain malignancies. Pleurodesis is the best option most of the time. The purpose of this study was to compare the choice of belomycin with povidone-iodine, which is not only determined by the efficacy of the agent but also by its cost, accessibility, safety, ease of administration and the number of administrations to achieve a complete response. We performed a randomized clinical trial on 39 patients presenting with symptomatic malignant pleural effusion. Patients were selected and randomly assigned to undergo chemical pleurodesis with either bleomycin or povidone-iodine. Primary characteristics of patients were assessed and graded before and after treatment concerning pain, dyspnea, and chest radiographs. A complete response was obtained in 79% of belomycin group and 75% of povidone-iodine group which was not statistically significant. Patients on belomycin treatment had a significantly lower score for dyspnea in one month follow up. This was significant after controlling for age, pain score and dyspnea score after drainage, using general linear model. Due to similar effect and significant cost advantage between bleomycin and povidone-iodine, we conclude that povidone-iodine is the agent of choice when utilizing pleurodesis for control of symptomatic malignant pleural effusions.

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Introduction

Pleurodesis with a chest tube drainage and intrapleural instillation of a chemical agent is the most effective methods for controlling a malignant pleural effusion (1,2). A wide variability exists in the choices of sclerosing agents. Talc, tetracycline and bleomycin have been widely used for pleurodesis (3).

Considering these agents, povidone-iodine, an iodine based topical antiseptic, is extensively used as an sclerosing agent (3). Many studies have shown the effectiveness of povidone-iodine to achieve a complete response rates 80-90% in the management of pleural effusion. On the other hand some side effects including thyroiditis and even visual loss has been reported (4), however it is the cheapest agent available. Previous studies have compared the effectiveness of talc with

other agents including *Corynebacterium parvum*, tetracycline, doxycycline and bleomycin (5).

Bleomycin is widely used among Iranian patients; however it is much more expensive compared to povidone-iodine. Besides there is not enough evidence demonstrating the efficacy of bleomycin compared to povidone-iodine. The purpose of this study was to compare the choice of the sclerosing agent, which is not only determined by the efficacy of the agent but also by its cost, accessibility, safety, ease of administration and the number of administrations to achieve a complete response (6).

The purpose of the present study was to compare the effectiveness of bleomycin with povidone-iodine, in the management of the pain after procedure; malignant pleural effusion and dyspnea after one month follow up.

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Materials and Methods

We performed a randomized clinical trial on patients with malignant pleural effusion. Patients in the study were selected from the pleural thoracic surgery outpatient

Clinic of Vali Asr Hospital affiliated with Tehran University of Medical Science between January 2009 and December 2009. Inclusion criteria were biopsy- or cytology-proven malignant pleural effusion; recurrent and symptomatic effusion; chest radiograph confirming lung expansion of 90% after therapeutic thoracentesis; and Karnofsky performance status index 70. The exclusion criteria were co morbidities that precluded general anesthesia; bleeding disorders; massive thoracic skin infiltration and active infectious disease. During the study, 40 patients with malignant or highly suspect pleural effusion were evaluated by a thoracic surgeon and selected. All participants gave written informed consent before participation. The research was carried out according to the principles of declaration of Helsinki; the local ethics review committee of Tehran University of Medical Science approved the study protocol.

The patients were assigned into 2 groups of bleomycin treatment or povidone-iodine treatment according to block randomization. Demographic and anthropometric data of the patients including sex; age; Karnofsky performance status index; time of pleural effusion; number of previous thoracentesis procedures; and type of primary malignancy were recorder for all studied patients.

Techniques

Patients underwent insertion of a 28 F chest tube at bedside under local anesthesia; IV opioids were administered when necessary. The next day, 1mg/kg of bleomycin (Nippon Kayaku laboratories; Japan) in a 60 mL saline solution, or povidone-iodine 10 % (Tolid Daru Pharm. Co. Iran) which was diluted to get povidone-iodine 2.5% , to which 5 mL of a 2% lidocaine solution was added and instilled through the chest tube according to the group of the patients. The tube was clamped for 1 h and then connected to a water seal. All patients were admitted to the same ward in the hospital, and underwent the same postpleurodesis respiratory therapy and pain control protocols. It is not our policy to use suction after pleurodesis; therefore, none of the patients underwent postoperative chest tube aspiration. The chest tube was kept in place until a daily output of 200 ml occurred; when the output was still high after 10

days, a Heimlich valve was connected to the chest tube. And the patient was discharged from the hospital. Numeric rating scale (NSR) was employed to score the pain at discharge and 30 postoperative days.

Radiologic analysis

Chest X rays were obtained after chest tube removal as the baseline chest X rays. Further chest X ray radiographs were performed on the 30th postoperative day after patients had undergone pleurodesis. The presence of pleural effusion was evaluated with chest X rays

Outcome analysis and follow-up

Pain after injection was evaluated by NSR as 0: no pain, 1: mild pain, 2: moderate pain and 3: sever pain. Dyspnea after drainage rather than before that was scored from 1 to 10. Dyspnea was scored from 1 to 10 one months later at patients routine follow up.

Statistical analysis

The statistical package SPSS 16 for windows (Chicago, Illinois, USA), was used for analysis. Kolmogorov-Smirnov test was employed to test the normality of the variables in each group. Variables distributed normally are presented as mean \pm standard deviation (SD). For comparison of dyspnea scores and other variables among the groups, Mann-Whitney U test and independent sample *t* test were employed, as appropriate. General linear model was employed to compare dyspnea score after in 30 days follow up controlling for age, pain and dyspnea score after drainage.

Results

Forty patients were selected to participate in the study, 19 underwent bleomycin treatment and 20 underwent povidone-iodine treatment and one did not accept to participate in the study. Pathologies of the studied population are presented in table 1. Chemotherapy was administered to all patients before pelurodesis, and pleural effusion remained refractory, none of the patients received chemotherapy after pleurodesis. A complete response was obtained in 79% of bleomycin group and 75% of povidone-iodine group which was not statistically significant. Characteristics of the groups are presented in table 2. Patients on bleomycin treatment had a significantly lower score for dyspnea in one month follow up. This was significant after controlling for age, pain score and dyspnea score after drainage using

Iodine povidone vs. bleomycine for pleural effusion

general linear model. There was not any significant difference between groups with respect of age, duration of thoracostomy, volume of pleural effusion, dyspnea score after drainage, fever and pleural effusion at discharge and pleural effusion one month later. ($P < 0.05$)

Discussion

Our finding from two groups of patients with malignant pleural effusion demonstrated that bleomycin is more effective in the management of dyspnea in one month follow up of the patients. On the other hand there was not any significant difference between groups in 1: pain score after procedure 2: dyspnea at discharge and 3: the recurrence of pleural effusion in one month follow up after procedure.

povidone-iodine an iodine-based topical antiseptic which is extensively absorbed from mucosal surfaces. It is associated with an increase in serum iodine concentrations (7). It may be absorbed by the thyroid gland and may appear in saliva, sweat, and milk, and is excreted unchanged in the urine (8). The exact mechanism by which povidone-iodine exerts its pleurodesis activity is uncertain; it is thought to be related to the low pH of the sclerosing solution (7,8). On the other hand bleomycin is an anti-neoplastic antibiotic from *Streptomyces verticillus*. Its mechanism of action is through inhibition of DNA synthesis (8). It is has sclerosing properties which is widely used for pleurodesis (2,8,9). It has minimal toxic reactions and is cleared by kidneys (8).

Previous studies have repeatedly shown the efficacy of povidone-iodine and bleomycin in the management of malignant pleural effusion separately (10-13). In a meta analysis conducted by Agrawal *et al.* the success rate of povidone-iodine pleurodesis was 90.6% which is almost equal to the efficacy of talc pleurodesis (5). Furthermore they showed that this effectiveness was regardless of the etiology or the techniques used to perform the pleurodesis (14,15). On the other hand it is showed that talc is the most effective chemical agent for the management of malignant pleural effusion (13,16,17). So it could be concluded that povidone-iodine is much more effective than bleomycin in the management of malignant pleural effusion. Kelly-Garcia *et al.* in a clinical trial of 20 patients, compared the efficacy of bleomycin with povidone-iodine in the management of malignant pleural effusion (18). They showed that povidone-iodine is as effective as bleomycin in the management of malignant pleural effusion in cases of recurrence (18). This was in consisted with our finding

that there was not any significant difference in the effectiveness of bleomycin compared to povidone-iodine.

Many studies have demonstrated that the significant side effects of povidone-iodine are the occurrence of the chest pain, postoperative visual loss and thyroiditis (4,10). We did not found any significant difference in the reported chest pain scores between our patients. However patients on the povidone-iodine group reported higher scores of dyspnea in one month follow up. So it could be questioned that when there was not any difference in the reported dyspnea scores at discharge, why patients on povidone-iodine treatment had higher scores in one month follow up. Future prospective studies may elucidate the dilemma.

In conclusion we have shown the similar effective of povidone-iodine compared to bleomycin in the management of malignant pleural effusion. The principal limitation of the present study was the small number of studied population and that the groups were not matched by age and sex, however we took advantage of close similarity between groups in most of the confounding variables and primary characteristics of the participants so as bleomycin may be administered to patients with sever dyspnea and povidone-iodine to others.

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