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Efficacy and safety of ethanol injection for endobronchial tumor debulking (a feasibility study)

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ABSTRACT

Background: Airway obstruction by malignant tumors may lead to dyspnea, cough, hemoptysis, atelectasis and pneumonia.
Aim: The aim was to assess safety and efficacy of ethanol injection in debulking of endobronchial malignant tumors.
Patients and methods: It included 20 patients with endobronchial malignant tumors and divided into 2 groups randomly: group A; 10 patients subjected to ethanol injection plus chemotherapy and group B; included 10 patients treated with chemotherapy alone.
Results: There was a significant improvement in dyspnea, cough and hemoptysis scores in group A after the end of the study (P1: 0.004, 0.014 and 0.014 respectively) and a significant improvement in group A compared with group B 2 weeks after the last session of chemotherapy as regard dyspnea and cough (P2 < 0.001 and 0.02 respectively) but with no significant difference between both groups two weeks after the last session of chemotherapy (P2: 0.21) for hemoptysis. In group A, there was a significant improvement in Karnofsky performance scale, FEV1 and FEV1/FVC ratio at the end of the procedure (P1 0.002, 0.024 and 0.03 respectively) with a significant improvement compared with group B (P2: 0.003, 0.04 and 0.05 respectively). Two patients in group A showed improvement in CT chest with no improvement in group B. Evaluation of response with revised RECIST; in group A, one patient showed good response, 5 patients showed partial response but in group B, only 2 patients showed partial response.
Conclusion: Intratumoral injection of ethanol 95% is effective and safe adjuvant to chemotherapy for tumor debulking.

Introduction

Most tumors of tracheobronchial tree are malignant [1] Lung cancer remains the leading cause of cancer mortality for both men and women [2]. Endotracheal or endobronchial obstruction may lead to cough, breathlessness and obstructive pneumonia. Endobronchial therapy may result in improvement of symptoms and quality of life [3]. Various forms of interventional therapies may be applied to the tracheobronchial tumors through the bronchoscope and percutaneous to the peripheral lung cancer. Image-guided tumor ablation is a treatment option for patients with hepatocellular carcinoma (HCC). Ablation induces tumor necrosis by injection of chemicals (e.g., ethanol, acetic acid) or temperature modification (ablation by radiofrequency, microwave, laser or cryoablation). Both ethanol injection and radiofrequency ablation achieve necrosis of HCC smaller than 2 cm [4]. The ablation activity for HCC is done by repeated injection of ethanol through a fine needle inserted into the lesion with US guidance.

Patients and methods

This prospective randomized controlled study enrolled 36 patients (only 20 patients completed the study and the other 16 patients refused to complete the study) with bronchial or tracheo-

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bronchial malignant tumors and conducted at chest medicine, oncology and pathology departments, Mansoura University, Egypt, during the period from October 2013 to December 2014 after approval of the local ethical committee of faculty of medicine, Mansoura University, Egypt, code number MS/437. Patients signed their written consents after detailed explanation of the procedure, they were 17 males and 3 females with age range from 32 to 74 (58.65 ± 9.51) years and divided into 2 groups randomly according to the enclosed envelope method: Group A; 10 patients subjected to intratumoral injection of ethanol according to site and size of the tumor in addition to treatment with the recommended regimen of chemotherapy according to their cell type. Group B; (control group): 10 patients treated with the recommended regimen of chemotherapy according to their cell type alone. The obstructing tumors must be endoluminal in the trachea, main bronchi or lobar bronchi and the margin between the tumor and the bronchial wall could be visible and there was a contraindication to surgery. Patients who were operable, uncooperative, with bleeding diathesis, intractable arrhythmia, severe pulmonary dysfunction or extraluminal obstruction of the airway were excluded from the study.

Methods

All patients were subjected to the following measures before and two weeks after the last session of chemotherapy in both groups:

1. Evaluation of dyspnea was done according American Thoracic Society [5], hemoptysis and cough were evaluated according to Walsh et al. [6] consolidation and collapse were evaluated according to Speiser and Spratling [7] and Karnofsky performance scale (KPS) according to Muers [8]. General and local examination were done.
2. Radiological investigations: as CT chest for staging and detection of post obstruction effects as consolidation or collapse.
3. Spirometry using device (Smart PFT CO) manufactured by medical equipment Europe – Hammelburg – Germany, with stress on FVC% and FEV1% of the predicted and FEV1/FVC ratio.
4. Fiberoptic bronchoscopy (FOB) was done for diagnosis of endobronchial tumors in both groups then for injection of ethanol for group A only and follow up for both groups 2 weeks after the end of chemotherapy using Pentax FB 18V. The number of sessions of ethanol injection was individualized according to the response with 2 weeks interval. Ethanol 95% was injected through aspiration needle of 1.8 mm diameter and 120 cm length (eNDO-FLEX GmbH Germany). Injected ethanol volume was calculated according to the size and location of the tumor according to the equation of Bruix and Sherman [12]: V (ml) = 4/3 π (D/2 + 0.5)3. (D = Diameter of the obstructing tumor). After injection of ethanol, flushing of the injection site with 20 ml saline 0.9% was done to dilute the possible spillover of ethanol. Bronchoscopic evaluation of airway opening was done every 2 weeks and forceps biopsy was taken before each session of ethanol injection from the targeted tumor to assess histopathological response. The primary end point of ethanol injection in group A was to achieve at least partial response according to criteria for evaluation of therapeutic effects (revised RECIST) [9] or a maximum of 5 injection sessions, patients refusing to complete the study, developing uncorrectable complications or death. The secondary end point of the study was 2 weeks after the last session of chemotherapy in both groups.
5. Evaluation of response after therapy:
   a. Subjective evaluation: by recording the changes in patients' symptoms and performance scale.
   b. Objective evaluation with radiologic, spirometric and bronchoscopic methods:
      I. Radiologic evaluation was done with chest CT scan.
      II. Spirometric evaluation with FEV1, FVC and FEV1/FVC.
      III. Bronchoscopic evaluation of airway patency was done according to Speiser's obstruction scoring [10] and achievement of the airway patency was evaluated according to response evaluation criteria in solid tumors (revised RECIST) [9] (Table 1).
6. Statistical analysis: Data was analyzed using SPSS (Statistical Package for Social Sciences) version 15 using the following tests: Chi-Square Tests, T-Test, Mann-Whitney Tests and Wilcoxon Signed Ranks Tests (see Tables 2–6 and Figs. 1–3).

Results

Twenty (20) patients, 17 males and 3 females, their age ranged from 32 to 74 years with a mean age of 58.65 ± 9.51 years were recruited in the study.

The patients were divided into 2 groups randomly according to the enclosed envelope method:

Group A; (interventional group): Included 10 patients with endobronchial malignant tumor who were subjected to injection of ethanol according to the site and the size of the tumor in addition to treatment with the recommended regimen of chemotherapy according to their cell type.

Group B; (control group): Included 10 patients with endobronchial malignant tumor who were treated with the conventional regimen of chemotherapy according to the cell type.

This table shows that all patients in group A with central airway obstruction were males (100%), with mean age 58.8 ± 8.62 years, meanwhile 7 patients in group B were males (70%), with mean age 58.5 ± 10.79 years. Regarding site of central airway obstruction, main bronchus obstruction in 5 patients (50%) in group A and 3 patients (30%) in group B and lobar bronchus obstruction in 5 patients (50%) in group A and 7 patients (70%) in group B.

This table shows; in group (A) there was a significant improvement in dyspnea, cough, hemoptysis, collapse severity scores and Karnofsky performance scale before and after the study. When

Table 1
Response evaluation criteria in solid tumors (revised RECIST).

Good response	More than 50% increase in airway lumen.
Partial response	25–50% increase in the caliber of the lumen
No response	Less than 25% increase in the caliber of the lumen
Progressive disease	A 25% or more increase in the size of one or more measurable lesions or the appearance of new lesions

Table 2
Demographic and pathological criteria of studied patients.

	Group A	Group B
Age: Mean ± (SD)	58.8 ± 8.62	58.5 ± 10.79
Gender		
Male	10(100%)	7(70%)
Female	0 (0%)	3 (30%)
Cell type of tumors causing CAO		
Large cell carcinoma	4(40%)	1(10%)
Adenocarcinoma	2(20%)	6(60%)
Squamous cell carcinoma	2(20%)	3(30%)
Undifferentiated carcinoma	2(20%)	0(0%)
Site of CAO		
Main bronchus	5(50%)	3(30%)
Lobar bronchus	5(50%)	7(70%)

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