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Research Article

FEV1 CHANGES IN CANCER PATIENTS UNDERGOING CHEMOTHERAPY

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ABSTRACT
The present study was aimed at determining the effect of chemotherapy on forced expiratory volume in 1 second (FEV_1) an important lung function parameter.
This study was conducted on 35 cancer patients with healthy lungs, who undertook cancer chemotherapy. The pulmonary function test parameters, forced expiratory volume in 1 second (FEV1). FVC ratio was recorded by using a computerized spirometer, Medspiror (Med Systems (P) Ltd. Chandigarh). All parameters showed a significant decline in the patients after the 1st and 2nd cycles of chemotherapy, as compared to those prior to the chemotherapy. The present study confirms the fact that chemotherapeutic drugs have a toxic effect on lungs.

Key Words: *Chemotherapy Pulmonary Function Tests*

INTRODUCTION
The incidence of respiratory illnesses has increased in the last 2-3 decades, thus leading to derangements of the lung functions, partly due to the increase in smoking, pollution and the life span and partly due to the use of various neoplastic drugs. At present, about 50% of the patients with cancer can be cured with chemotherapy, thus contributing to a cure in about 17% of the patients (Dimopoulou, 2002). The ideal anticancer drugs can eradicate the cancer cells without harming the normal tissues, but unfortunately, no currently available agents meet this criterion and the pulmonary toxicity which is caused by the administration of chemotherapy is usually irreversible and progressive. So, the present study was undertaken to estimate the extent of damage which is done by anticancer drugs on the lungs.

MATERIALS AND METHODS
The present study included 35 patients of either sex, who were diagnosed to have malignancy, but had healthy lungs. This study was conducted in the Department of Radiotherapy/Oncology, Shri Guru Teg Bahadur (S.G.T.B) Hospital, which is attached to the Government Medical College, Amritsar.
Patients with pulmonary metastasis and lung disease or those who had been previously exposed to radiotherapy during the treatment were excluded from the study.
All the subjects were explained about the procedures which were to be undertaken and written informed consent was taken from them as per the Helsinki declaration. This study was approved by the institutional ethics committee.
The patients were randomized into the following three groups: Group I (1st visit): before the start of chemotherapy. Group II (2nd visit): 3-4 weeks after the 1st visit (1st dose). Group III (3rd visit): 3-4 weeks after the 2nd visit (2nd dose).
Pulmonary function tests (PFT) were performed on the patients in the three groups at the baseline (before chemotherapy), 3-4 weeks after the start of chemotherapy and again, after the next 3-4 weeks. The tests were done on a computerized spirometer, Medspiror (Med Systems (P) Ltd. Chandigarh), with the patients in a standing posture.

Recording of FEV1
The relaxed subject in a standing position, were prepared to grip the sterile mouthpiece, as was demonstrated to him/her prior to the recording. When the subject was confident and familiar with the

procedure, he/she was asked to perform a maximum inspiration after a deep expiration. The subject was then instructed to expire with maximum effort (maximum expiration).The mouthpiece was then removed and the following spirometric parameters were recorded for analysis.

Forced expiratory volume in first second (FEV_1): The fraction of vital capacity which is expired during the 1st second of a forced expiration.

The data was collected, tabulated and analyzed by using the paired t-test for the comparison of the means and by the Chi-square test for the two-by-two tables. A 'p' value of 0.05 was taken as the cut off for the measure of significance. The patients on whom the study was undertaken were on various chemotherapy regimens.

Table 1: Patient distribution: C.M.F: Cyclophoshamide, Methotrexate, Fluorouracil; C.A.F: Cyclophoshamide, Adriamycin, Fluorouracil.

Chemotherapy regime	No of patients
1. Carcinoma breast(C.M.F regimen)	10
2. Carcinoma breast(C.A.F regimen)	5
3. Carcinoma stomach	5
4. Multiple myeloma	4
5. Carcinoma Ovary	4
6. Carcinoma Endometrium	2
7. Carcinoma Oesophagus	1
8. Non Hodgkins lymphoma	2
9. Carcinoma Pancreas	2

RESULTS

The mean age of the subjects in all the groups was 51.71+9.97 years (range 30 to 70 years).The number of male subjects was 13 and that of the female subjects were 22.

Forced Expiratory Volume in the First Second (FEV1) Litres

The difference in the value of the FEV1 in the group I cancer patients and group II patients was statistically highly significant, while the difference of its value between the group I and group III cancer patients was also statistically highly significant.

DISCUSSION

In the present study, it was seen that the value of the FEV1 was high in the group I cancer patients (before chemotherapy) in comparison to the group II and group III patients (after chemotherapy).

The usual pulmonary injury with cytotoxic therapy is probably due to progressive pulmonary fibrosis, with relatively little of an inflammatory component and with a tendency to cause irreversible lung damage. Bleomycin and Mitomycin are cytotoxic antibiotics which cause pulmonary fibrosis in up to 5-10% of the patients (Marruchella *et al.*, 2002) while the pulmonary toxicity from the combination of Gemcitabine and Paclitaxel is reported to be approximately 5% (Rivera *et al.*, 2009 and Friedberg *et al.*, 2003). Several cytotoxic drugs that act by the alkylation of DNA have also been shown to cause alveolitis and pulmonary fibrosis e.g. Busulphan, Chlorambucil, Cyclophosphamide^] and Melphalan. These effects have also been seen with Methotrexate and Carmustine.

We found a similarity in our findings with those of Jensen *et al.*, (1990) who suggested that mantle-field irradiation was associated with a primary obstructive and minor restrictive lung function impairment, whereas chemotherapy and combined modality therapy was associated with a restrictive lung function impairment. Also, Nysom *et al.*, (1998) who studied acute lymphoblastic leukemia patients, observed slight restrictive pulmonary disease which developed after the intake of chemotherapy.

Table 2: Comparison of FEV_1 in the three groups of cancer patients

Parameter	Group I Cancer patients (before)		Group II (after 1st cycle of chemotherapy)		Group III (after 2nd cycle of chemotherapy)		'p' Value
	Mean	SD	Mean	SD	Mean	SD	
FEV1(L)	1.95	0.18	1.79	0.18	1.66	0.16	<0.001

Pulmonary toxicity is usually irreversible and progressive as a result of the administration of chemotherapy. The initial site of damage seems to be the endothelial cells, with an inflammatory type reaction resulting in drug induced pneumonitis (Marruchella *et al.*, 2002), (Rivera *et al.*, 2009). Another type of damage occurs as a result of an immunological mechanism, resulting in an allergic type reaction. Either the lung or the drug may act as an antigen in an allergic type reaction. Chronic exposure to chemotherapy causes extensive alteration of the pulmonary parenchyma, with changes in the connective tissue, obliteration of the alveoli and dilatation of the air spaces, which is known as honeycombing. Continuous lung injury and repair result in restrictive lung disease, the increased work of breathing and a functionally reduced lung volume, thus leading to an impaired gas exchange. The chest X-ray may be within normal limits, but it can show a pattern of diffuse interstitial markings. The pulmonary function tests can show a restrictive pattern when pulmonary fibrosis has occurred before the clinical symptoms have appeared. But few studies have been carried out, which do not show similar results. Ooi *et al.*, (2001) found lung function indices including FVC, FEV_1, TLC and DLCO, in patients who received chemotherapy, but did not have significant declined lung function indices. According to Dimopoulou *et al.*, (2002) after chemotherapy, there were no significant changes in the forced vital capacity (FVC), FEV_1, TLC or the alveolar volume.

Conclusion

The present study highlights the observation that most of the spirometric parameters in cancer patients after chemotherapy showed a significant decline. Some drugs may cause direct damage to the lung parenchyma, like Bleomycin, Cyclophosphamide and Nitrofurantoin, which can cause the generation of toxic oxygen free radicals. Others may act on the system, whereby the lung matrix repairs itself, interfering with or increasing collagen formation. In some cases, this restrictive type of abnormality is associated with an obstructive pattern as well. In case of intrinsic drug induced lung diseases, the physiological effects of the diffuse parenchymal disorder reduce all the lung volumes, probably by the excessive elastic recoil of the lungs, in comparison to the outward recoil of the chestwall. The expiratory airflow is reduced in proportion to the lung volumes. This decline after chemotherapy is probably due to the toxicity of the various chemotherapeutic drugs.

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