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Osteoporosis among Asthmatic Patients Exposed to Mustard Gas Compared with Non-Exposed Asthmatics

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ABSTRACT

Background: Chemical warfare victims with history of exposure to sulfur mustard gas comprise a considerable number of our young asthmatic population. They are at risk of adverse effects of the gas including asthma; diffuse pulmonary fibrosis, chemical bronchitis, skin lesions and ophthalmic complications, with a great part of their treatment depending on corticosteroid compounds.

Objective: To evaluate the rate of osteoporosis in a group of asthmatic victims of sulfur mustard gas and to compare it with non-chemical asthmatic patients, in order to determine the distribution, site of involvement, intensity of effects, and difference with the non-exposed group.

Materials and Methods: In this prospective study, 100 asthmatic male patients who had a history of exposure to sulfur mustard gas were selected according to inclusion and exclusion criteria, and matched with 100 non-chemical asthmatic male patients in regard to age, duration of disease, duration of corticosteroid therapy, and the form of therapy. Bone Mineral Density (BMD) test was performed on hip and lumbar vertebrae of case and control groups according to WHO criteria. Independent-samples T test was used to analyze the results.

Results: There was a significant difference ($p < 0.05$) between the two groups in the range of osteoporosis and osteopenia. No significant correlation was found between age and complications. Most changes (65%) were observed in the vertebral column, and hip involvement (5%) was much more severe in the case group.

Conclusion: Considering the morbidities caused by this chemical warfare agent, the osteoporotic complications in chemical warfare victims can intensify their disabilities. Therefore, preventive measures must be undertaken to reduce complications.

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Key words: Asthma, Osteoporosis, Corticosteroid, Sulfur mustard gas

INTRODUCTION

Asthma is a chronic inflammatory disease of airways, for which corticosteroids have a great role in treatment and control (1,2).

In long term; however, inhaled and oral corticosteroid have significant adverse effects including osteoporosis in skeletal system (3,4).

The victims of the chemical warfare agent, sulfur mustard gas, are at great risk of its impacts and complications such as diffuse pulmonary fibrosis,

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chemical bronchitis, skin lesions, ophthalmic complications, airway irritability and asthma (5,6,7); once again corticosteroids have a central role in their therapy. However the rate of osteoporosis among the chemical warfare victims treated with corticosteroid is not yet clear.

This study aims at comparing the rate and intensity of osteoporosis among chemical warfare victims with asthma treated by corticosteroid, and non-chemical asthmatic patients.

MATERIALS AND METHODS

This prospective case-control study was performed between April and November 2003 in Loghman Hakim Hospital, Shaheed Beheshti University of Medical Sciences, Tehran, Iran.

A chemical warfare victim was defined as one who has a history of at least one-hour exposure to sulfur mustard gas, and an official statement confirming his injury. One hundred male chemical warfare victims who suffered from bronchial asthma were selected from the volunteer cases referred to chemical warfare victims' clinic. The American Thoracic Society's definition of asthma was used as the standard scale (8). A questionnaire was given to all volunteers covering demographic data, nutrition, history of smoking, history of endocrine problems (thyroid, parathyroid, and sex hormones), use of osteoporosis therapeutic drugs or diuretics, GI and /or renal diseases, exposure to chemical warfare agents, duration of exposure, duration of corticosteroid therapy and the form of therapy received. A standard chest X-ray and spirometry were performed and recent medical history was evaluated to confirm long-term complications of sulfur mustard exposure such as diffuse pulmonary fibrosis and ophthalmic lesions. All those lacking the criteria for a chemical warfare victim, or having a history of smoking and using osteoporosis inducing or therapeutic drugs were excluded from the study,

and eventually 100 patients were selected for the case group.

From non-chemical asthmatic male patients who volunteered for the study, 100 persons were selected as the control group. Considering the same inclusion and exclusion criteria, age, duration of corticoid therapy and, as much as possible duration of disease were matched between case and control groups.

Bone Mineral Density test (BMD) with Dual Energy X-ray Absorptiometry (DEXA) method was performed on all subjects for hip and lumbar vertebrae. Detection of metal density in back, abdomen and hip was considered as an exclusion criterion. Test results were interpreted as osteoporosis (>2.5 SD lower than normal T score), osteopenia or low bone density (between 2.5 to 1 SD T score) and normal condition (<1 SD lower than normal T score), The T score is an SD from peak bone mass according to the definition provided by the World Health Organization. A Lunar DPX system, produced by Lunar Company, was used for densitometry.

Data were analyzed using SPSS software version, 11.5, based on independent sample t-test with a significance value of $p < 0.05$.

RESULTS

The study was performed on 100 chemical warfare victims in a period of six months. The average age was 40 ± 12 SD years, and diffuse airway irritability was confirmed in all of them using spirometry. The duration of exposure to sulfur mustard gas is shown in Table 1.

The selected individuals had no history of smoking; had not used calcium, vitamin D, hormonal medicines or diphosphonids in the past two years and had received corticosteroid therapy with at least 10 mg equivalent of prednisolon for over one year. Of all cases, 62% received corticosteroid for 5-10 years,

32% for 10-15 years, and 6% for more than 15 years. Among them, 60 used inhalant corticoids only, 32 patients used inhalant and oral agents, and 8 received long-acting injection drugs.

Table 1. The duration of exposure to sulfur mustard gas in chemical warfare victims

Duration of exposure (hours)	1	2-4	4-6	6-8	8-10	>10
Number (%)	25	10	30	15	18	2

In the case group, 59 patients had normal BMD results, 36 had osteopenia and 5 were osteoporotic. The BMD results for the control group were 91% normal, 7% osteopenia and 2% osteoporosis. The difference in the rate of both osteopenia and osteoporosis between the two groups was statistically significant ($p < 0.05$).

There was no significant correlation between age and osteoporosis.

In chemical warfare victims group, the most reduced bone density was seen both in hip and vertebrae in 22 patients (65%), vertebral column only in 9 patients (22.5%) and hip only in 5 persons (12.5%). Of osteoporotic patients, three (60%) had a reduced bone density in hip and vertebral column, and in two persons (40%), the vertebral column was the only place of involvement.

DISCUSSION

Numerous studies have been performed in regard to pulmonary diseases, especially asthma, and the side effects of corticosteroid use on bone density (9,10,11,12). There are also some studies concerning the effects of sulfur mustard gas on the respiratory, reproductive, and nervous systems (13). However studying the effects of this agent on bone density and

comparing it with corticosteroid-using non-chemical warfare victim patients is a new area that the 8-year imposed war between Iraq and Iran (in which chemical warheads were used by the Iraqi side), and the considerable number of chemical warfare victims in our country, provide a unique opportunity to explore.

Chemical warfare victims are faced with some underlying diseases such as diffuse pulmonary fibrosis or asthma, which necessitates the use of corticosteroid compounds. They also have a sedentary lifestyle due to physical disabilities caused by their condition. Both these factors can have a direct influence on the progress of osteoporosis. The results of our study confirm this hypothesis, and show that exposure to sulfur mustard gas clearly increases the rate of osteopenia and osteoporosis.

Decreased BMD in the vertebral column, especially between L2- L4, was seen in both case and control groups, but an important point is that there was a significantly higher rate of BMD decrease in the hip in the victim group.

Considering the young age of the chemical warfare victims, the progress of osteoporosis can impose complications other than those related to their exposure to chemical agents.

Since these agents have a long-term effect on bone density as compared with corticosteroids, it is feasible and necessary to prevent and diagnose the condition as soon as possible to avoid its progression. This necessitates a more extensive study to develop a strategy for preventing drug side effects.

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