Glucocorticoid-related osteoporotic fractures

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ABSTRACT

Introduction: This study was conducted to evaluate the prevalence of fractures secondary to steroid use.

Methods: A total of 165 patients (100 male and 65 female) who received glucocorticoid therapy at a dose of 7.5 mg or more, or its equivalent, for more than six months were identified from July 1, 2007 to December 30, 2007. Data extracted included age, gender, dose of glucocorticoid, concomitant diseases, the use of anti-resorptive therapy, calcium and vitamin D supplementation, and the results of bone mineral density (BMD) tests, if performed. Any fragility fractures, the site involved and the treatment administered were also recorded. The data was entered and analysed using the Statistical Package for the Social Sciences.

Results: 140 patients had no fractures while 25 (15.2 percent) sustained an osteoporotic fracture. The age (p-value less than 0.5), dose of steroids (p-value less than 0.001) and duration of glucocorticoid therapy (p-value less than 0.001) were significantly higher among patients who sustained fractures. Of these, 12 were male and 13 were female. None of the patients in both groups was started on antiresorptive therapy. The dosage of glucocorticoids was higher among women than men (11.5 versus 24.5 mg/day, p-value is 0.05). The commonest sites of osteoporotic fracture were the spine (44 percent) and proximal femur (24 percent). Eight out of 11 patients had more than one vertebra involved.

Conclusion: Fractures due to steroid-induced osteoporosis could have been prevented if appropriate measures were taken.

Keywords: glucocorticoids, osteoporosis-related fractures, secondary osteoporosis

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INTRODUCTION

Postmenopausal osteoporosis and male osteoporosis have recently been found to be common among the Saudi Arabian Society.[1-4] Secondary osteoporosis, particularly glucocorticoid-induced osteoporosis (GIOP), has started to gain attention among physicians; however, GIOP-related fractures have not been well studied, especially in the Middle East. Corticosteroids cause low bone mass by directly affecting osteoblastic activity and hence, reducing bone formation that predominantly affects the trabecular bone.[5] It has been well established that the long-term use of glucocorticoids increases the risk of all osteoporotic fractures, and thus, it is recommended that the use of prednisolone ≥ 5 mg for three months or longer requires proper investigation and treatment so as to prevent osteoporosis.[6-9] Even with these recommendations, patients continue to be poorly managed.[10-12]

In a large meta-analysis study of glucocorticoid users, van Staa et al[13] found a relative risk increase of 1.91 for any fracture, 2.86 for vertebral fracture, 1.61 for hip fracture, and 1.13 for forearm fracture. There is limited information from Middle Eastern countries regarding the prevalence of steroid-induced fractures, and in a study from our institution, we found that no prophylaxis was administered to patients on steroids. We hypothesised that osteoporotic fractures resulting from the prolonged use of steroids may be a common occurrence among our patients. Hence, this study was carried out to evaluate the prevalence of osteoporosis-related fractures due to glucocorticoid use and to determine the site of fractures involved.

METHODS

This was a retrospective study involving adult patients treated at King Fahd University Hospital, AI-Khobar, Saudi Arabia, who were prescribed prednisolone ≥ 7.5 mg or its equivalent for more than six months between July 1, 2007 and December 30, 2007. The medical records of the patients were reviewed, and data, including age, gender, dose and duration of glucocorticoid therapy, was extracted. A history of concomitant diseases that could primarily cause osteoporosis, such as endocrine diseases, sickle cell disease, rheumatological and gastrointestinal diseases and a history of malignancy or trauma were

Table I. Baseline characteristics of all the patients (n = 165).

Parameter	No. (%)		p-value
	Without fractures	With fractures	
No. of patients	140 (84.9)	25 (15.1)	
Mean age ± SD (yrs)	39 ± 14.1	41.1 ± 10.6	0.05
Mean dose of prednisolone ± SD; range (mg daily)	17.1 ± 21.3; 7.5–80	23.8 ± 17; 7.5–60	0.001
Mean duration of prednisolone administration ± SD; range (mths)	40.8 ± 31.3; 6–108	65.3 ± 34.9; 9–121	0.001
Bone mineral density	21 (15.0)	5 (20.0)	0.001
Treatment with calcium	106 (75.7)	17 (68.0)	0.001
Treatment with vitamin D	46 (32.8)	16 (64.0)	0.001
Antiresorptives	0	0	

SD: standard deviation

Table II. Data of patients with fractures (n = 25).

Parameter	Male (n = 12)	Female (n = 13)	p-value
Mean age ± SD (yrs)	42.6 ± 11.6	40.5 ± 10	0.6
Calcium (mg/dl)	9.2	7.5	0.3
Alkaline phosphatase (IU)	73	88.5	0.3
Mean dose ± SD (mg daily)	11.5 ± 9.7	24.5 ± 21.2	0.05
Duration (mths)	63	62.6	0.2
Fractures	12	13	0.2

SD: standard deviation

Table III. Sites of fractures (n = 25).

Site of fracture	No. (%)
Colle's (distal radius)	3 (12)
Proximal femur	6 (24)
Spine	11(44)
Proximal humerus	3 (12)
Tibia and fibula	2 (8)

recorded, and these patients were excluded from the study. The medications used to prevent bone loss, including antiresorptive therapy, calcium and vitamin D supplementation, were noted. The results of bone mineral density measurements, as well as any fragility fractures, the site involved and the treatment administered, were also recorded. The patients were divided into two groups; Group A consisted of patients without fractures and Group B consisted of those with fractures. Vertebral fractures were diagnosed and classified as mild, moderate or severe according to the semi-quantitative technique assessment of the anterior-posterior and lateral spine radiographs described by Genant et al.[14] Osteoporotic fracture was defined as a fracture that results from a force equivalent to a fall from a standing height.

The data was entered into a database and analysed. The two-tailed, non-paired student's *t*-test was used to compare the means of the patients who sustained osteoporotic fractures with those who had no fractures and to make comparisons among the male and female patients who had fractures. The analyses were conducted using the Statistical Package for the Social Sciences version 14.0 (SPSS Inc, Chicago, IL, USA). A p-value < 0.05 with a 95% confidence interval (CI) was used to indicate statistical significance.

RESULTS

A total of 165 patients (100 male and 65 female) received glucocorticoid therapy at a dose ≥ 7.5 mg or its equivalent for more than six months during the study period. Of these, 140 patients had no fractures and 25 (15.2%) sustained an osteoporotic fracture (Table I). The age, dose of steroids and duration of glucocorticoid therapy were significantly higher among patients who sustained fractures (p = 0.5, p = 0.001 and p = 0.001, respectively). Of the 25 patients who sustained fractures, 12 were male and 13 were female (Table II). None of the patients in either group was started on antiresorptive therapy. The analysis showed no statistically significant differences between the male and female patients who sustained fractures apart from the dose of glucocorticoids received, which was significantly higher among women (11.5 ± 9.7 vs. 24.5 ± 21.2 mg/day, p = 0.05). 29% of the patients were receiving steroids due to rheumatoid arthritis, while the rest of the patients had other diseases. The commonest site of osteoporotic fracture was the spine (44%), where fracture occurred in seven women and four men, followed by the proximal femur (24%) (Table III). Four men and two women had proximal femur fractures. The majority of spinal fractures occurred at the thorax spine. Eight out of 11 patients had more than one vertebra

Table IV. Comparison of Z-scores in the general population with those among patients with and without fractures.

Parameter	Mean ± SD (range)		
	General population (n = 25)	Patients without fractures (n = 5)	Patients with fractures (n = 25)
Hip Z-score	0.06 ± 0.7 (−1.0 to 1.6)	−2.5 ± 0.6 (0.2 to −3.5)	−2.7 ± 0.7 (−1.2 to −3.6)
Spine Z-score	−1.0 to 1.0 ± 0.61 (−1.0 to 1.5)	−2.9 ± 0.9 (−1.2 to −5.1)	−3.05 ± 0.7 (−1.5 to −5.1)

SD: standard deviation

involved. Table IV shows the stratified Z-scores of the healthy participants compared to the patients with and without fractures.

DISCUSSION

The overall prevalence rate of GIOP-related fractures was found to be 15.1% in this study, and the vertebral column was the most affected, with 44% of fractures. The average number of osteoporosis-related fractures for our hospital was 12.6 per year compared to an average of 15.1 per year for steroid-induced fractures. The true prevalence rate of fractures due to GIOP is not known, but a rate of 13.3%–28.0% has been reported for vertebral fractures.[15,16] The heterogeneity in the prevalence rate in some studies is likely related to differences in the population studied, the dose, route and duration of glucocorticoid therapy, the sites of fracture reported and the diagnostic methods employed. The prevalence rate of osteoporotic fractures in the current study is within the reported range, but it is possible that the number may be higher due to the retrospective nature of the study and the possibility that some fractures may have been missed.

Luengo et al found no relationship between the dose of steroids and the prevalence of vertebral fractures,[17] whereas other reports have observed that the glucocorticoid dose is strongly related to the risk of fracture.[18,19] Moreover, de Vries et al have found that the risk of GIOP and its associated fracture increased substantially with increasing accumulative exposure, and among patients who received a daily glucocorticoid dose ≥ 30 mg and whose cumulative exposure was more than 5 g. They also found that the relative risk of osteoporotic fracture was 3.63 in patients who received a daily glucocorticoid dose ≥ 15 mg, and patients whose cumulative exposure was ≤ 1 g had a slightly increased risk of osteoporotic fractures.[20] In the current study, the glucocorticoid dosage and the duration of therapy were significantly higher among all patients who sustained fractures compared to patients who had no fractures. Our study confirmed an increased risk of fracture among relatively young adult patients with a mean age of 40 years; however, the patients who sustained fractures were significantly older.

In our study, vertebral fracture was found to be the commonest type of fracture, and this is consistent with that reported in the literature. Steinbuch et al found a 17-fold increased risk of vertebral fractures and a 7-fold increased risk of hip fractures in patients who received > 10 mg of prednisolone equivalents per day for a period of more than 90 days.[19] Vertebral fractures related to glucocorticoid use are mostly asymptomatic.[21] We were not able to assess the number of patients who were asymptomatic since this was a retrospective study.

There were some limitations to this study, including the fact that it was a retrospective study with a relatively small sample size. In addition, the results were not adjusted for the effects of other factors that may have influenced bone mass and fracture risk independently. In spite of the above limitations, to our knowledge, this was the first study carried out to evaluate the osteoporotic risk of fractures among the Arab population who were undergoing long-term glucocorticoid therapy. This study has documented an increased risk of osteoporotic fractures related to GIOP among relatively young adult Saudi patients. It was found that men can have osteoporotic fractures with smaller doses of glucocorticoids compared to women. Thus, prevention of such fractures is required in the management of steroid-induced osteoporosis.

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