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Original Article

Evaluation of Osteoporosis in a Selected Group of Iranian Patients with Ulcerative Colitis

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ABSTRACT

Background: Osteoporosis is a preventable and treatable disorder, reported with higher prevalence patients with ulcerative colitis but their relationship is controversial. Osteoporosis in these patients may be attributes to corticosteroid use, malnutrition and reduced intake of calcium and Vitamin D, lower levels of sex hormones, chronic inflammation and inflammatory cytokines. The aim of study was to compare bone mineral density (BMD) of femoral neck and lumbar spine in ulcerative colitis patients with age and sex matched controls.

Materials and Methods: This was a case-control Fifty patients with ulcerative colitis referred to Shariati Hospital and four private clinics from 2003 to 2006, were selected. Patients with history of long term corticosteroid use and postmenopausal women were excluded. The short term corticosteroid users (less than 3 month in the past 2 years) were included. Age and sex matched healthy Shariati Hospital staffs and their families were selected as control group. The Bone Mineral Density (BMD) was measured in lumbar spine (L1-L4), femoral neck and total hip sites. The effect of different factors such as age, sex and short-term corticosteroid use and disease duration and disease activity on BMD was evaluated in patient group. All variables were encoded and analyzed by SPSS -13.

Results: There was no significant difference between the case and the control groups in BMD of lumbar spine, femoral neck and total hip. There was no difference in decrease of BMD between males and females (P:NS). Short term corticosteroid use and disease activity at the time of densitometry had no impact on BMD of lumbar spines, femoral neck and total hip. (P:NS). Disease duration had negative effect on BMD of lumbar spine, femoral neck and total hip ($P \leq 0.02$). Aging decrease BMD of lumbar spine and femoral neck and total hip in these patients ($P \leq 0.03$).

Conclusion: Ulcerative colitis patients that are not prolonged users of corticosteroids, don't need screening for osteoporosis unless in special circumstances such as aging and long disease duration.

Keywords: Ulcerative colitis, Osteoporosis, Bone mineral density.

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INTRODUCTION

Ulcerative colitis is the most common inflammatory bowel disease (IBD) with the prevalence of 80 to 120 in 100000 in high incidence countries and is defined by recurrent episodes of inflammation in colonic mucosa. (1) Osteoporosis is one of the complications seen in ulcerative colitis. It may be attributed to corticosteroid use, malnutrition and reduced intake of calcium and vitamin D, chronic inflammation and inflammatory cytokines, lower levels of sex hormones as well as other well known risk factors of osteoporosis. (2-5), Organ cultures of involved IBD mucosa

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spontaneously produced increased amounts of TNF-alpha, IL-1 beta, and IL-6 compared to normal mucosa Increased inflammatory cytokine production by lamina propria mononuclear cells (LPMCs) and mucosa treated with EDTA suggests that these cytokines originate mainly from LPMCs. These results confirm the role of inflammatory cytokines in IBD and shed a new light on the role of TNF-alpha in IBD. (6), On the other hand, interleukin 1beta and its natural antagonist have been implicated in the pathogenesis of IBD. Both cytokines influence bone formation. IL-1beta stimulates osteoclast activity while interleukin 1 receptor antagonist enhances bone formation. (7)

Pathologic fracture is the most important complication of osteoporosis with the relative risk of 2.4 in lumbar spine and 2.6 in femoral neck, along with its surgical complications, individual and social burden of patient care and hospitalization. (8,9), Due to controversy about low bone mineral density in ulcerative colitis, comparison of BMD between UC patients and controls, and the effect of various factors on BMD of UC patients seems to be worthwhile.

Some studies have been performed about bone mineral density in IBD patients in Iran and other countries but they have no control group and they enrolled all IBD patients, both ulcerative colitis (UC) and Crohn`s disease (CD) and some of their patients had involvement of small intestine and were used to receive long term corticosteroids that may cause malabsorption and osteoporosis but we decided to evaluate the effect of chronic inflammation on bone mineral density and enrolled selected UC patients and compared them with control group.(10,11)

MATERIALS AND METHODS

This was a Case-Control study: Fifty ulcerative colitis patients 29 (58%) male and 21(42%) female referred to gastroenterology clinic of Shariati Hospital and four private clinics from 2003 to 2006 in Tehran were selected. They were 19 to 60 years old patients with ulcerative colitis whose diagnosis was confirmed by clinical, endoscopic and pathologic criteria. Disease activity was grouped into mild, moderate and severe at the time of bone densitometry, according to Roux et al criteria (table 1). (12)

Table 1: Classification of disease activity in ulcerative colitis, according to physician global assessment

Sign or symptom	Mild	Moderate	Sever
Bowel movements per day	< 4	4 < < 6	> 6
Blood in stool	Little	Intermediate	Many
Average of temperature in one day	–	< 37.5^{0}C	≥ 37.5^{0}C
Pulse rate per minute	–	< 90	≥ 90
Hematocrite of patient to normal average	–	> 75%	≤ 75%
Erythrocyte sedimentation rate	< 30 mm/h	–	>30 mm/h
Endoscopic view	Redness, decreased vascular marking, fine granularity	Sever redness, loss of vascular marking, course granularity, bleeding with contact	Spontaneous bleeding, presence of ulcer

Those with history of long term corticosteroid use and postmenopausal women were excluded to eliminate the effects of these factors on evolution of osteoporosis. The short term corticosteroid users (less than 3 month in the past 2 years) were included. All patients that fullfilled these criteria and accepted to perform bone densitometry consecutively were inrolled in the study until the total number of fifty patients was achieved. Bone mineral density (BMD) of these patients was compared with the BMD of sex and age matched controls (50 people) who were Shariati Hospital staff and their families. Controls were selected with stratified random sampling method.

For each patient, one of the sex and age matched controls were selected among 281 healthy people and investigated while we did not know about BMD results at the time of selection. These controls had no known predisposing factor for osteoporosis, like long–term corticosteroid use and menopause. The BMD of lumbar spine, femoral neck and total hip in the case and the control groups were evaluated by dual energy x-ray absorptiometry method with Hologic QDR-4500W machine. In the case group, the effect of different factors such as age, sex, short-term corticosteroid use, disease duration, and disease activity (at the time of densitometry) on BMD was evaluated. All variables were encoded and analyzed by SPSS 13, standard deviation (SD) was calculated for means and the comparisons were done by paired and independent sample t-test, correlation and one way ANOVA formulas.

RESULTS

Fifty patients were included in this study and compared with age and sex matched controls. In both groups, 58% were male and 42% were female. The mean age of males and females were 36.55±13.27 and 22±6.03 years respectively (total mean±SD:35.06 ±10.90 years).Thirty-four patients (68%) had mild, fifteen (30%) had moderate and one (2%) of them had severe disease activity. The mean disease duration was 6.43 ± 4.81 years in the case group (6.67±5.12 in men and 6.10±4.45 in women). According to World Health Organization criteria, four(8%) of all patients were osteoporotic, thirty(60%) were osteopenic and sixteen(32%) were normal .The mean BMD of the patients lumbar spine, femoral neck and total hip were 0.95 ± 0.11, 0.84 ± 0.15 and 0.93 ± 0.14 g/cm^2, respectively. The mean BMD of the controls lumbar spine, femoral neck and total hip sites were 0.96 ± 0.05, 0.85 ± 0.04 and 0.95 ± 0.04 g/cm^2, respectively (table 2).

Table 2: The mean BMD of the case and control groups

Site of Bone density	Case group mean±SD	Control group mean±SD	PV
Lumbar spine	0.95±0.11	0.96±0.05	NS
Femoral neck	0.84±0.15	0.85±0.04	NS
Total hip	0.93±0.14	0.95±0.04	NS

There was no significant difference between the case and the control groups in lumbar spine, femoral neck and total hip sites. Gender had no significant effect on BMD of lumbar spine, femoral neck and total hip sites. Disease activity at the time of densitometry- had also no effect on BMD in the measured sites. Short-term corticosteroid use also had not any impact on BMD of mentioned sites. Disease duration had negative effect on BMD of lumbar spine, femoral neck and total hip sites ($P \leq 0.02$). Aging significantly decreased BMD of lumbar spine, femoral neck and total hip sites in these patients ($P \leq 0.03$).

CONCLUSION

Osteoporosis has reported in patients with ulcerative colitis but their relationship is not clear. Osteoporosis may be related to corticosteroid use, sex, age, duration and activity of the disease.

In the present study, disease activity (at the time of densitometry) had no effect on BMD of lumbar spine and femoral neck. It could be due to estimating of the disease activity at the time of bone mineral densitometry instead of total course of the disease but the negative effect of disease duration on BMD of lumbar spine and femoral neck was predictable and confirmed in this study, like the study conducted by Pollak RD et al that showed disease duration was related to reduced BMD. (13)

There was no significant difference in BMD between men and women in another Iranian study. (13), this outcome was identical with our results. In a similar study from Iran, treatment

with corticosteroid increased low bone density possibility in Iranian patients. Corticosteroid use, age, smoking, and BMI are predictive factors for low bone density in IBD patients. (14), Ulivieri FM et al also showed that in female ulcerative colitis patients whole body and lumbar spine BMD have significant negative correlation with the steroid intake and the number of relapses after 6 years.(15) Duration of corticosteroid use would be a better indicator for disease activity in the total course of the disease than previous criterion because this criteria, could estimate the disease activity in each episode of ulcerative colitis rather than the disease activity in the total course of the disease. In our study, short-term corticosteroid use had no significant effect on BMD of the lumbar spine and the femoral neck. This is in contrary to the study conducted by Frei P, et al. According to the study conducted by Frei P, et al, osteopenia and osteoporoses are commonly found in IBD patient. Steroid treatment was significant risk factors for osteoporosis of the lumbar spine. (16), Leticia H, et al. evaluated bone mineral density of the lumbar spine in 40 patients with IBD and found low bone mineral density in 25% of patients correlated with corticosteroid cumulative dose in milligrams. (11)

Tsironi E, et al. also studied bone density in 122 IBD patients and cumulative steroid dose and increasing age proved to be the most important predictive factors of low bone mineral density. (17) In contrary to the studies conducted by Pigot F, Vestergaard P, et al. ulcerative colitis had no significant effect on BMD of lumbar spine and femoral neck (18,19), In our study, disease duration showed a negative effect on BMD that this result was like the result of study conducted by Schoon EJ, et al. that explained duration of complaints longer than 6 months before diagnosis significantly correlated with low BMD. (20)

Aging could have negative effect on BMD in our result. According to the studies conducted by Schoon EJ, et al. and Riggs, et al, the negative effect of age on BMD of lumbar spine and femoral neck was confirmed too. (21,22), Ben Hamida et al. also showed that the age and duration of evolution of inflammatory bowel disease superior to 10 years were risk factors of osteoporosis. (22)

In de Silva ,et al. study from Srilanka 111 inflammatory bowel disease (IBD) patients were screened for osteoporosis and were compared to 333 healthy controls .They find that the occurrence of osteoporosis among IBD patients was significantly higher than that among controls($p= 0.001$).

However on multivariate analysis only age, menopause and use of systematic steroids were found to be associated independently with the occurrence of osteoporosis. While like our study IBD and treatment other than systemic steroids were not associated with osteoporosis. (20)

Mohammadreza Zali, et al. studied the prevalence of decreased bone density in 126 Iranian IBD patients (126 UC and 39 CD patients). A total of 53 IBD patients (32.1%) had diminished bone mineral density. Of These, 9(5.4%) had osteoporosis however, 44(26.7%) were osteopenic. (24), They had no control group in their study. Khadgawat, et al. studied bone mineral density (BMD) among Indian patients with IBD. Two third of these patients had low BMD. Since the intake of dietary calcium was inadequate in a majority of these patients, they advised to increase the intake of dairy products. (25)

We did not consider all of the risk factors of low BMD like inadequate dietary calcium and this is the limitation of our study, but this limitation can be at least partially compensated by enrollment of control group from the similar Iranian population.

Our study confirms that age and disease duration associated with reducing BMD but short-time corticosteroid, disease activity and sex did not have significant effect on BMD.

Recommendations: This study showed that

ulcerative colitis is not an indication for screening of osteoporosis, unless in special circumstances such as long disease duration, severe disease resulting in prolonged corticosteroid use and the presence of other risk factors for osteoporosis. A staging system is required not only for disease activity in each episode but also for the severity of the ulcerative colitis course which must be held in other studies. Clear cut disease duration that affects the BMD of the lumbar spine and the femoral neck must be clarified in the future studies too.

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