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ORIGINAL ARTICLE

Effect of omeprazole on bone mineral density and frequency of osteopenia and osteoporosis

Homayoun Zojaji, Saeed Mohammady Bonehy

Research Institute for Gastroenterology and Liver Disease, Shahid Beheshti University, M.C., Tehran, Iran

ABSTRACT

Aim: The goal of the present study was to assess the effect of omeprazole on bone mineral density and frequency of osteopenia and osteoporosis.

Background: The effect of omeprazole on bone turnover and the role of stomach pH alteration in calcium absorption have not been completely understood.

Patients and methods: In a case-control study, 58 patients who were referred to Loghman hospital, Tehran, for bone densitometry between July 2005 and July 2006 and were administered omeprazole (20 mg/12hours for at least one month) were entered into the study. The control group comprised 239 matched (for gender, age, weight, history of cigarette smoking, history of milk or egg consumption within the week preceding the study) patients who were not administered Omeprazole. Bone mineral density (BMD) was measured at the lumbar spine (LS) (L2-L4, anterior-posterior position) and hip using dual-energy X-ray absorptiometry (DXA) with a Lunar Prodigy densitometer.

Results: The mean T-score of lumbar spine was not significantly different between patients who received omeprazole and controls (-0.802±1.38 versus -0.808±1.56, P=0.977). Also, mean T-score of hip was similar between patients who received this drug and control group (-0.431±1.050 versus -0.245±1.18, P=0.241). There were also no significant relationships between the consumption of omeprazole and prevalence of osteopenia or osteoporosis.

Conclusion: Short-term administration of omeprazole has no significant influence on bone density and does not increase the incidence of osteopenia and osteoporosis.

Keywords: *Omeprazole, Bone mineral density, Osteopenia, Osteoporosis.*

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INTRODUCTION

Previous experiments have revealed that the concentration of proton pump inhibitors (PPI) can be high in osteoclasts. In vitro investigations have shown that administration of omeprazole, the most frequently used drug in the group of PPI, can lead to leukocyte dysfunction and inhibition of osteoclast-mediated bone resorption (1-4). Furthermore, it has been clear that one week administration of 20 mg omeprazole daily significantly decreases fractional calcium absorption under fasting conditions that might be due to the alteration of stomach pH and gastrointestinal motility (5). However, the effect of omeprazole on bone turnover has been investigated in a few studies (6) and the role of stomach pH alteration in calcium absorption is controversial. In the present study, we assessed the effect of short term omeprazole administration on bone mineral density and incidence of osteopenia and osteoporosis in a case-control study.

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Reprint or Correspondence: Saeed Mohammady Bonehy, MD. Research Institute for Gastroenterology and Liver Diseases, Shahid Beheshti University, M.C.,Tehran, Iran
E-mail: ssmmbb293@yahoo.com

PATIENTS and METHODS

Fifty-eight patients who were referred to Loghman hospital for bone densitometry between July 2005 and July 2006 and were administered omeprazole (20 mg/12hours for at least one month) were entered into the study. Patients who were administered other types of drugs that could alter the bone resorption or metabolism, were excluded. In addition, patients with renal failure, osteomalacia or recent pathological fracture were also excluded. Among other referred patients, 239 patients who had no past history of omeprazole administration and were matched for sex, age, weight, history of cigarette smoking, history of milk or egg consumption within the last week were entered as control group. The purpose of the protocol was explained both to the patients and control subjects, and informed consent was obtained before beginning the study. The study was approved by the Ethics Committee of Shahid Beheshti University of Medical Sciences.

Demographic characteristics, clinical data and patients' drug history were collected by a self-administered questionnaire. Bone mineral density (BMD) was measured at the lumbar spine (LS) (L2-L4, anterior- posterior position) and hip using dual-energy X-ray absorptiometry (DXA) with a Lunar Prodigy densitometer (GE Lunar, WI, U.S.A.). A real BMD was expressed in g/cm2 and in standard deviations from the young normal mean (T-score), based on the Iranian Reference Population. The sample of subjects was grouped into two groups based on the WHO recommended criteria: osteoporosis if T-score was equal to or less than -2.5 and osteopenia if $-2.5 < \text{T-score} \leq -1.0$ (7).

Results were reported as mean ± standard deviation (SD) for the quantitative variables and percentages for the categorical variables. The groups were compared using the Student's t-test or Mann-Whitney U test for the continuous variables and Chi-square test for categorical variables. P values of 0.05 or less were considered statistically significant. All the statistical analyses were performed using SPSS version 13 (SPSS Inc., Chicago, IL, USA).

RESULTS

Case and control groups were matched for demographic criteria, the mean consumption of milk and egg, and also frequency of cigarette smoking. The history of underlying diseases was also similar between the two groups. In addition, daily intake of drugs was similar between them (Table 1).

Table 1. Demographic characteristics and clinical data of patients who received omeprazole and control group

	Omeprazole Group (n=58)	Control Group (n=239)	P-value
Age (year)	54.2±9.5	53.4±10.8	0.201
Body mass index (kg/m^2)	28.5±4.0	22.7±4.2	0.683
Milk intake (glasses per week)	7.6±4.1	8.3±5.2	0.073
Egg intake (number per month)	5.4±5.2	5.5±4.4	0.337
Cigarette smoking (pack-year)	3 (5.2%)	12 (5.0%)	0.329
Underlying diseases			
Diabetes mellitus	4 (6.8)	13 (5.4)	0.753
Hypertension	5 (8.6)	14 (5.9)	0.552
Hyperlipidemia	4 (6.8)	8 (3.3)	0.268
Hypothyroidism	7 (12.1)	14 (5.9)	0.158
Joint rheumatism	2 (3.4)	12 (5.0)	0.999
Renal stone	2 (3.4)	6 (2.5)	0.658
Heart failure	1 (1.7)	2 (0.8)	0.483
Drug history			
Aspirin	2 (3.4)	3 (1.3)	0.259
Beta-blocker	6 (10.3)	13 (5.4)	0.237
Statins	4 (6.8)	8 (3.3)	0.268
Calcium	21 (36.2)	63 (26.4)	0.288
Steroids	6 (10.3)	22 (9.2)	0.805
Glibenclamide	4 (6.8)	12 (5.0)	0.532
Levothyroxin	6 (10.3)	14 (5.9)	0.256

Data are presented as mean ± SD or number (%)

The mean of BMD of lumbar spine (T-score) in patients who received omeprazole and other group was not significantly different (-0.802±1.38 versus -

0.808±1.56, P=0.977). Also, mean of BMD of hip (T-score) was similar between case and control groups (-0.431±1.050 versus -0.245±1.18, P=0.241). There were also no significant relationships between the consumption of omeprazole and prevalence of osteopenia and osteoporosis (Table 2).

Table 2. Prevalence of osteopenia and osteoporosis in patients who received omeprazole and control group

	Omeprazole group (n=58)	Control group (n=239)	P-value
Osteopenia			
Lumbar spine	19 (32.8)	82 (34.3)	0.828
Hip	16 (27.6)	61 (25.6)	0.755
Osteoporosis			
Lumbar spine	5 (8.6)	30 (12.5)	0.408
Hip	2 (3.4)	3 (1.3)	0.269

Data are presented as number (%)

DISCUSSION

Omeprazole administration is one of the standard protocols for treatment of acid-related disorders such as gastroesophageal reflux disease, peptic ulcer disease, Zollinger-Ellison syndrome, and idiopathic hypersecretion. This drug is also successfully administered for Helicobacter pylori eradication and treatment of upper gastrointestinal bleeding (8).

In the present study, we tried to highlight the side effects of omeprazole administration on bone density. However, our study found no relationship between the administration of omeprazole and the decrease in BMD and incidence of osteopenia and osteoporosis. Similarly, Kocsis et al. reported that omeprazole, at a dose of 20 mg/day, did not significantly influence the investigated biochemical parameters of osteoclastic and osteoblastic function in pediatric patients (9). However, in another study by Mizunashi et al. urinary excretion of calcium decreased after omeprazole treatment in the study group and serum intact parathyroid hormone, alkaline phosphatase, osteocalcin, and tartrate-resistant acid phosphatase (TRAP) increased, whereas in the control group, there were not any changes in these parameters (6).

It seems that the lack of significant association between the use of omeprazole and its bone side effects (as in Mizunashi study and the present one) is due to the short course of therapy; whereas this association has been reported in long-term omeprazole therapy. Yang et al. indicated that the risk of hip fracture was significantly higher among patients prescribed long-term high-dose PPIs and the strength of the association increased as the period of PPI therapy prolonged (10). Side effects of long-term omeprazole administration can be related to the decrease in bone resorption due to the inhibition of osteoclastic vacuolar H+ - K+ ATPase (4, 6, 11). This effect has also been investigated in animal models. In a study on male rats, Cui et al. showed that the body weight gain was suppressed by omeprazole administration and the bone area and BMD were reduced, while the lengths of the spine and the femur and the body composition were unchanged (12). We believe that short-term use of omeprazole is well tolerated and can be accompanied by no bone side effects, while excessive long-term use of this drug may cause the lack of hydrochloric acid which is essential for the body to properly absorb nutrients, especially calcium. Therefore, for long-term administration of this drug, long-term side effects especially in the elderly should be considered. Moreover, according to a few available investigations about short-term effects of omeprazole on bone structure, more studies for assessment of these probable side effects and its-related predictors are recommended.

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