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Original Article

Zinc Status as a Risk of Osteoporosis

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ABSTRACT

Objectives: There is increasing evidence on association between lowzinc (Zn) status and osteoporosis, but the impact of zinc status as a risk of osteoporosis has not been reported. The aim of the study was to measure the concentration of serum zinc in patients with osteoporosis, and to ascertain the impact of zinc status on bone mineral density.
Methods: Serum concentration of Zinc and anthropometric parameters (age, gender, and body mass index) were measured in 55 apparently healthy subjects and 200 patients completed bone mineral density (BMD)measurements of the hip area and the limber spine using the dual energy x-ray absorbtiometry(DEXA) scan. Osteoporosis was defined as a BMD≥2.5 SDs below the mean of young subjects (a T-score ≤ -2.5).
Results: Significantly lower zinc concentrations (p=0.001), together with higher prevalence of hypozincemia(p=0.01) were found in patients with osteoporosis than in both osteopenic patients and healthysubjects. There was no statistically significant difference observed between the osteopenic and healthy subjects with respect to zinc levels. In the osteoporosis group, a positive correlations of zinc was observed with BMD(p<0.001) and a negative correlation was observed with age (p=0.01).
Conclusion: The low zinc status in conjunction with abnormal BMD may be strongly associated with osteoporosis in the studied patients. It thus indicates the need for the effectiveness of zinc supplements to patients with osteoporosis.
Keywords: zinc, osteoporosis, osteopenia, bone density

1. INTRODUCTION

Osteoporosis is a disease commonly encountered in the general practice, and considered a common cause of fractures mainly among women[1].it is also an important public health problem in elderly men, so about thirty percent of fractures of hip occur in men[2].several risk factors have been incriminated in the causation of the disease including age, hypogonadism, drug containing steroid, tobacco smoking, alcohol intake, lack of physical activity and excess or lack of certain components of diet[3].The organic matrix in bone is mainly composed of protein and most of the bone mineral content is calcium[4].Moreover, some other minerals may be needed to maintain a healthy state of the bone,

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including zinc, which is an essential trace element of bone growth and mineralization[5].This element may be associated with bone strength and bone mass[6].Since zinc is an established trace metal of bone health, it is important to analyze its association with bone mineral density in patients with osteoporosis.

2. METHODS

Study population

Two hundred patients (ages 45-70 years) who prepared for diagnostic BMD measurement at osteoporosis unite, Duhok Center of Rheumatic Disease and Medical Rehabilitation, Duhok, Kurdistan region, Iraq; were enrolled in the study.On the basis of patient history, medical history, clinical examination and radiological assessment, the participants were included and screened for osteoporosis. Osteoporosis is defined as BMD score of -2.5 and lower, and osteopenia between -1 to-2.5 SDs. Participants who had a history of secondary osteoporosis were excluded from the study, as well as those who used hormonal replacement therapy, zinc supplement or none fasting. Fifty five apparently healthy subjects of comparable age, sex and BMI were also included in the study.

All the participants provided written informed consent. The study protocol was approved by the Ethics Committee of the Medical Faculty, University of Duhok.

Anthropometric Measurements

Anthropometric measurements-body height (cm), body weight (Kg) were obtained. Body mass index (BMI) was calculated as weight in kilograms divided by height in meter squared. Study patients were divided into 3 groups: a normal weight group (n=29, BMI<25 kg/m20) overweight (n=50, BMI25-29.9) and an obese (n=121, BMI>30 kg/m2).

Biochemical Measurements

Phlebotomy was performed in the morning 8-10 o'clock, after a 12-14 h overnight fast. Serum specimens were collected in tubes containing no anticoagulant. Samples were allowed to clot for 30 minutes and then centrifuged at 3000 rpm for 10 minutes. Serum samples were divided into aliquots and stored at -80 c without prior thawing and refreezing before analysis.

Serum zinc was measured by flame atomic absorption spectrophotometer (PyeUnicam 2900, PyeUnicam Ltd, Cambridge, CB12PX, England). The intra- and inter-assay coefficient of variation (CV) for zinc was 3.0% and 6.5% respectively.

Statistical Analyses

Statistical analyses were performed using SPSS statistical package (version 15.0 for windows, SPSS, Chicago, IL, USA). Data are presented as mean +standard deviation. Differences between groups were evaluated with Student's t-test. A correlation analysis by Pearson's (r) correlation coefficient was used to determine the relationship between zinc levels and other variables in patient group.Categoral variables were analyzed by Chi square test. A p value of <0.05 was considered statistically significant. The power and sample size were calculated for zinc and BMD score, the values exceeded 0.90.

3. RESULTS

Table 1 shows the general characteristics of healthy subjects and patientgroups.No significant differences were found with respect to age BMI, and gender between the healthy subjects and patient groups. Significantly lower zinc level was observed in patient groups compared to healthy subjects.(p=0.01). A significantly higher prevalence (17.0%) of hypozincemia (serum zinc<70 ug/dl) was found in the patient groups compared with (1.8%) in the healthy subjects (p=0.001).

Table 2, shows the patient groups categorized as osteoporosis groupexhibited lower zinc levels than did the osteopenia group (p=0.01).Significantly higher prevalence of hypozincemia and lowervalues of BMD score was observed inosteoporosis group compared to osteopenia group. The 2 groups were also differ significantly with respect to age (p=0.01).

To determine which of the anthropometric parameters was significantly associated with the serum zinc level in patient groups, we distributed patients according to low and normal zinc levels.(**Table 3).**Among the different age groups, patients in >65 year age group had a higher prevalence of low zinc levels (41.2%) than those with normal zinc levels (21.1%). A significantly lower mean zinc level was found in the patients with age>65 years compared with the other age groups (p=0.013).No significant difference was found with respect to gender and BMI between the low and normal zinc groups.BMD score for the hip and spine were significantly lower in osteoporotic patients in the lowest serum zinc level (<70 ug/dl) than in osteoporotic patients with higher serum zinc concentrations.

The relationship between zinc and related parameters including age, BMI and BMD score in patient groups is presented in **Table 4.**As shown, in the osteoporosis group, zinc correlated positively with BMD (p=0.001), and negatively correlated with age(p=0.01).

4. DISCUSSION

This study provided definitive evidence that patients with osteoporosis had low serum zinc levels. The results confirm a correlation between hypozincemia and osteoporosis, as the prevalence of hypozincemia observed in osteoporosis cases was about 8 times higher than that observed in osteopenia cases or healthy subjects.These results are in accordance with previous studies[7, 8].Moreover, we reported a significant relationship between zinc and the BMDmeasurement and age. In ourstudy, zinc correlated with BMD score in osteoporosis group: the association was stronger with BMD score than with age, suggesting that hypozincemia has a role in accelerating or producing osteoporosis. By contrast, the

other studies suggested osteoporosis may lead to hypozincemia [9].However; the impact of zinc deficiency on the etiology of the disease is still unclear [10].Zinc has been demonstrated to have a simulator effect on bone formation and mineralization; the metal activates aminoacyl-tRNA synthetase in osteoblastic cells, and stimulates cellular protein synthesis. Moreover, zinc inhibits osteoclastic bone resorption by inhibiting osteoclast-like cell formation from marrow cell[11].Another study implies that zinc can increase osteogenic effect by stimulating cell proliferation, alkaline phosphatase (ALP) activity and collagen synthesis in osteoblastic cells[12].

It is important to note that stronger association between BMD and zinc values have been reported for women compared with men[13].In our study, patients with osteoporosis were predominantly women, 125/160(F/M ratio abut 3.5).This may suggest an important mechanism through which sex can influence higherrisk of hypozincemia in patients withosteoporosis. But, however, we did not observe a significant difference in mean zinc levels between males and females. These finding maysuggests that gender could not explain the hypozincemia observed in cases with osteoporosis.

Mild-moderate zinc deficiency appears to be an important public health problem in many developing countries including Iraq[14]. Several studies have shown that nutritional zinc deficiency is prevalent in several developing countries[15].This might be due to the commonly consumed staple foods have low content of zinc and rich in phytate. The latter inhibit the absorption and utilization of zinc in GIT.Indeed, patients with osteoporosis are known to be more vulnerable to zinc depletion and suboptimal zinc status than other groups[16] .A high proportion(17.0%) of patients with osteoporosis, but not healthy subjects(1.8%) or patients with osteopenia(2.5%), had serum zinc levels <70 ug/dl. These results suggest an important mechanism through zinc can influence higher risk of osteoporosis in our population, although, measurement of the other relevant minerals has not been determined, which is a limitation of this study. This mightunderestimate the definitive conclusion regarding the role of zincspecifically (or other relevant minerals) related to these patients with osteoporosis.

Table1: Patient and healthy subject data.

Patients (n=200)	Healthy subjects (n=55)		*p*-value
Age, y, mean±SD	58.9±8.7	50.6±5.4	0.09
Female, n (%)	165(82.5)	43(78.1)	0.53
BMI,(kg/m^2,mean±SD	31.7±6.1	28.7±6.7	0.07
Zinc, ug/dl, mean±SD	79.4±11.4	85.3±8.1	0.01
Hypozincemia, n (%), (Zinc<70 ug/dl)	34(17.0)	1(1.8)	0.001
Osteoporosis, n (%)	160(80.0)	-	-
Osteopenia, n (%)	40(20.0)	-	-

Table2: Demographic data and zinc status in patients with osteoporosis and osteopenia

Parameter	osteoporosis (n=160)	osteopenia (n=40)	*p* value
Age, y, mean ±SD	60.2±8.6	53.6±7.1	0.01
Female, n (%)	130(81.2)	5(87.5)	0.485
BMI,kg/m^2, mean±SD	31.8+6.2	31.5+6.1	0.809
Zinc, ug/dl, mean±SD	77.9+11.3	85.7+9.1	0.01
Hypozincemia, n (%), (Zinc<70 ug/dl)	34(21.1)	1(2.58)	0.001
BMD, gm/cm^2, T score	3.60	2.01	

Table3: Distribution of osteoporotic patients with low and normal zinc concentrations by age, gender, BMI and BMD score

Serum zinc (ug/dl)				
<70 ug/dl	≥70 ug/dl			
No. (%)	no. (%)	mean (SD)	*p*-value	
Age,y				
45-54 7(20.6)	46(36.5)	81.0 (10.5)	0.013	55-64 13(38.2)
53(42.1)	80.6(10.8)			
≥65 14(41.2)	27(21.4)	75.3(12.8)		
Male	9(26.5)	20(15.8)	76.9(11.9)	0.147
Female	25(73.5)	106(84.2)	80.2(11.2)	
BMI, kg/m^2				
<25	6(17.7)	17(13.6)	78.8(13.5)	0.674
25-29.9	13(38.2)	28(22.2)	78.4(11.7)	
≥30	15(44.1)	81(64.2)	80.0(10.8)	
BMDs				
< 2.5	34(100)	95(75.4)	77.9(11.4)	0.001
-2.5 <-1.0 0(0.0)	31(24.6)	85.7(9.1)		

Table 4: Pearson's Correlation Coefficients (r) between zinc and age, BMI and BMDs in osteoporotic patients.

Variable	r	*p*-value
Age	-0.227	0.010
BMI	-0.021	0.771
BMDs	0.344	0.001

5. CONCLUSION

To our knowledge, ours is the first study to examine the association of zinc status with measurements of bone mineral density among patients with osteoporosis, at least in our population. As expected, BMD score is associated with lower levels of zinc and unfavorable changes in the zinc status, suggesting zinc may play a central role in the pathogenesis of osteoporosis-related pathologies. Inthis sense, these findings mayindicate the need for the effectiveness of zinc supplementation.However, its effects on bone density remain to be evaluated in a large sample group.

6. ACKNOWLEDGEMENT

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