

A Study of Serum Prolactin in Reduced Bone mineral Density

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Abstract

Objective: Pituitary hormones have direct and indirect effects on bone remodeling, and skeletal fragility is a frequent complication of pituitary diseases. The osteoporotic effect of excessive prolactin is being recognized. The present study proposed to determine association of bone mineral density with serum prolactin levels.

Methods: A total of 124 subjects were included in this cross-sectional study. Bone mineral density was estimated using ultra sound of os calsis. Blood samples were collected from each of the subjects and serum prolactin levels were estimated by enzyme-linked immune sorbent assay. The specimens were analyzed for serum calcium, serum phosphorus, and serum alkaline phosphatase also.

Results: The mean levels of the analysed biochemical parameters were 10.08 ± 6.82 for serum prolactin, 9.71 ± 0.731 for serum calcium, 3.91 ± 0.459 for serum phosphorus, 101.71 ± 14.69 for serum alkaline phosphatase and -0.2 ± 0.77 for bone mineral density from normal elderly individuals. Serum prolactin level is increased above the reference range in osteopenia and osteoporosis with the elevation being significant in the osteoporotic group. (p-value: 0.001).

Conclusion: As hyperprolactinemia is found to be associated with osteoporosis and osteopenia, estimation of serum prolactin can be a useful tool for assessment of reduced bone mineral density. The correlation of serum prolactin with bone mineral density, serum calcium, and serum phosphorus was inversely proportional in osteopenia and osteoporosis.

Key words: BMD- Bone mineral density; SD- Standard Deviation

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Introduction

Pituitary hormones have direct and indirect effects on bone remodeling, and skeletal fragility is a frequent complication of pituitary diseases. The osteoporotic effect of excessive prolactin is being

recognized. Reduced bone mineral density is found to be associated with hyperprolactinemia.¹⁻¹²

The osteoporotic effect of excessive prolactin may be due to hypoestrogenism, calcium mobilization from bone, prolactin receptors in the bone and prolactin dependent increase in parathyroid hormone-related peptide level¹³⁻¹⁴.

The present study was undertaken to find association of hyperprolactinemia with reduced bone mineral density.

Material and Methods

Total of 124 subjects were included in this cross-sectional study with following criteria:

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Inclusion Criteria

1. Apparently healthy elderly subjects
2. Both male and female subjects
3. Subjects between 60 - 80 years of age

Exclusion Criteria

1. Diabetes Mellitus
2. Chronic Renal failure
3. Acute and chronic liver disease
4. Alcoholism
5. Drugs - anticonvulsants

Study Centre: Rajiv Gandhi Govt. General Hospital / Madras Medical College.

Bone Mineral Density (BMD) was estimated using ultrasound of the os calcis and depending on the speed of sound the subjects were diagnosed as having either osteopenia or osteoporosis, based on the T-score. At present, the gold standard test for assessment of bone density is DEXA Scan. (Dual Energy X-ray Absorptiometry) which can also predict the fracture risk. However, a developing nation like India cannot afford to diagnose fracture risk in the general population with the help of DEXA scan due to the high cost. Therefore a test which will be less expensive and reliable has to be opted in our country to screen 'high risk' elderly individuals who are prone to develop osteopenia and osteoporosis and the resultant complication 'fracture'.

T Score: The number of standard deviations above or below the mean bone mineral density of young controls.

Z-score: It is the number of the standard deviation of BMD of the person compared with the mean of healthy age matched population.

The subjects were grouped as normal, osteopenia and osteoporosis according to criteria defined in table 1.

Specimen Collection and Storage

After obtaining the informed consent of the subjects, five ml of peripheral venous blood samples was collected from each of the 124 subjects under strict aseptic precaution into clean, dry test tubes without adding any anticoagulant and the samples were allowed to stand for half an hour. The serum was separated by centrifugation at 2500 rpm for 10

min. Samples were labeled and allotted identification number. 1 ml of the serum from each sample was transferred with the help of a micro pipette into clean, dry tubes and preserved at -20°C for analysis at a later date. Samples were analyzed in two batches within 30 days of collection. Serum prolactin levels were estimated in two batches by ELISA. The remaining specimens were analyzed for serum calcium, serum phosphorus and serum alkaline phosphatase.

The reference range obtained among subjects with normal BMD was compared with the mean levels of the parameters obtained from the osteopenic group and osteoporotic group. The statistical significance of the study parameters was obtained from the corresponding 'P' value, which was arrived at using the students 't' test. The correlation of serum prolactin with the other parameters of the study was arrived at using the Karl Pearson correlation coefficient.

Table 1.

Category	Definition
Normal	A value for BMD \pm 1 SD of the young adult reference mean
Osteopenia	A value for BMD > 1 SD and < 2.5 SD lower than the young adult mean
Osteoporosis	A value for BMD > 2.5 SD lower than the young adult mean
Severe Osteoporosis	A value for BMD > 2.5 SD lower than the young adult mean in the presence of one or more fragility fractures

Results

Bar diagrams depicting the mean values of the parameters in the different groups of study along with their standard deviation have been shown in figure 1a to c. Box and Whisker plot showing BMD and serum prolactin in different groups are shown in figure 2a and 2b respectively.

The mean levels of the analyzed biochemical parameters were 10.08 ± 6.82 for serum prolactin, 9.71 ± 0.731 for serum calcium, 3.91 ± 0.459 for serum phosphorus, 101.71 ± 14.69 for serum alkaline phosphatase and -0.2 ± 0.77 for BMD from apparently normal elderly individuals.

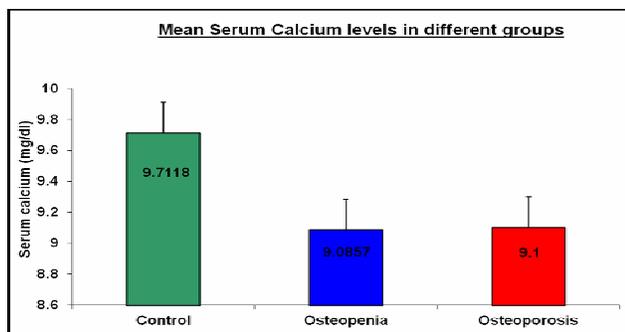


Figure 1a.

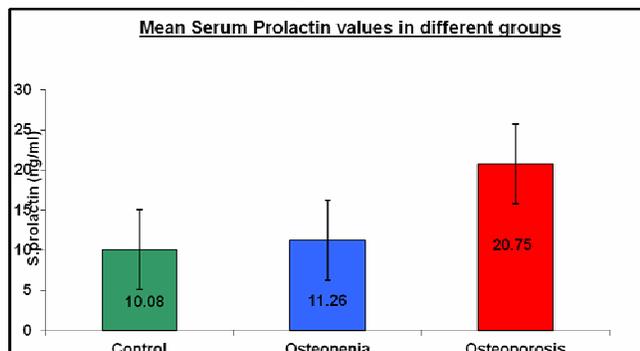


Figure 1b.

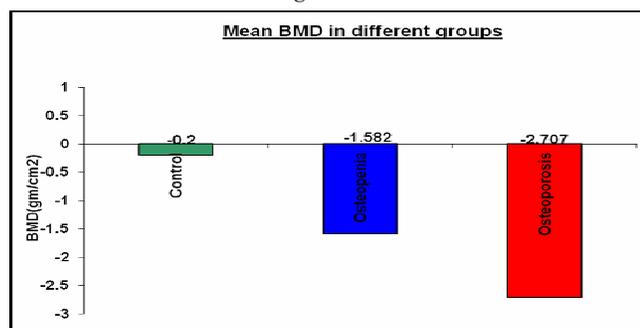


Figure 1c.

Discussion

The mean levels of the analyzed biochemical parameters in subjects with osteopenia revealed a significant decrease in serum calcium (p value: 0.03) significant increase in serum alkaline phosphatase (p-value: 0.03) and a significant decrease in BMD (p value: 0.01) as compared to the normal. The significant decrease of serum calcium observed in the osteopenic elders is due to impairment in calcium absorption and renal conservation being more predominant in the control elders leading to its significant decrease. The mean level of BMD (T-score) in the osteopenic group is -1.58.

When the levels in osteoporosis are compared with the reference range highly significant increase of serum alkaline phosphatase (SAP) (p-value: 0.001) and serum prolactin (p-value 0.001) were

observed against a highly significant decrease in BMD (p-value 0.001) with T-score of -2.7 obtained in the study of the osteoporotic group.

The highly significant increase in SAP and serum prolactin can be attributed to the increase in osteoblastic activity as the cause for the increase in SAP, decline of dopamine in the elders is said to be the cause for hyperprolactinemia. In the elderly, it has been reviewed that there is a rise in serum prolactin at the rate of 5.3% per year due to loss of hypothalamic pituitary regulatory function that occurs with aging. The increase in prolactin level has been ascribed to an age related decline in dopamine, the neurotransmitter responsible for inhibition of prolactin secretion.¹⁴

BOX AND WHISKER PLOT

Figure - 2 (a)

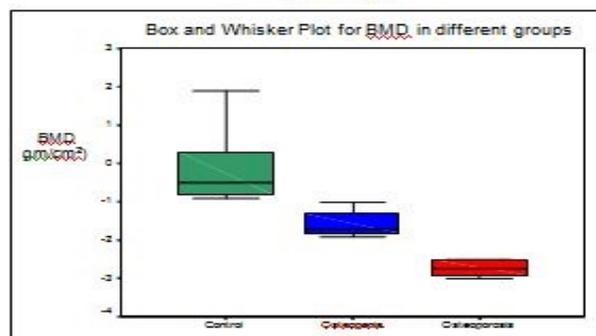


Figure - 2 (b)

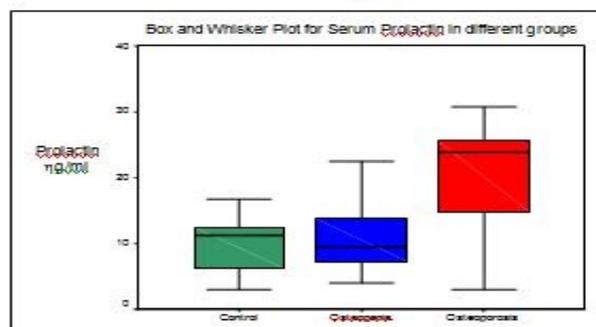


Figure 2a and 2b. Comparison of the levels in osteopenia and osteoporosis reveals a highly significant increase of serum prolactin (p value .001) against a highly significant decrease (p-value .001) of BMD in osteoporosis than osteopenia.

Hyperprolactinemia in the osteoporotic group of the study correlates well with the finding of Bernard et al. that the metabolic manifestations of hyperprolactinemia include a decrease of BMD.⁷ Klibanski. A et al. opined that this association can be due to the direct action of prolactin on calcium mobilization through prolactin receptors which are

independent of vitamin D and parathormone and that the hyperprolactinemic subjects have an increased risk of developing osteoporosis.²

Similarly, the highly significant increase in serum prolactin levels of this group over that of the osteopenic group and as well over that of controls can be the relevant cause for the greater deterioration of BMD in osteoporosis. So it is presumed that greater the increase of serum prolactin level, greater is the decrease in BMD. Analysis by the Karl Pearson correlation coefficient revealed an inverse correlation of prolactin with BMD. As hyperprolactinemia is found to be associated with osteoporosis, estimation of serum prolactin can be a useful tool for assessment of reduced bone mineral density.

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