1, 25-DIHYDROXYCHOLECALCIFEROL (1,25-(OH)₂ D₃) LEVELS IN OSTEOPOROSIS

A.P.S. Narang* , S. Batra**, S. Sabharwal** and S.C. Ahuja**

*Department of Biochemistry and **Orthopaedics, Dayanand Medical College & Hospital, Ludhiana - 141001, Punjab

ABSTRACT

In the present study primary involution osteoporosis and vitamin D levels were studied in 60 subjects including thirty controls. The biochemical analysis of serum calcium, phosphorus, ALP, albumin and vitamin D₃ (1,25-(OH)₂ D₃) levels were significantly decreased in osteoporotic patients when compared to non-osteoporotic control group. There was a significant correlation of magnitude of sun exposure with 1,25-(OH)₂ D₃ levels. Similarly, vitamin D intake in the diet has a significant correlation with 1,25-(OH)₂ D₃ concentration. However, no correlation could be obtained between vitamin D₃ levels with increasing age. Among the biochemical markers serum calcium, phosphorus, ALP and albumin could not be correlated with 1,25-(OH)₂ D₃ levels.

KEYWORDS

Osteoporosis 1, 25-Dihydroxycholecalciferol

INTRODUCTION

Osteoporosis is a skeletal disorder characterized by low bone mass and micro architectural deterioration of bone tissue with a consequent increase in bone fragility and susceptibility to fracture risk. In Indian population, the bone mass begins to diminish after third decade and the decline continues throughout life (1). The primary osteoporosis has been classified into three categories viz. Idiopathic Juvenile, Idiopathic in young and Involutional adult osteoporosis. Involutional osteoporosis is the commonest form, which begins in the middle life and has two distinct syndromes (2). Type I (Post menopausal osteoporosis) affect women after menopause in which fractures occur at sites rich in cancellous bone, crush fractures of vertebrae, fractures of distal forearm and of the ankle (3). The increased bone resorption leads to decreased Parathyroid Hormone (PTH) secretion which in turn leads to decreased production of 1,25-dihydroxy cholecalciferol and increased renal calcium

excretion. In human beings, cholecalciferol (Vitamin D₃) is synthesized from 7-dehydrocholesterol located under skin on the exposure to sunlight. Cholecalciferol get hydroxylated at 25-position in liver and at 1-position in kidneys, resulting in active form of vitamin D-1,25-dihydroxycholecalciferol (1,25-(OH)₂ D₃). The function of 1,25-diOH D₃ is to increase uptake of calcium by the intestine, minimize loss of calcium by the kidney and stimulates resorption of bone when necessary. Type II (Senile) osteoporosis is the predominant form in men and women after the age of seventy, it is twice as common in females. It is characterized by fractures at sites containing substantial proportion of both cortical and cancellous bone. Main manifestations are hip and vertebral fractures. Although proximal humerus and tibia are also common sites (4-6).

The relationship between calcium absorption, parathyroid function, age with 1,25-(OH)₂ D₃ action has been reported (7,8). In the older patients with osteoporosis, PTH and 1,25-(OH)₂ D₃ levels are much lower when compared to older controls. The calcium absorption is impaired in men with spinal osteoporotic fractures and is associated with low 1,25-(OH)₂ D₃ levels (9). However, this is not low enough to account entirely for decrease in calcium absorption and there is in addition resistance of the gut to respond normally to 1,25-(OH)₂ D₃. The role of vitamin D in pathogenesis and treatment of osteoporosis in postmenopausal women has been

Author for correspondence :

Dr. A.P.S. Narang
Prof. & Head,
Department of Biochemistry,
Dayanand Medical College & Hospital,
Ludhiana 141 001 (Punjab), INDIA
E-mail: dmch_ldh@satyam.net.in

reported (10).

It was planned to evaluate the $1,25-(OH)_2 D_3$ levels in patients with clinical features suggestive of reduced bone mass with evidence of osteoporosis and the result were compared between osteoporotic patients with normal healthy controls in male and female subject.

MATERIAL AND METHODS

The present study was conducted in Dayanand Medical College & Hospital, Ludhiana on 30 (15 males and 15 females) patients in the age group of 40-80 years. An equal number of age and sex matched healthy controls were included in the study.

The patients of primary osteoporosis were selected who were having low backache or malaise with radiological evidence of osteoporosis at one or more sites. Detailed clinical examination including physical, systemic and local examination was carried out on the patients. The laboratory investigations included Hemogram with ESR, serum sugar, renal function tests, liver function tests, calcium, phosphorus, ALP and uric acid, x-rays as relevant for the patients viz. x-ray pelvis, spine and clinical interest were done. $1,25-(OH)_2 D_3$ levels were estimated in all sixty subjects by Radioimmunoassay method using kits supplied by Biosource. Serum samples were treated with extraction solvent and applied on cartridges to separate $1,25-(OH)_2 D_3$ from other vitamin D metabolites. The samples, standards and controls were incubated with the tracer solution in coated tubes. A fixed amount of ^{125}I labelled $1,25 (OH)_2$ vitamin D competes with $1,25 (OH)_2$ vitamin D from either standard or extracted samples for a fixed amount of specific antibody coated on the inner surface of incubation tubes. After an overnight incubation, an aspiration followed by washing, the reaction was stopped. The amount of $1,25(OH)_2 D_3$ was calculated from the standard curve in picogram/ml. The levels of $1,25-(OH)_2 D_3$ were compared with age, vitamin D intake, sun exposure, serum calcium, phosphorus, albumin and ALP levels.

RESULT

The mean ($\pm$ SD) of $1,25-(OH)_2 D_3$ in healthy control male patients was $29.5 (\pm 7.17)$, whereas in patients of osteoporosis was $22.6 (\pm 5.75)$ pg/ml. (Table 1). It was significantly low in osteoporosis ($p < 0.05$). Similarly, in females subjects it was significantly decreased in osteoporosis when compared to controls ($p < 0.05$).

Table 1. Levels of $1,25-(OH)_2 D_3$ in controls and patients of Osteoporosis (pg/ml)

Group	Controls	Patients with Osteoporosis
Males	29.5 ± 7.17	22.6 ± 5.75
Females	21.4 ± 4.96	16.5 ± 2.47

The levels of $1,25-(OH)_2 D_3$ were significantly higher in male subjects as compared to females in both of patients and controls ($p < 0.05$).

The increase in age did not show any significant decrease in vitamin D levels. The supplementation of vitamin D (5-10 microgram per day) showed a significant correlation with the levels of $1,25-(OH)_2 D_3$. The levels of serum albumin, calcium, phosphorus, ALP showed no correlation with $1,25-(OH)_2 D_3$.

DISCUSSION

The $1,25-(OH)_2 D_3$ levels were found to be decreased in patients of osteoporosis of both sexes. In female subjects, levels of vitamin D_3 are low in comparison to males which is due to little sun exposure in female subjects. In a study on hypervitaminosis D, a clear out relationship was established between sun exposure and vitamin D levels measured in winter and summer months (11).

The vitamin D dietary intake significantly increase the $1,25-(OH)_2 D_3$ concentration. The women by increasing the intake of vitamin D can significantly reduce the bone loss and improve net bone density. In the studies on hypovitaminosis D (11) and on impaired vitamin D metabolism with aging women (12), a low serum calcium was found to be significant univariate predictor of hypovitaminosis D. In another study on occult vitamin D deficiency in postmenopausal US women with hip fractures, low circulating serum calcium levels were found (10). In the present study, however, no significant correlation was observed between serum calcium and vitamin D levels. Similarly, no significant correlation could be found between $1,25-(OH)_2 D_3$ with serum albumin, phosphorus and ALP levels.

A general awareness among the people is required to stress the importance of sun exposure and intake of diets rich in vitamin D, all of which have a bearing on osteoporosis index. This can help to generate preventive strategies towards the growing epidemic of osteoporosis for the entire population as well as for those at higher risk.

REFERENCES

1. Ahuja, M. (1969) Normal variation in the density of selected human bones in North India. *J. Bone Joint. Surg.* 51, 719-735.
2. Riggs, B.L. and Melton, L.J. (1983) Evidence for two distinct syndromes of involutional osteoporosis. *Am. J. Med.* 75, 899-901.
3. Van Hoop, H.J.C. and Van der Mooren, H.J. (1999) Females sex hormone replacement therapy increases serum free 1,25-dihydroxyvitamin D₃, a 1 year prospective study. *Clinical Endocrinology* 50, 511-516.
4. Manolagas, S.C., Howard, J. and Culler, F. (1982) Cytoreceptor assay for 1,25-(OH)₂ D₃ a simple rapid and reliable test for clinical application. *Clin Res.* 30, 527.
5. Quesada, J.M., Coopmans, W., Ruis, B. and Alizam, P. (1992) Influence of vitamin D on Parathyroid function in the elderly. *J. Clin. Endo. Metab.* 75, 494-561.
6. Nareyana, K., Goswami, R. and Gupta, N. (2000) Prevalence and significance of low 25-(OH)D concentration in healthy subjects in Delhi. *Am. J. Clin. Nutr.* 72, 472-475.
7. Zerwekh, J.E., Sakhee and Glass, K. (1983) Longterm 1,25-(OH)₂ D₃ therapy in postmenopausal osteoporosis: Demonstration of responsive sub groups. *J. Clin. Endo Metab.* 56, 410-413.
8. Ebelling, P.R. and Sandgren, L.B. (1992) Evidence of an age related decrease in intestinal responsiveness to vitamin D relationship between 1,25-(OH)₂ D₃ and intestinal VDR concentration in normal women. *J. Clin. Endo. Metab.* 75, 176-182.
9. Need, A. G., Nordsis, H. A. and Horowitz, N. (1998) Intestinal calcium absorption in men with spinal osteoporosis. *Clin. Endo.* 48, 163-168.
10. Leboff, S.M. and Lynn K. (1999) Occult vitamin D deficiency in postmenopausal US women with acute hip fracture. *JAMA* 281, 1505-11.
11. Mellisea, K.T. and Donald, M. (1998) Hypovitaminosis D in medical in patients. *New Engl. J. Med.* 338, 777-783.
12. Tsai, K.S., Riggs, P.L. and Kumar, R. (1984) Impaired vitamin D metabolism with aging in women. Possible role in pathogenesis of senile osteoporosis. *J. Clin. Invest.* 73, 1668-1672.