OSTEOCALCIN LEVELS IN GRAVES' DISEASE AND EUTHYROID CONTROLS

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SUMMARY

As a result of accelerated osteoclastic and osteoblastic activities in hyperthyroid state, loss of bone mass occurs. Osteocalcin levels were investigated in Graves' disease and euthyroid individuals. Average serum osteocalcin levels were found to be 13.3±4.3 ng/ml and 7.6±2.4 ng/ml for the Graves' and the euthyroid group respectively. Serum osteocalcin appears to be a sensitive marker of hyperthyroid osteopathy and more suitable and precise than the usual markers of bone metabolism.

Key Words: Osteocalcin, Bone GLA protein, Graves' disease, Hyperthyroidism

INTRODUCTION

Osteocalcin or bone gamma-carboxyglutamic acid protein (GLA protein) is a noncollagenous bone matrix protein and is a specific and sensitive biochemical marker for bone metabolism (1). Osteocalcin is a small (5800 Da) protein, synthesized by osteoblasts and the plasma levels are biochemical indicator of bone formation (2,3). Intensive research was done to establish serum osteocalcin levels in the physiological and pathological situations like osteoporosis (4), Paget disease, Osteogenesis Imperfecta, renal insufficiency, and various endocrine diseases (5-7). Serum osteocalcin is elevated in diseases characterized by an increase in bone turnover, such as primary hyperparathyroidism, renal osteodystrophy and Paget's disease of bone. It can also be used as a bone metastasis marker (8). Urinary excretion of calcium and phosphorous is known to increase in Graves' disease (9). Hyperthyroidism is associated with increased bone resorption and reduced bone density. Serum osteocalcin levels are found to be high in hyperthyroidism and reduced in hypothyroidism (10). Thyroid hormone-induced osteoporosis is characterized by increases in both osteoclastic and osteoblastic activities especially in cortical bones. The aim of this study was to find out the plasma levels of osteocalcin in Graves' disease.

MATERIAL AND METHODS

Thirty nine patients who were diagnosed to have Graves' disease with clinical findings, scintigraphy and thyroid hormone levels and 8 euthyroid women with no nodules were included in this study. Thirty one of the Graves patients were women with ages between 13 and 61, average age being 36.2±13.5. Men with Graves' disease were between 29 and 52, the average age being 39.4±9.9.

Women consisting the control group had applied with suspect of hyperthyroidism but were found to be euthyroid. The ages of the control group were between 21 and 63, the average being 37.1±10.1. Thirty five of the patient group was newly diagnosed, 2 received radioactive iodine, and 2 had antithyroid therapy before.

Following the diagnosis of Graves' disease phlebotomy was carried in the morning by tourniquet. Because serum osteocalcin levels show a cirrcadian rhythm, care was given to obtain blood samples between 9:00-10:00 a.m. (11). Sera was kept in -40°C prior to osteocalcin assay which was done with Nichols Human Osteocalcin Radioimmunoassay kit. The expected range of osteocalcin values were: 1.2-10.5 ng/ml with mean value being 3.6 ng/ml for women and 2.3-13.8 ng/ml with mean value being 5.7 ng/ml for men.

Statistics were done with the Students' t test.

RESULTS

Average osteocalcin values was found to be 13.3±4.3 ng/ml for the Graves group and 7.6±2.4 ng/ml for the control group. The range being 4.4-29.4 ng/ml and 4.8-11.3 ng/ml for the two groups respectively (Fig.1).

Significant difference was found between the osteocalcin levels of the Graves and the control groups (Students' t test $p<0.01$). Within the Graves group no significant difference was found between the average osteocalcin levels of the women and the men ($p>0.05$). No significant difference was found between the average ages of the patient and the control group and between the ages of the women and men in the patient group.

DISCUSSION

Osteocalcin levels are used to monitor the patients' response to therapy in many bone and endocrine diseases. Bone pains are not given serious attention in Graves' disease. It is known that bone density decreases in Graves' disease. Indirect markers of bone resorption in hyperthyroidism are: increased

serum alkaline phosphatase values with normal parathyroid hormone values and increased excretion of sodium and phosphorous with urine and feces (6).

Increased serum osteocalcin levels of the Graves' patients in this study is a direct evidence of the bone resorption and formation mainly with the influence of high thyroid hormone status.

Our results correlate well with Kojima's (12) study done with Graves' patients. It may be appropriate to monitor serum osteocalcin levels and to give prophylactic calcium to prevent bone resorption due to hyperthyroidism along with the therapy for hyperthyroidism (13).

Experimental studies done with rats have shown that administration of thyroxine and triiodothyronine has caused increase in osteocalcin levels (14). The bone resorption effect of thyroid hormones has also been shown in vitro (15). Thyroid supplementation given to patients with euthyroid goiter may lead to a decrease in bone mineral density and an increase in osteocalcin levels. Calcium supplementation given as a result of serum osteocalcin monitoring can help prevent iatrogenic decrease of bone mineral density.

In conclusion serum osteocalcin is a sensitive and direct marker of hyperthyroid osteopathy and it is certainly more suitable and precise than the indirect markers like serum alkaline phosphatase, urinary calcium and phosphorous.

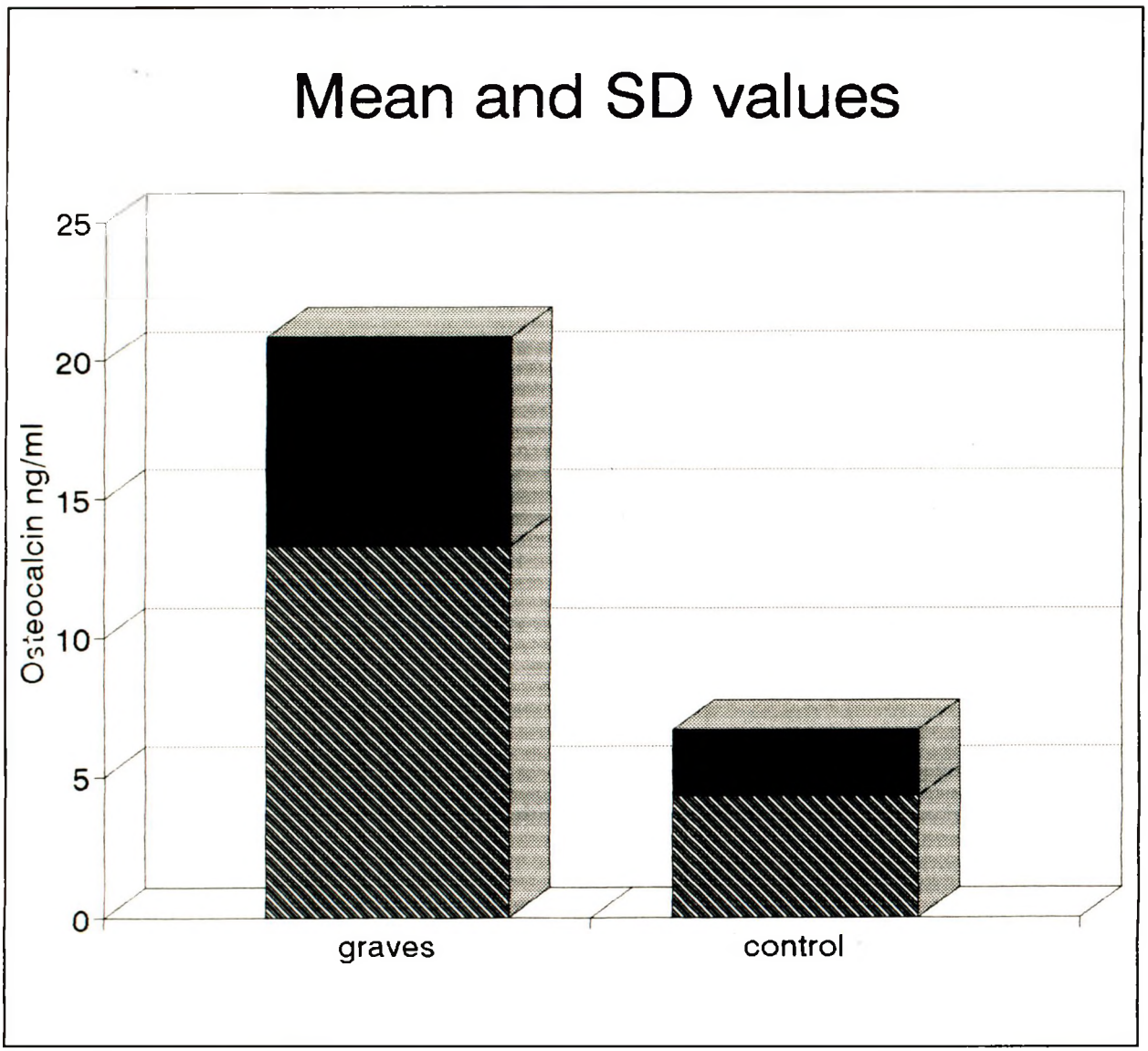

Fig 1. Average Osteocalcin Values.

: SD

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