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PREVALENCE OF HYPERCALCEMIA AND HYPERCALCIURIA IN THYROTOXIC PATIENTS OF A REFERRAL ENDOCRINE CLINIC

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ABSTRACT

Many patients with thyrotoxicosis develop hypercalciuria and nypercalcemia. Urine calcium excretion depends on diet, latitude and sunshine exposure. With regard to variation of these indices in different geographical regions, we conducted a one-year study on 202 patients, 65 males and 137 females, with thyrotoxicosis of varying severity. The mean age of patients was 35.24±11.95 and 35.87±12.21 years for men and women respectively. Free T4 index, serum calcium and phosphorus, PTH and alkaline phosphatase were measured in all patients. The mean for FTI was 7.48±1.98. Serum Ca and P mean was 9.31±0.46 mg/dL and 4.11±0.61 mg/dL respectively. 3 patients (1.5%) had hypercalcemia and hyperphosphatemia was detected in 38(18.6%) patients.

The mean of urine Ca and P were 190±106.7 mg/24h and 626±246.73 mg/24h respectively. Increased urine Ca and P was detected in 20(9.8%) and 4(4.4%) patients respectively. PTH was suppressed in 34(16%) and alkaline phosphatase was increased in 50(24.5%) patients.

There was no significant relation between FTI with serum and urine Ca and P and serum PTH and alkaline phosphatase in thyrotoxic patients. There was also no appreciable difference in serum Ca and P and urine Ca between the two sexes with respect to the lower exposure of muslim women to sunlight.

These results contrast with the high frequency of hypercalcemia (27%) and hypercalciuria in patients with thyrotoxicosis in previous studies and might be due to habitual low calcium diet and sunshine exposure in this area.
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INTRODUCTION

Thyrotoxicosis induces an increased bone turnover and carries a high risk of osteoporosis. The prevalence of hypercalcemia and hypercalciuria in thyrotoxicosis has been reported to be 3-27% and 20% respectively in different studies.[2,17-22] Urine Ca depends on diet, latitude and sunshine exposure. With regard to variations of these indices in different geographical regions, we conducted this study in Rasht, one of the northern cities of Iran.

MATERIAL AND METHODS

All the patients with thyrotoxicosis of different severity referring to an endocrine clinic for a period of 1 year were included in the study. There were 202 patients, 65(32.2%) males and 137(67.8%) females, with an age range of 12-63 years, mean (35.44±11.25) for males and 7-76 years, mean (32.87±12.2) for females. The patients were divided into 3 groups with respect to severity of thyrotoxicosis. An FTI equal to 4.49-5.49 was considered mild, 5.5-7.49 moderate and above 7.5 severe thyrotoxicosis.

All the patients had blood drawn for TSH (N= 0.3-5 mU/L), T3 (N= 0.8-2.7 nmol/L), FTI (N= 1.4-4.5), serum Ca (N= 8.1-10.4 mg/dL), P (N= 2.3-4.7mg/dL), Alk.ph (N= 80-310U/L), and PTH (N= 40-100 pmol/L). 24h urine collection was done for urine Ca (N= up to

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275 mg/d for males, up to 250 for females), urine P (N= up to 1300 mg/d) and creatinine (N= 0.7-1.8g/24h). Patients with T3 toxicosis and incomplete urine collections were excluded from the study.

Results were expressed as mean±SD; for statistical analysis the chi-square, t-test, analysis of variance and Sheffe's test were used.

RESULTS

Mild, moderate and severe thyrotoxicosis was detected in 26, 76 and 98 patients respectively. 4 patients had T3 toxicosis with a normal FTI.

Overall free T4 index (FTI) range was 3.97-14.7 with a mean of 7.48±1.98. There was no significant difference between the severity of thyrotoxicosis and sex.

Serum Ca range was 8.2-11mg/dL with a mean of 9.3+0.46 mg/dL. Hypercalcemia (Ca>10.4 mg/dL) was detected in 3 (1.5%) patients, 2 males and 1 female (Table I).

Serum P range was 2.8±5.9 mg/dL with a mean of 4.1±0.61 mg/dL. Hyperphosphatemia (P>4.7 mg/dL) was observed in 38 (18.6%) patients, 14 males and 24 females (Table I)

The mean serum Ca in males and females was 9.37±0.45 mg/dL and 9.27±0.46 mg/dL and the mean for serum P in both sexes was 4.16±0.59 mg/dL and 4.09±0.61 mg/dL respectively.

There was no significant difference between serum Ca and serum P in both sexes (Table II) and also no noticeable relation between these two indices and the severity of thyrotoxicosis.

The mean seasonal variation in serum Ca and P is shown in Table III. There was no significant seasonal difference in serum Ca (p= 0.08), but this difference for serum P was significant (p= 0.04) and accounted for the variation between serum P in the summer and fall (4.27 mg/dL vs. 3.95 mg/dL respectively).

The mean seasonal variation in urine Ca and urine P is shown in Table IV. Overall the difference was noticeable statistically for both indexes (p= 0.02 vs. p= 0.011 respectively). For urine Ca this difference accounted for the variation between urine Ca in the spring and winter (161 mg/d vs, 244.9 mg/d respectively) and for urine P it accounted for the variation between urine P in the summer vs. fall and fall vs. winter (697 mg/d vs. 528.8 mg/d and 528 mg/d vs. 721.6 mg/d respectively).

Serum alkaline phosphatase mean was 221.3±121.7 u/L and we had an increased alkaline phosphatase level in 15.8% of patients. The mean for PTH was 50±18 pmol/L and 34 (16.7%) patients had suppressed PTH levels. There was no significant relation between severity of thyrotoxicosis with PTH and alkaline phosphatase in both sexes.

Hypercalciuria and hyperphosphatemia was detected in 20 (9.8%) and 9 (4.4%) patients respectively. Urine Ca and P range for males and females is shown in Table I. There was no noticeable difference between urine Ca in both sexes but urine P was appreciably increased in males (p= 0.01).

There was no significant relation between urine Ca and urine P with FTI in both sexes (Table V).

DISCUSSION

Thyrotoxicosis induces an enhancement of bone turnover and carries a high risk of osteoporosis.[13] Mild hy-

Table I. Prevalence of hypercalcemia and hyperphosphatemia in thyrotoxic patients.

	Male	Female
Ca > 10.4	2	1
P > 4.7	14	24

Table II. The mean ± SD of serum Ca, serum P, urinary Ca and urinary P in patients with thyrotoxicosis.

Sex / Mean±SD	Male	Female	
Serum Ca	9.37±0.45	9.27±0.46	NS
Serum P	4.16±0.59	4.09±0.61	NS
Urine Ca	206±116	185±10.8	NS
Urine P	689.6±245.4	593.7±238.8	0.01

Table III. The mean ± SD of seasonal variation of serum Ca and serum P in thyrotoxic patients.

Mean±SD / Serum	serum Ca	serum P
Spring	9.2±0.36	4±0.57
Summer	9.2±0.32	4.2±0.58
Autumn	9.4±0.52	3.9±0.59
Winter	9.3.6±0.56	4.1±0.65

Table IV. The mean ± SD of seasonal variation of urinary Ca and urinary P in thyrotoxic patients.

Mean±SD / Season	UCa (mg/d)	UP (mg/d)
Spring	161.4 ± 86.4	606.5±230.7
Summer	204±68.4	969.9±219
Autumn	202±118.4	528.8±190
Winter	244.9±116	721.6±287.5

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Table V. The mean ± SD of SCa, SP, UCa and UP in thyrotoxic patients with different grades of thyrotoxicosis.

Severity	SCa (mg/dL)	SP (mg/dL)	UCa (mg/d)	UP (mg/d)
Mild	9.34 ± 0.34	3.9 ± 0.53	223.4 ± 137.4	636.8 ± 214.6
Moderate	9.29 ± 0.46	4.2 ± 0.46	186.6 ± 77.2	611.8 ± 223.7
Severe	9.32 ± 0.48	4 ± 0.6	208.6 ± 105.5	654.2 ± 257

percalcemia is reported in 23% of patients with thyrotoxicosis.[4]

Although symptoms of thyrotoxicosis predominate those of hypercalcemia, patients sometimes develop severe hypercalcemia, anorexia, vomiting, polyuria, nephrocalcinosis and even impaired renal function,[8] and rarely hypercalcemic crisis.[9,10] Coexistence of thyrotoxicosis and hyperparathyroidism has also been reported,[5,11-13] otherwise symptoms of thyrotoxicosis might not be so evident in geriatric patients and others who may present with unexplained hypercalcemia.[14,15] So it is crucial to determine serum Ca levels in patients with thyrotoxicosis and thyroid function tests (TFT) in patients with unexplained hypercalcemia.

Our patients with hypercalcemia were asymptomatic and had a mild increase in serum Ca (max= 11mg/dL); this is in accordance with other studies.[4,6,7]

The prevalence of hypercalcemia in our patients was 1.5% (3 patients). This is in contrast with some studies showing an increased total serum Ca in 10-20% of patients.[10,11,17] Hypercalcemia is also reported in 27% of thyrotoxic patients in Burman et al.'s study.[18] Our findings are in agreement with Lalau et al.'s study who reported 3% hypercalcemia in 31 patients.[20]

In accordance with Defronze et al.'s study,[19] 18.6% of our cases (38 patients) had hyperphosphatemia.[19]

In this study as in others[2,19,21,22] an appreciable number of patients had hypercalciuria (20%), increased Alk.ph (24.5%) and suppressed PTH levels (16%). A direct relation between thyroid hormone levels and bone turnover indices has been shown in different studies,[2,23] among thyrotoxic patients vs. normal controls. In our study we did not find any significant correlation between indices of increased bone turnover (like increased urine and serum Ca and P, increased Alk.ph and suppressed PTH) with severity of thyrotoxicosis.

We could not find a significant seasonal difference for serum Ca; in contrast, serum P was increased more often in the summer. The seasonal variation for urine Ca and urine P was noticeable but surprisingly the greatest increment was in the winter which we expected to have low urine Ca and P levels at this time of the year.

There was also no appreciable difference between serum Ca and P and urine Ca between the two sexes with respect to the lower exposure of muslim women to sunlight due to their style of dressing.

The low prevalence of hypercalcemia in our study might be due to a habitual low Ca diet and low sunshine exposure in this area.

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