Letters to the Editor

Influence of L-Thyroxine Therapy on Parathyroid Hormone Concentrations

To the Editor:

In our RIA laboratory, we serendipitously observed that an unusual number of patients referred from the outpatient endocrinology clinic of the St. Savas Oncology Hospital had parathyroid hormone (PTH) concentrations exceeding the recommended upper reference limit of 6.90 pmol/L (65 ng/L) of our assay (ELSA-PTH, Cisbio International). Further work-up failed to show any evidence for hyperparathyroidism, but these patients were all receiving L-thyroxine for various thyroid problems, and their thyrotropin (TSH) concentrations were very suppressed (<0.4 mIU/L).

To investigate this phenomenon further, we obtained blood samples from all patients on thyroxine therapy (for goiter, hypothyroidism, thyroiditis, or thyroid cancer) referred to our laboratory. As a reference population, healthy blood donors, matched for age and sex and on no medication, were also included in our study. The study was conducted after institutional review board approval, and all participants gave their informed consent. The PTH was assayed in plasma samples obtained in EDTA-containing plastic tubes (Vacutainer®, Beckton Dickinson) and immediately centrifuged (1000g) for 10 min at 4 °C. Plasma was then separated and stored at −20 °C. The PTH assay (ELSA-PTH, Cisbio International) is a 2-step IRMA, with a monoclonal capture antibody specific for the mid region and the carboxyl-terminal part (39–84) of the PTH molecule and a radio-labeled polyclonal antibody that recognizes the N-terminal part (1–34) of the PTH molecule. Serum was also collected and sent to the high-volume hospital laboratory for calcium, phosphorus, albumin, creatinine, and hepatic enzyme determination, and another portion was assayed for TSH (IRMAZENco TSH-S, Zentech; detection limit: 0.025 mIU/L), thyroxine, and triiodothyronine (free and total). For PTH concentrations, 95% CIs were derived for each population using the MedCalc® software package. Owing to the known skewness in the distribution of the PTH values, logarithmic transformation of the data was used in calculating the 95% CIs. The patient population (n = 95, 9 males and 86 females, age range 42–75 years, mean age 58 years) on L-thyroxine therapy was subdivided (n = 64) into those with excessively suppressed TSH concentrations (<0.4 mIU/L, mean, 0.28 mIU/L) and those (n = 31) with TSH concentrations kept within normal limits (mean, 0.87 mIU/L). A 95% CI for PTH was also derived for healthy blood donors (n = 39). Patients on calcium-altering medications and/or with abnormal calcium/phosphorus concentrations, obese patients, and those with abnormal renal and/or hepatic function were excluded from this study (1).

Our results are shown in Fig. 1. The 95% CI for patients with excessively suppressed TSH concentrations was 2.12–12.27 pmol/L (20.0–115.7 ng/L), whereas for patients with normal TSH concentrations and healthy blood donors the 95% CIs were 1.37–7.54 pmol/L (12.9–71.4 ng/L) and 0.96–7.53 pmol/L (9.1–71.0 ng/L) respectively (mean PTH concentration ±2 SD, calculated from the log-transformed data). The means of the PTH values of the 2 L-thyroxine–treated groups of patients were compared using the unpaired t-test (with Welch correction), and the derived P value (P = 0.0197) indicated a statistically significant difference of the means of the 2 data sets. Comparison of the means of the PTH values of the healthy blood donors and the L-thyroxine–treated patients, with normal TSH values, showed no statistical significance (P = 0.4658).

Overtreatment of patients with L-thyroxine and hyperthyroidism is a well-known cause of accelerated bone loss with increased serum calcium, although the anticipated PTH suppression in these patients does not appear to be unequivocally supported in the literature (2, 3). The findings in this report could be attributable to a nongenomic action of the supraphysiological peak L-thyroxine concentrations on the parathyroid cells, possibly via mitogen-activated protein kinase, bypassing the calcium-sensing receptor regulation (4). Commercial kit–related parameters, such as the concurrent measurement of the intact PTH molecule along with its carboxy-terminal degradation products in the plasma, may also play a role, although further studies are definitely required to clarify this issue, because PTH assays are known to vary in their specificity (5).

In conclusion, we have observed PTH concentrations to be higher in patients receiving L-thyroxine therapy who have highly suppressed TSH concentrations. Further studies of this phenomenon with other PTH assays are...
needed to confirm our observation and to clarify its underlying mechanism. Knowledge of this effect may help clinicians to avoid unnecessary and expensive work-ups for suspected hyperparathyroidism.

Grant/Funding Support: None declared.
Financial Disclosures: None declared.

References


Adonios Zanglis*
Demetrios Andreopoulos
Nikolaos Baziotis
St. Savas Oncology Hospital
Nuclear Medicine Department
Athens, Greece

* Address correspondence to this author at:
St. Savas Oncology Hospital
Nuclear Medicine Department
171 Alexandras Ave.
Athens 115 22, Greece
e-mail azanglis@yahoo.gr

DOI: 10.1373/clinchem.2007.102194

Acute Variation of Osteocalcin and Parathyroid Hormone in Athletes after Running a Half-Marathon

To the Editor:

Parathyroid hormone (PTH) and osteocalcin (OC) play important roles in bone remodeling and bone metabolism. Although the physiological functions and clinical significance of these markers are well established, the influence of other biological variables aside from diurnal and seasonal variability has been less well investigated (1). Because little information is available on the kinetics of such markers after physical exercise, we measured PTH and OC in 15 athletes performing a half-marathon run. The study population consisted of 15 healthy trained white males, (mean age, 47 years) who had been engaged in specific endurance training for at least 5 years. Participants performed a 21-km, half-marathon run under competition conditions, while equipped with a heart-rate monitor [mean (SE) VO2 max 85% (3%)]. Prior to the race, preexercise baseline fasting blood samples were collected from the volunteers after a 48-h rest from the last training, 30 min before they warmed up for the race. Post exercise samples were collected immediately after the race, and 3 h, 6 h, and 24 h thereafter. All study participants gave informed consent for being tested, and the study was approved by the ethics committee.

Fig. 1. Box and whisker plots of the derived PTH 95% CIs for patients on L-thyroxine therapy.

(A), Patients (n = 64) with excessively suppressed TSH (<0.4 mIU/L) concentrations [mean (SD) TSH = 0.29 (0.14) mIU/L]. The true calcium concentration (albumin-corrected) for this group of patients was 9.61 (0.26) mg/dL. (B), Patients (n = 31) with TSH concentrations within reference limits [mean (SD) TSH = 0.87 (0.36) mIU/L]. Means of the PTH concentrations for each group were compared with the application of the t-test for independent samples, with logarithmic transformation of data, assuming unequal variances (Welch-test, P = 0.0197). Data for the healthy blood donors (n = 39) are not shown.