Logroño, Spain

Laboratorio Central
Hospital San Millán
Logroño, Spain

Relationship of T-Uptake and Thyroxine in Hyper- and Hypothyroid Patients

To the Editor:

Radioimmunoassay is an accurate and direct method for assessing thyroxine (T₄) binding globulin concentrations. Because such techniques are costly, time consuming, and use radioactive materials, nonisotopic assays are often favored. Although it is an indirect measure of T₄ binding protein (TBP) concentration, resin triiodothyronine uptake (RT₃U) has been the most widely used test, to date, for this assessment. However, RT₃U is heavily influenced by the total T₄ concentration in the specimen. RT₃U and total T₄ are expected to change proportionately (but not linearly) when TBP concentrations are within the reference range (1). Hypothyroid patients are expected to have normal or high RT₃U concentrations, whereas the converse is expected in hyperthyroid patients.

To automate thyroid hormone testing on a single instrument, many laboratories measure T-uptake on the Abbott IM analyzer (Abbott Park, IL), replacing the RT₃U assay. In the fluorescence polarization immunoassay (IM₄ method) for T-uptake, fluorescein-labeled T₄ is added to the patient’s serum and equilibrates between the TBP-bound and free fractions. As a result, T-uptake is directly proportional to the concentration of TBP. According to the Abbott IM₄ T-uptake test product insert, a reciprocal relation between RT₃U and T-uptake is anticipated: transformed % uptake = mean normal range + (0.8 (T-uptake)² + 0.2)²/2.

To investigate the effects of hyper- and hypothyroidism on T-uptake values, we reviewed 1766 consecutive thyroid profiles performed in our clinical laboratory over a three-month period. All assays were performed on the IM₄ analyzer [reference ranges for thyrotropin (TSH) = 0.1–5.0 mIU/L and T₄ = 45–120 μg/L]. Biochemically hyperthyroid subjects were identified as patients with concentrations of TSH <0.1 mIU/L and T₄ >120 μg/L (n = 30, 1.7% of all thyroid panels studied). Biochemically hypothyroid subjects were defined as patients with concentrations of TSH >5.0 mIU/L and T₄ <45 μg/L (n = 43, 2.4% of all thyroid panels studied). Linear correlations were sought between T-uptake and T₄. Within each patient group, T-uptake was inversely proportional to T₄ (in the hyperthyroid group, r = 0.79, P = <0.00001; in the hypothyroid group, r = 0.32, P = 0.04), whereas the majority of individual T-uptake results fell within the reference range (Figure 1).

The T-uptake assay is performed with approximately a 50-fold excess of fluorescein-labeled T₄ tracer; therefore, changes in the absolute T₄ concentration should have a negligible analytical effect. We surmise that the inverse relation between T-uptake and T₄ probably reflects the metabolic effects of thyroid hormone on TBP concentrations either through changes in TBP production or as a result of degradation. These findings are consistent with a study by Ahmed and Smethurst (2), in which TBP concentrations were essentially inversely proportional to the total T₄. Analogous results were reported by Ishida et al. (3) regarding concentrations of thyroxine-binding prealbumin in various thyroidal conditions. Together, these data predict that as TBP concentrations decrease with increasing T₄ concentrations, the proportion of unbound T₄ will rise more rapidly than the increase in total T₄. The inverse effect would apply for decreases in T₄ concentrations in hypothyroidism as well. Medical practitioners should be aware of the metabolic effects of thyroid hormones on TBP concentrations in the management of patients with thyroid dysfunction.

References

William E. Winter
Joel Weber
Joseph Sleater
Roger L. Bertholf

University of Florida
Dept. of Pathol. and Lab. Med.
Box 100275
Gainesville, FL 32610-0275

Fig. 1. Correlation of T-uptake with T₄.
In hyperthyroid patients, r = 0.79, P = <0.00001; in hypothyroid patients, r = 0.32, P = 0.04; shaded areas represent the reference range. Top: hyperthyroxinemic patients with suppressed TSH concentrations; bottom: hypothyroxinemic patients with increased TSH concentrations.