Functional Sensitivity and Recovery of Thyroid-stimulating Hormone

To the Editor:

Comparisons of the Vitros ECI thyroid-stimulating hormone (TSH) method with the AxSym (1), Immulite (1, 2), Elecsys (2), and ADVIA Centaur (2) have shown an unexplained progressive negative bias <0.2 mIU/L, a phenomenon that we have also observed (Fig. 1A). To investigate the bias, we diluted the TSH International Reference Preparation 80/558 (predominately pituitary TSH) and serum from a patient with untreated hypothyroidism (a mixture of pituitary and hepatic sialylated TSH) in serum pooled from patients receiving suppressive doses of thyroxine for thyroid cancer and with undetectable TSH values by the ADVIA ACS:180, Vitros ECI TSH, and Roche Elecsys methods. To obtain accurate dilutions at concentrations <0.1 mIU/L TSH, we used the technique of Vaks (3).

Measured TSH with both the patient serum sample and the International Reference Preparation mirrored the progressive negative bias found in the method comparison studies for the Vitros ECI TSH method (Fig. 1B). For both the Elecsys and ADVIA ACS:180, recovery of TSH was as high as 120% at concentrations <0.1 mIU/L. For the Vitros ECI method, recovery of TSH was as low as 60% at concentrations <0.1 mIU/L. The pattern of recovery did not appear to be related to the TSH concentration used for the low calibrator concentration (ECi, 0.002 mIU/L; ACS, 180: 0.01 mIU/L; and Elecsys 2010, 0 mIU/L).

If an assay’s functional sensitivity (4) is found to be 0.01 mIU/L but dilution of TSH at this concentration is 50% or 150%, the true functional sensitivity of the assay is 0.02 or 0.005 mIU/L, respectively. Dose-dependent recovery, as seen here, will therefore produce an inaccurate estimate of an assay’s functional sensitivity. Clinicians could be overconfident in the reliability of TSH results at low concentrations. We suggest that it is essential that the recovery of TSH be quoted at the claimed functional sensitivity of an assay.

When the TSH-30 (5) assay, which uses the same antibody combination as the Vitros ECI TSH assay (personal communication from Ortho Clinical Diagnostics), was widely used in the United Kingdom, it produced results that were 30–40% lower than those obtained with other methods (6), and this difference was thought to be attributable to the TSH-30 preferentially measuring certain forms of TSH (7). Therefore, the average difference between the Vitros ECI and the ADVIA ACS:180 and Elecsys TSH assays of 40% above 0.2 mIU/L is as expected. We find it difficult to understand that the average difference found (1, 2) is close to unity at >0.2 mIU/L. An explanation might be that the Vitros ECI method is supplied with different calibration factors in different parts of the world.

Fig. 1. TSH concentrations obtained from different assay methods. (A), percentage difference of TSH values produced by the Vitros ECI from Elecsys 2010 (n = 436; ○) and the ADVIA ACS:180 (n = 263, □). (B), dilution study of TSH International Reference Preparation 80/558 (dashed line) and of serum from a patient with untreated hypothyroidism (solid line) diluted in serum pooled from patients receiving suppressive doses of thyroxine for thyroid cancer and with undetectable TSH values by all methods. Results are shown for the ADVIA ACS:180 (□), Roche Elecsys (○), and Vitros ECI TSH (△) methods. Each dilution was analyzed five times by each method.

References


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