Measurement uncertainty for the analysis of serum 25-hydroxyvitamin D

H. C. M. Stepman · L. M. Thienpont

Received: 7 October 2009 / Accepted: 15 October 2009 / Published online: 17 November 2009

© International Osteoporosis Foundation and National Osteoporosis Foundation 2009

Dear Editor,

In a recent article in this journal, Cavalier et al. “report a relatively high “measurement uncertainty” for the measurement of serum 25-OH vitamin D (25(OH)D) levels for four different analytical techniques. Due to “measurement uncertainty”, the “true” 25(OH)D of a patient (whatever the commercially available assay tested) will be >80 nmol/L if its measured concentration is >100 nmol/L [1].” This leads them to the statement, “if a physician considers that a normal vitamin D status is a 25(OH)D level ≥ 80 nmol/L, he should ensure that the patient's results are ≥ 100 nmol/L”. This raises several questions.

First, what is a “relatively high measurement uncertainty” for 25(OH)D measurements? We have addressed this question recently by investigating several common approaches to establish analytical performance goals for 25(OH)D measurements, one of the major concepts being the establishment of analytical goals from biological variation [2]. Based on data from within subject biological variation under strictly controlled conditions ($CV=8\%$), a maximum analytical CV of 4% would be desirable for short-term monitoring of individuals with strictly controlled vitamin D status, such as for certain clinical studies [2]. Based on data of population distributions of 25(OH)D (CV 20–40%), a maximum analytical CV of 10% would be desirable for

diagnosis [2]. This shows that a “relatively high” measurement uncertainty should be related to the underlying biological variation of an analyte and the clinical purpose of the measurement. The “relatively high measurement uncertainty” (true concentration of 25(OH)D >80 nmol/L at a measurement result of 100 nmol/L) described by Cavalier et al. [1] translates into an analytical CV of $\sim 8\%$. This, indeed, may be considered “relatively high” for short-term monitoring of individuals with strictly controlled vitamin D status, but not for longer-term monitoring under routine conditions or diagnosis.

Second, it is surprising that the burden of poor analytical quality is put on the patient by proposing higher treatment levels for 25(OH)D. In our opinion, instead of putting the burden on the patient, the burden should be put on the analytics by improving the analytical methods and by taking advantage of averaging results from repeated sampling (for example, when monitoring vitamin D supplementation).

Although not strictly related to the publication of Cavalier et al. [1], it is worth noting that bias (or lot-to-lot calibration variation) is a major problem in the analysis of 25(OH)D and may need to be kept under 5% [2].

References

1. Cavalier E, Rozet E, Gadisseur R, Carlisi A, Monge M, Chapelle JP, Hubert P, Souberbielle JC, Delanaye P (2009) Measurement uncertainty of 25-OH vitamin D determination with different commercially available kits: impact on the clinical cut offs. *Osteoporos Int*. doi:10.1007/s00198-009-1052-5
2. Stöckl D, Sluss PM, Thienpont LM (2009) Specifications for trueness and precision of a reference measurement system for serum/plasma 25-hydroxyvitamin D analysis. *Clin Chim Acta* 408:8–13

A reply to this letter can be found at doi:10.1007/s00198-009-1098-4.

H. C. M. Stepman · L. M. Thienpont (✉)
Laboratory for Analytical Chemistry,
Faculty of Pharmaceutical Sciences, Ghent University,
Harelbekestraat 72,
9000 Ghent, Belgium
e-mail: linda.thienpont@ugent.be