Letters and Replies

Advance Access publication 11 November 2009

Comment on ‘Lanthanum deposition in a dialysis patient’

Sir,

Davis and Abraham report the detection of microscopic lanthanum particles in macrophage infiltrates of the mesenteric lymph node at autopsy of a dialysis patient, 3 years after a 7-month period of treatment with lanthanum carbonate [1]. Based on the limit of detection of their scanning electron microscopy/energy dispersive x-ray spectroscopy (SEM/EDS) analytical technique, they speculate that the concentration of lanthanum must be at least 10–100 µg/g wet weight, a level far higher than previously reported in the liver of lanthanum-treated patients (0.6–2.0 µg/g) [2].

Extreme caution must be used when attempting to compare a ‘point’ concentration determined for individual cellular particles using a spatial analytical method like SEM/EDS, with a bulk tissue concentration determined on a larger tissue sample using methods such as inductively coupled plasma-mass spectrometry, as was applied to the bone and liver measurements in the earlier studies cited by the authors. The concentration of lanthanum in a sub-cellular particle will be substantially diluted at the cellular level and even to a greater extent at the tissue level. It is therefore quite possible that the bulk mesenteric lymph node concentration is similar to or even lower than the concentrations reported for other tissues. Furthermore, the point lanthanum concentration given for the mesenteric lymph node must be regarded as speculative in the absence of appropriate calibration standards.

In view of the short period of lanthanum treatment and the long period of time that elapsed before the patient died from gadolinium-induced nephrogenic systemic fibrosis, other possible explanations for the presence of lanthanum in the mesenteric lymph nodes should be considered. Lanthanum occurs naturally in the diet, and daily faecal excretion in healthy individuals can be high. In a recent Phase 1 study, the background faecal lanthanum excretion was up to 4330 ± 5340 ng/day [3]. At the extreme end of this range, this could equate to excretion of ~20 µg/day (mean ± 3 standard deviations). The level could be substantially higher in individuals who eat foods that are naturally rich in lanthanum. Occasional high tissue concentrations have been reported for dialysis patients who have never been exposed to treatment with lanthanum carbonate as a phosphate binder, for example bone concentrations of up to 1.0 µg/g wet weight were reported in haemodialysis patients by D’Haese et al. [4]. Similarly, occasional high background plasma lanthanum concentrations have been reported in haemodialysis patients. Hutchison et al. found concentrations of up to 0.6 ng/ml (very similar to the levels achieved after lanthanum carbonate treatment) in the comparator control arm of a Phase 3 study [5].

In summary, this report of the presence of lanthanum in the mesenteric lymph node is notable, but caution should be applied both in interpreting the bulk tissue concentration and in attributing the levels found to historical phosphate-binder therapy.

Conflict of interest statement. SD is an employee of Shire Pharmaceuticals; PD’H has received research grants from Shire Pharmaceuticals.

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Reply

Sir,

We appreciate the chance to clarify any questions regarding our report [1] in response to the letter from D’Haese and Damment. To do so, we need to explain our results more fully than the initial limitations of space in our published letter allowed.

D’Haese and Damment stated that we ‘speculate that the concentration of lanthanum (La) must be at least 10–100 µg/g wet weight, a level far higher than previously reported in the liver of lanthanum-treated patients (0.6–2.0 µg/g)’ [2]. We did not mean to speculate but rather gave