Author's response to reviews

Title: Lanthanum associated abnormal liver function tests in two patients on dialysis

Authors:

Girish Namagondlu (drgirish@hotmail.co.uk)
Norman Main (norman.main@whnt.nhs.uk)
Lucy Yates (lucy.yates@whnt.nhs.uk)
Joanne Mooney (jaonne.mooney@whnt.nhs.uk)
Sangita Sathyamurthy (sangita.sathyamurthy@whnt.nhs.uk)
Indiver Daryanani (indiver.daryanani@whnt.nhs.uk)
Alex Crowe (alex.crowe@nhs.net)
Tom Ledson (thomas.ledson@coch.nhs.uk)
Anindya Banerjee (anindya.banerjee@coch.nhs.uk)

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Author's response to reviews:

The JMCR Editorial Team

Ref: 1978816942337447 - Lanthanum induced abnormal liver function tests in 2 patients on dialysis

Dear Editor,

Many thanks for your letter.

We have now revised our manuscript and are re-submitting it. All changes are in bold and underlined.

Reviewer 1 suggested our paper ought not to be called a ‘case series’ – we agree and we have now changed the Title of the report as well as in the Discussion section where now we say ‘cases’ instead of case series.

We also agree with Reviewer 1’s comments that ‘causality’ is not well established and we now mention this in our Conclusion.

As per Reviewer 1’s comments about clarity in the LFT changes with Lanthanum we now provide 2 Tables for each case obtained over several months before and after starting and stopping Lanthanum.

We disagree with Reviewer 1’s views that ‘fluid overload’ may explain abnormal LFTs in Case 2; as we have now mentioned in the Discussion section, both cases had a residual urine output and adequate fluid balance in between dialysis sessions. The rapid deterioration and jaundice in Case 2 occurred only after commencement of Lanthanum.
Reviewer 1 wanted speculative mechanisms of Lanthanum toxicity; we have now included additional References to support theories of trivalent cation related membrane rigidification (11) and liver enzyme changes in chicken livers even at exceedingly low concentrations (12) in the Discussion section of our paper.

Reviewer 2 has commented on our conviction that the abnormal LFTs in our 2 cases are definitely related to Lanthanum. We agree that in absence of definitive tests this effect of Lanthanum is probably speculative on our behalf; we therefore now mention in the Introduction that liver function derangement with Lanthanum is a 'possible' association. Additionally we have now changed our Discussion and Conclusion sections to reflect these speculative views.

We agree with Reviewer 2 that in presence of reasonable urine output and adequate dialysis clearances accumulation of Lanthanum leading to hepatotoxicity over only a few weeks of its use is less likely and hence we mention this in the Discussion section of our paper.

We do however believe that such hepatotoxic effects of this new drug, albeit speculative, should be highlighted, such that other practitioners are aware of such side effects. Only time can tell for certain about the future safety of this new phosphate binder in patients on dialysis.

Kind regards,

Anindya Banerjee and coauthors

14/02/2009