Author's response to reviews

Title: There is (still) too much aluminium in infant formulas

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Author's response to reviews: see over
To the Editor of BMC Pediatrics

Please find attached our revised manuscript;

There is (still) too much aluminium in infant formulas

Please find below our detailed response to the comments made by the two referees. We would like to point out that neither of these reviewers have any expertise in the field of aluminium and human health and some of their comments reflect this lack of understanding. Though Fewtrell is the first author on a recent paper on this subject she would, I am sure, be the first to admit that the paper in question is her only experience of aluminium and human exposure to aluminium. Greer’s background, though impressive in the field of paediatrics is completely outwith of the field of our research.

While we did not find there to be any substantive criticisms of the science in our manuscript by the reviewers, we have done our best to use their comments to improve its message and clarity. The changes in the revised manuscript have been indicated using Track Changes.

Reviewer: Mary S Fewtrell

The reviewer is thanked for their positive and thoughtful comments. Like many of us they ask about the potential consequences of infants ingesting significant amounts of Al in infant formulas. Several examples of aluminium toxicity caused by ingestion of infant formulas are included as references in the manuscript (10,11,12,13,25) as well as information relating to the potential toxicity of an elevated body burden of Al (22). The Al content of infant formulas are at least 10-40 times higher than that of breast milk. They are several times higher than the maximum allowed content of potable water! The point we are raising here is that these levels of Al will contribute significantly to the body burden of infants. Unlike parenteral nutrition these milks are ingested several times each day over many months and the consequent addition of Al to the infant’s body burden over such extended time periods is actually
equivalent to that which infants receive while on parenteral nutrition over a much shorter period of time. Your own follow-up work has shown that such exposures to Al can be damaging both in the short and long term. There has not been any recent research to investigate if there are any direct correlations between infant health (in the short or long term) and exposure to Al in infant formulas. A lack of such recent research does not preclude the possibility that some children receiving Al-rich infant formulas will suffer some health consequence in the future.

Reviewer: Frank Greer

While we respect the reviewer’s opinions and, indeed, his expertise in other areas of paediatrics we cannot agree with the negative and disinterested tone of his review. His general opinion on our results is ‘so what’ but this is only an opinion and it not an informed opinion where exposure to Al is concerned. I have been working on the ecotoxicology of Al for 25 years and I can inform the reviewer that there are many hundreds of published works which support the toxicity of Al both in conditions of chronic and acute exposure. There are many works, some of which are cited in our brief report, which demonstrate the toxicity of Al in infant formulas to infants. The reviewer accepts that Al exposure through parenteral nutrition is toxic while not accepting that Al exposure through infant formulas could be toxic. The former was only shown to be toxic because it was (recently) investigated by experiment. There have not been any experiments to investigate the toxicity of Al in infant formulas for almost 20 years. However, the lack of any recent investigations does not equate with their safety. Regarding the manufacturers of infant formulas, they may not be aware of the Al content of their products. We contacted each of them and asked them this question and those that replied made it clear that they did not add any Al to their products and were not aware of its presence. This possibility is alluded to in our manuscript. Regulatory bodies act upon the latest and most complete evidence of a problem when and if it is highlighted and it is not impossible that such in the UK and elsewhere may do so following publication of our findings. The formulas chosen represent the most popular formulas used in the UK and they are made by international companies and sold worldwide under their respective brand profiles.

With reference to the numbered ‘minor’ points;

1. THGA is explained in the script.
2. Breast milk is not really a ‘control’ for this study. The Al content of breast milk is usually ca 20 µg/L. Many, many times lower than the Al content of ALL infant formulas.
3. Not sure which 3 lines are referred to as a reference [1] is included? If the reviewer is referring to the abstract then we have added the reference [17] though we are not sure if references are usually included in abstracts?
4. All formulas investigated herein were for infants between preterm and 12 months. Some could be used for older infants but were not exclusive for older children. We have the manufacturers packaging and instructions if required.
5. Even a well-shaken liquid formula cannot guarantee a completely even distribution of its contents within the milk ‘slurry’. Al will be associated with different components of the milk including proteins, amino acids, vitamins, small organics as well as potentially particulates.
6. As explained previously, there is only a ‘clear link’ (recently) between Al in parenteral nutrition and infant toxicity because there have been investigations of this link. While there
has not been any recent investigation there have been investigations of Al toxicity in infants taking infant formulas and these have demonstrated toxicity. These cases are documented in the manuscript.

7. I am not sure which ‘commonly fed complementary foods’ the reviewer is referring to but we have not investigated this. Perhaps we will?

8. This is the reviewer’s personal opinion and it is based upon no knowledge of the field. If I was to make similar uninformed comments relating to the known and considerable expertise of the reviewer then they would probably reply in the same manner. We are the world leaders in what we do and nothing that we have written has been written without the due care and consideration it deserves. We are not speculating, we are not sensationalising. We are reporting results of first class provenance without prejudice because we believe them to be important. We understand Al and we are of the opinion that there is too much Al in infant formulas for them to be absolutely safe for preterm and term infants.

9. We have used the mean value to determine an average daily intake of Al from formula feeds. This is normal practice. What gain would there be from using presenting this data as a range as opposed to average daily intake?

We thank the Editor for the opportunity to respond to the reviewers and to submit a revised manuscript. We do hope that we have addressed all legitimate concerns and that the Editor will agree with us and one of the reviewers that the results of our work are important and should be made available to a wider audience as soon as is possible.

Yours faithfully

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