Reviewer's report

Title: High frequencies of elevated alkaline phosphatase activity and rickets exist in extremely low birth weight infants despite current nutritional support

Version: 1 Date: 31 March 2009

Reviewer: Reginald Tsang

Reviewer's report:

This is an important study in view of the survival of extremely low birth rate infants, and the lack of data on estimates of rickets and fractures in this population. The original study (of Koo et al, which should be referenced) set the stage for the detection and highlighting of these problems in very low birth rate infants, but since then there has been no clarification of the existence of these problems using current modes of nutritional support.

Page 5, First paragraph, The descriptions are imprecise in many regards. What do the authors mean about infants who have “persistently high APA”: what is persistent?

What is the definition of “evidence of persistent or long term inadequate mineral intake”?

What is the definition of “inability to tolerate a full volume”?

What is “a few infants with lower APA…”?

The authors need to give a better definition or better series of definitions in order for the reader to understand the clinical modus operandi in this particular nursery.

Page 6, Paragraph 4, The authors need to stress that radiographic evaluation was not done on a broad comprehensive basis, but only for those who had high APA, so this is a biased population.

What is the definition of osteopenia?

Page 7, Paragraph 1, the details of these subjects are clearly seen on the table, and probably need not be elaborated in the text, which actually does not help.

Page 7, Paragraph 2, Presumably when the authors say “when the infants were not evaluated for rickets,” in this paragraph they mean that no x-rays were done – is that correct?

Page 8, Last Paragraph, comments of “diagnosis of rickets and how physical examination is not useful etc, unless evidence of the fracture is present”, needs to be referenced – what exactly do the authors mean about that sentence anyway? That physical examination is not useful in predicting osteopenia or rickets, unless evidence of a fracture is present?

Page 9, Paragraph 2, the authors need to clarify why they say that the biochemical data were 60% specific, since the data were retrospective, without a comprehensive evaluation of all clinically relevant measures etc.
Furthermore, the authors indicate that “it is likely that these parameters will identify most infants with radiologic rickets” – how do they justify this comment?

Paragraph 3, the authors indicate that “preterm formulas, fortified human milk, and TPN typically provide about 60 to 100 mg/kg/d of retained calcium”….the question would be what about this particular population? What was the actual intake?

The sentence, “the large difference in APA within a narrow range of birth weights indicates ….”is not justified, nor proven, by the study. In fact it is unclear what the sentence means.

Furthermore, the authors state that “it is likely that there is a unique and extremely elevated short term demand for minerals in these smallest infants that is not met.” This is an unusual statement, with no proof, as is the comment that it is “often apparent to clinicians, but has not been documented”, whatever that means.

Page 10, the first paragraph is very speculative and unproven, and with no references. The comment that “bone growth may be rapid at some phase in these infants leading to very high APA etc” is not proven, nor referenced.

The comment “we did not attempt to document the feeding or TPN course of these infants as it would not be feasible to categorize these” is an unusual statement – why is it not feasible?

And what is the relationship with the last sentence of the paragraph, about the acute events being not increased? “However, ….”. “However” implies a connection that escapes the reader.

Last paragraph, the sentence that “our data generally support the use of APA as a useful parameter in this screening of rickets” is a loose statement with no real data provided in the study.

Page 11, First paragraph, Paragraph 2, the authors say that “further indications for radiographs would be any infant with an extremely prolonged course of parenteral nutrition. Do the authors have any data on this? And what do they mean by extremely prolonged?

The authors’ recommendations, while interesting, are not really based on their data, but on a clinical suggestion.

Specifically, the last sentence should be rephrased “we suggest” rather than “our data suggest;” in any case the authors paper do not give any indication that early nutritional intervention has a direct effect on the APA rise or the development of rickets. This comment as expressed in the conclusion is also incorrect, and it should be expressed as a speculation if the authors so wish.

Page 16 might be something that could be available on the website or something similar, or “available on request.”

The last figure while interesting is not what this study proves, and at most is a suggestion/speculation that these authors wish to make.
Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

i have no competing interests