Reviewer's report

Title: Enteral vitamin A for reducing severity of bronchopulmonary dysplasia in extremely preterm infants: a randomised controlled trial

Version: 2 Date: 27 May 2017

Reviewer: Jonathan Slaughter

Reviewer's report:

Thank you for allowing me to review the randomized clinical trial protocol, "Oral (enteral) vitamin A for prevention of bronchopulmonary dysplasia in extremely preterm infants: a randomized controlled trial."

The trial will be important to the field of neonatology by assessing whether enterally administered, water soluble vitamin A (retinyl palmitate) is effective in preventing or reducing the symptoms of bronchopulmonary dysplasia (BPD). This is a very important, clinically relevant question since intramuscularly administered vitamin A has been shown to reduce BPD, but is unpopular due to the need for repeated intramuscular injections in fragile preterm infants. The investigation also evaluates salivary vitamin A measurement as a less invasive way to evaluate preterm infants for vitamin A deficiency. If shown to be valid, salivary vitamin A measurement has the potential to be an important biomarker for future vitamin A trials that may aim to randomize populations of "high-risk" vitamin A deficient infants.

The authors have registered their trial online (Australia and New Zealand Clinical Trial Registry; ACTRN12616000408482) and have followed the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) checklist in reporting their trial protocol. The trial rationale, methods, and sample size as described appear appropriate to answer the questions posed by the investigators.

Specific comments:

The Background section may read easier if the description, of the potential of vitamin A in its water-soluble form to have higher intestinal absorption relative to the fat-soluble form, is moved prior to the description of the previous investigations that looked at the enteral administration of vitamin A.

I noted a minor typographical error on p. 5, line 32. "shows that passive diffusion as a predominant model," should be "shows that passive diffusion is a predominant model."
Are the methods appropriate and well described?  
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?  
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?  
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