Reviewer’s report

Title: The impact of different doses of vitamin A supplementation on male and female mortality. A randomised trial from Guinea-Bissau.

Version: 2 Date: 1 June 2011

Reviewer: Aamer Imdad

Reviewer’s report:

This paper addresses an important question related to effectiveness of vitamin A supplementation in reducing mortality in children 6 months to 5 years. Overall the paper reads well but revisions in certain sections of the paper can improve authenticity of findings and therefore that of conclusions. I have few major queries about the hypothesis and the conclusions of the paper and then certain suggestions to improve methods, results and discussion section.

Major Comments
• The literature described in the background focuses on proposed increased effectiveness of vitamin A supplementation in children who had recent vaccination (especially DTP) and that the low dose can be as effective as higher dose and then the hypothesis that “a low dose of vitamin A compared with the recommended dose is associated with lower mortality in girls. We also hypothesised that the lower dose would be particularly beneficial in girls who had DTP vaccine as their most recent vaccine.” I would like that the authors clarify the following questions
  1. Are they testing the hypothesis that low dose is as effective as higher recommended dose irrespective of immunization status/history or the hypothesis that low dose vitamin A will be enough/equally effective in children who have been immunized or they testing both of the above hypothesis together?
• In conclusions, authors claim that they didn’t find conclusive evidence in favor of low dose vitamin A supplementation for reducing mortality (in girls). Can the results be interpreted as “There was no differential effect of low or high dose vitamin A supplementation for reducing mortality (in girls, who have been immunized)?

Other Comments
Abstract:
• Result’s section: Please clearly state that the results were statistically insignificant. A “Tendency” in favor/against of an intervention is not conclusive evidence.

Full text

Introduction:
• 1st paragraph last line, please give the recommended frequency of
supplementation (i.e. every 4-6 months)
• Third paragraph, please also refer to other studies that investigated low dose (more frequent) vitamin A supplementation for reducing mortality (Rahmathullah, L., B. A. Underwood, et al. (1990). "Reduced mortality among children in southern India receiving a small weekly dose of vitamin A." N Engl J Med 323(14): 929-35)
• Comments on hypothesis as above

Methods:

Study settings
• What was the baseline mortality rate in the study area
• A brief description of health facilities in the area, were there hospitals around and sick got immediate health care etc?
• Baseline stunting rates?

Enrollment and randomization:
• How was the sequence generated?
• How was allocation concealed?
• Blinding?
• Who delivered the intervention and who collected the data?
• Were the data analysts blinded to allocation?

Outcomes
• What were the secondary outcomes? Did authors look at morbidity outcomes? Were any side effects noted as it is important to investigate that were there less side effects (especially vomiting) with low dose of vitamin A?

Results:
• Please give data according to age groups, as it has been shown previously that there is no effect of vitamin A supplementation in children 6 months to 1 year of age "Vitamin A and Pneumonia Working Group. Potential interventions for the prevention of childhood pneumonia in developing countries: A meta-analysis of data from field trials to assess the impact of vitamin A supplementation on pneumonia morbidity and mortality." Bull World Health Organ(73): 609-19.
• State clearly that results were not statistically significant
• Please show data for cause specific mortality (may be as webtable). When the authors have done verbal autopsies, then why the data have not been presented in complete details?

Discussion
• Please also site and defend your hypothesis/findings against the literature where scientists don’t agree with the hypothesis that effect of vitamin A supplementation may be mediated through immunization and there is a differential effect of vitamin A on girls. Please see the following references as an


Conclusion:
• The statement “The trial confirmed that the impact of VAS may differ by sex” is not supported by the findings of the study. Please rephrase

Level of interest: An article of limited interest

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

I declare that I have no competing interests