Reviewer's report

Title: A randomized cross over trial of tolerability and compliance of a supplement with low iron separated from calcium vs high iron combined with calcium in pregnant women [ISRCTN56071145]

Version: 5 Date: 11 December 2005

Reviewer: Andrew E. Czeizel

Reviewer's report:

General
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My first point is connected with the term of multivitamin. All experts know that the so-called multivitamins contain – beyond vitamins – minerals and trace elements. Thus, in my opinion, it would be better to use the term micronutrient combination.

A serious weakness of the study is the high drop-out rate. It is a pity but the arguments of authors can be accepted to explain it and mainly that this dropout does not disturb the message of the study.

The major problem of the primary prevention of congenital abnormalities by periconceptional folic acid or folic acid-containing multivitamin supplementation is the preconceptional onset of supplementation. An important task is therefore to educate the potential parents for the preconceptional onset, however, the protocol of this trial evaluated the prenatal (i.e. postconceptional) use of two micronutrient combinations.

Previous studies showed – among possible ADE – diarrhoe as well. Authors did not evaluate this possible ADE. Why?

I would need a reference regarding 15% reduction of birth defects in page 4 lines 10-12. Botto et al (2004) estimated 15-20%, while WHO Expert Committee (Folic acid: from research to public health practice 2004) 33% reduction of congenital abnormalities. The spectrum of nausea and vomiting during pregnancy is wide from slight food aversion and heartburn to hyperemesis gravidarum. It would be useful to differentiate mild, severe and very severe degree (hospitalisation) of nausea and vomiting during pregnancy.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

Discretionary Revisions (which the author can choose to ignore)

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article of importance in its field
Quality of written English: Needs some language corrections before being published

Statistical review: Yes

Declaration of competing interests:

I declare that I have no competing interest.