Reviewer's report

Title: Early nasogastric tube feeding in optimising treatment for hyperemesis gravidarum: the MOTHER randomised controlled trial (Maternal and Offspring outcomes after Treatment of HyperEmesesis by Refeeding)

Version: 3  Date: 9 December 2014

Reviewer: Caroline Maltepe

Reviewer's report:

Major compulsory revisions

1. For the primary outcomes, the authors state that the validated PUQE score will be used. However, the authors are not using the correct version of the PUQE scale. The authors need to change to the PUQE-24 scale. Please look at the following paper and Table 1 in the paper: Ebrahimi N et al. Nausea and vomiting of pregnancy: using the 24-hour Pregnancy-Unique Quantification of Emesis (PUQE-24) scale. J Obstet Gynaecol Can. 2009 Sep;31(9):803-7.


3. Will all maternal demographics be collected, such as education, marital status, work, gravidity, parity, BMI, vitamin use pre-pregnancy, smoking, medical history, etc…?

4. Many women stop taking their medications when they become pregnant, due to fear that it may affect the baby. How will that be assessed? Will women be treated or asked to resume their medication(s)? For women with pre-existing history of depression and/or anxiety, how will they be counseled and/or treated?

5. If the women score high in the psychopathology scales, will they be provided psychological counseling and/or antidepressant/anti-anxiety medication(s)? Experiencing hyperemesis gravidarum (HG) may cause women to be more depressed, however, if they have an existing history of depression, their symptoms could spiral to greater depression, hence increasing their NVP/HG symptoms.

6. The authors’ exclusion criteria for study should also include if NVP symptoms begin for the first time after 10 weeks of gestation. How will differential diagnosis for NVP/HG be assessed for the participants?

7. It is concerning when a woman is hospitalized or readmitted at 5+0 weeks (as per the inclusion criteria), as typically, nausea and vomiting of pregnancy (NVP) begins between 4 and 9 weeks of gestation and symptoms (nausea, vomiting and/or retching) peak between 7 and 12 weeks of gestation. How can this be explained? What is the inclusion criterion for start of NVP symptoms?
8. Are women undergoing fertility treatment included? If yes, then please state fully all criteria for participation in the study. Additionally, fertility drugs increase symptoms of NVP. Authors should ensure to report women who had fertility treatment(s).

9. How will dietary intake be assessed for the woman prior to their hospitalization? Will women be asked how often they were eating and drinking fluids throughout the day when they found out they were pregnant?

10. Will the participants be tested for Helicobacter pylori infection? In a study published earlier this year, Niemeijer and colleagues demonstrated a significant association with occurrence of HG. Please see following papers:


11. If a woman is tested positive for helicobacter pylori infection, will she receive antibiotics?

12. Many pregnant women do not recognize symptoms of heartburn, dyspepsia or reflux (such as burping, nausea at night, belching, something stuck at back of throat, etc…), which affect 40-85% in the first trimester. In 2009, Gill and colleagues demonstrated a reduction of the NVP severity when adding acid-reducing pharmacotherapy to the existing antiemetic regimen(s). It may be beneficial for authors to ask the participants if they are experiencing any symptoms, and if yes to treat with an H2 Blocker and/or PPI.

13. Additionally, with all the excessive vomiting, a woman’s throat becomes raw. She will be afraid to eat or drink. It may be beneficial for the participants to receive an H2 Blocker and/or PPI in their IV and to continue their use once sent home.

14. The authors state “Standard care consists of intravenous rehydration and, when considered necessary, laboratory monitoring, electrolyte and/or vitamin supplementation, antiemetic medication and dietetic advice”, however, there is no information on the antiemetics that will be given, dietary advice, oral electrolytes provided, vitamins, etc… that will be provided? What are the guidelines/protocol?

Please see paper by Lamondy, Anne “Hyperemesis Gravidarum and the Role of the Infusion Nurse”

15. Will any of the women receive ondansetron? If yes, how will these patients be monitored? Will there be an ECG be done prior to its use? With its conflicting safety profile, and recent papers demonstrating increase risk of cardiac defects,
how will participants be informed about safety?

16. Will the participants, once sent home, continue with dietary changes, oral electrolyte solutions, antiemetics?

17. The authors should clarify what the following acronyms/abbreviations HIS, NVPQoL, HADS, SCL-90, SF-36, EQ5D, are in the data collection paragraph in methods/designs.

18. Authors stated that the patients will be provided information in Dutch and English. Will any of the questionnaire the authors have listed for this study [validated NVP symptom and NVP specific quality of life measures (PUQE, HIS, NVPQoL), psychopathology (HADS, SCL-90) and general health related questions (SF-36, EQ5D)] be provided only in English? Have any been translated to Dutch? If yes, has it been validated?

19. Please revise the reference #15, as the correct listing of authors are “Hsu JJ, Clark-Glena R, Nelson DK, Kim CH.”

20. If long-term follow-up will be done, such as neurodevelopment of child, will the authors also test for maternal IQ and socioeconomic status?

**Level of interest:** An article of outstanding merit and interest in its field

**Quality of written English:** Needs some language corrections before being published

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

**Declaration of competing interests:**

I declare that I have no competing interests