Reviewer's report

Title: Evaluation Of Splanchnic Oximetry, Doppler Flow Velocimetry In The Superior Mesenteric Artery And Feeding Tolerance In Very Low Birth Weight IUGR And Non-IUGR Infants Receiving Bolus Versus Continuous Enteral Nutrition

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Reviewer: Gerd Schmalisch

Reviewer's report:

The study protocol submitted by Valentina Bozzetti and co workers is addressed to the important clinical problem of the optimal enteral nutrition of VLBW infants. In a registered, randomized single-center, cross-over study the authors intend to compare bolus and continuous enteral nutrition using sophisticated measuring techniques (Doppler flow velocimetry in the superior mesenteric artery, cerebral and abdominal near-infrared spectroscopy (NIRS)). At least abdominal NIRS in VLBW is very new and only few information exits about the biological variability of the measured parameters, their reproducibility and the effect of the inter-observer variability.

The protocol is in general well designed and well written and the manuscript adhere to the relevant standards for reporting and data deposition.

It is planed to include 20 VLBW infants in the study and three paired and unpaired group comparisons (primary and secondary endpoints) are intended. Some concerns to reach all endpoints remain.

Major points

1. A single-center study has several advantages. However, the number of VLBW infants of a unit is limited and some of the infants are already enrolled in other trails. Has the unit the potential to recruit 10 IUGR and 10 Non-IUGR VLBW infants within 2 years according the inclusion criteria?

2. Abdominal NIRS has several disturbances (see page 9) and it is difficult to standardize. Is the sample size calculation for this parameter a realistic one?

3. As stated (page 16) neonatologists with the same expertise and manual ability will perform the measurements. Are the inter-observer variability known and which efforts have been taken for their reduction?

Minor points

• VLBW is defined as birth weight <1500g (see inclusion criteria)
• Infants which are already included in other trials should be excluded from this study.
• How is the intra-uterine growth restriction (IUGR) defined?
• Page 9, last sentence. Ref. 15 is not under review and does not consider splanchnic oximetry.
• It is not clear how the effect of the order of the feeding regimes (Group A versus B) will be compared.
• Missing values (page 20): How missing values will be estimated? Such estimations should be done with caution and the number should be limited on 1 - 2. Sometimes it is better to evaluate the reduced number of patients.

**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 declare that I have no competing interests'