Reviewer's report

Title: LETTER TO THE EDITOR: CLARIFYING SOME ASPECTS AND THE TERMINOLOGY OF INDIVIDUALIZED HUMAN MILK FORTIFICATION

Version: 0 Date: 20 Aug 2018

Reviewer: Gemma McLeod

Reviewer's report:

Thank you for asking me to review this letter to the editor.

Members of the EMBA Working Group in their letter to the editor aim to (i) draw attention to the importance of the use of a metabolic marker to adapt protein intake in preterm infants and (ii) clarify terminology and some specific aspects regarding individualised human milk fortification.

The EMBA seek to achieve their aims by

(i) acknowledging the efforts made by Mathes et al. (2018) to obtain a practical, non-invasively measured metabolic marker reflecting the short term protein intake of preterm infants;

(ii) reminding the authors of a randomised trial (Arslanoglu et al. 2006) that employed twice-weekly measurements of BUN as the basis for adjusting protein fortification and improving protein intake; and

(iii) referencing the two models of human milk fortification recommended by the World Association of Perinatal Medicine (Arslanoglu et al. 2010) i.e. (a) Adjustable method: adjusting protein fortification based on regular BUN measurements; and (b) Targeted method: protein fortification based on milk macronutrient analysis.

Whilst the intent of the EMBA is no doubt to promote standardisation of clinical practice and consensus around research terminology, methodology and endpoints, it is important to encourage continued exploration into new methods and technologies that will enhance research design and continue to promote best clinical practice. Although BUN is used as a metabolic marker of protein adequacy, the adjustable method of individualising protein fortification on the basis of BUN measurements has not been universally adopted across neonatal units, potentially because BUN is also an indicator of renal impairment and sensitive to fluid status, its measurement is invasive and, when used in the context of protein fortification, translates to regular blood sampling of the infant. It is interesting that Mathes et al. (2018) have demonstrated a highly positive correlation between plasma urea concentrations and the urinary urea-creatinine-ratio,
and between actual protein intake and plasma urea concentrations and the urinary urea-creatinine-ratio. Methods employed to individualise fortification of milk fed to preterm infants should continue to be rigorously explored, and adjusting protein fortification on the basis of urinary urea-creatinine ratio may warrant further investigation.


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