Reviewer’s report

Title: Genetic variants of the vitamin K dependent coagulation system and intraventricular hemorrhage in preterm infants

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Reviewer: Susanna Ranta

Reviewer’s report:

The authors present an ambitious study addressing genetic risk factors for IVH, a serious and common complication in preterm babies. However, the reference values for coagulation factors in preterm infants vary according to gestational age and are influenced by clinical factors. Further, as the authors state, IVH is multifactorial with a lot of confounding factors which complicate the analysis making it challenging to analyse individual factors. Interestingly, the carriers of the A-allele for VKORC1 gene, had lower IVH rate than infants the wild type G/G genotype. The speculation that differences in vitamin K metabolism seems reasonable and, as the authors state in the conclusions, warrants further research.

Minor comments:

In Table 1, the authors show that infants with IVH had significantly lower FII and FX. However, they were also born at lower gestational age. Therefore I would suggest adjusting also these coagulation factor values for gestational age as done in tables 2 and 3.

Infants with F7-323Ins10 variant had lower FVII levels as anticipated, but not higher IVH rate. Surprisingly, they also had lower FX levels and even lower FII activity even though this was not statistically significant. In the discussion, could the authors please speculate if there could be some other factors which influence liver function/the vitamin K dependent coagulation factors in the F7-323Ins10 variant group?

Discretionary Revisions

In the abstract, methods section “coagulation factor 7” refers to the protein (not the gene) and could be written with Roman numerals.

Some of the abbreviations are not given in the main (for example SGA, NICU, GA)

Table 3, differences in CRO and hematocrit are marked in bold as significant although they were not significant when adjusted with gestational age. This could be added to the table for clarity.

Level of interest: An article of importance in its field
Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

I declare that I have no competing interests