NEONATAL ENCEPHALOPATHY: AN ASSOCIATION BETWEEN ALTERED SERUM CYTOKINES IN THE FIRST WEEK OF LIFE AND NEURODEVELOPMENTAL OUTCOME AT TWO YEARS

T. Strickland,¹⁻² D. Sweetman¹⁻³, C. Onwuneme^{3,4}, Z. Zareen¹⁻³, M. Slevin³, R.W Watson⁴, J. Murphy^{3,4}, E.J. Molloy¹⁻⁶

Discipline of Paediatrics, Trinity College Dublin¹ Trinity Translational Medicine Institute, St James Hospital² Neonatology, National Maternity Hospital³ UCD School of Medicine and Medical Sciences, University College Dublin⁴ Tallaght University Hospital⁵ Coombe Women’s and Infants University Hospital, Dublin⁶ Our Lady’s Children’s Hospital, Crumlin, Dublin, Ireland⁷

Introduction

- Neonatal encephalopathy (NE) is clinically defined syndrome characterized by disturbed neurologic function in the term infant, manifested by a reduced level of consciousness or seizures, often accompanied by difficulty with initiating and maintaining respiration, and by depression of tone and reflexes. (1)
- Predicting neurodevelopmental outcome in the earliest days of life following NE is notoriously difficult. Previous studies have implicated inflammation in the onset of NE. (2) It has also been highlighted that perinatal serum cytokines are altered and may predict abnormal neuroimaging in NE. (3,4)
- We investigated a panel of four biomarkers in serum, namely, VEGF, IL-8, Epo and GM-CSF. We chose these particular serum biomarkers as they represent the two sides of the pro-inflammatory (IL-8, GM-CSF) and anti-inflammatory/neuroprotective (Epo, VEGF) response to hypoxia-ischaemia. The aim of this study was to evaluate associations between perinatal serum IL-8, GM-CSF, VEGF and EPO and neurodevelopmental outcome at 2 years.

Methods

- 45 of 82 infants from our previous study (3) were followed up at 2 years post-NE and had their cognitive, language and motor abilities assessed via Bayley Score of Infant Development III (BSID-III) by a developmental psychologist (5) 4 infants died before follow up and the remainder did not attend assessment.
- Spearman correlations and multiple t-tests were used to assess associations between BSID-III and serum cytokines (EPO, VEGF, GM-CSF and IL-8) previously measured via multi-spot ELISA at day 1, 2, 3 and 7 of life
- Developmental delay was defined as a score of <85 while normal was >85 as per Johnson et al (6) VEGF, IL-8, EPO and GM-CSF concentrations from these patient subsets were compared Significance was considered at p < 0.05

Table 1: BSID Parameters	Mean	SD	Composite Score >85	Composite Score <85
Composite Cognitive	101.1	18.7	37 of 45 (82%)	8 of 45 (18%)
Scaled Cognitive	10.2	3.7		
Composite Language:	102.2	22.4	37 of 45 (82 %)	8 of 45 (18%)
Scaled Expressive	9.8	4.0		
Scaled Receptive	10.9	4.0		
Scaled Total	20.7	7.6		
Composite Motor:	103.4	20.0	40 of 45 (89%)	5 of 45 (11%)
Scaled Gross	9.4	3.3		
Scaled Fine	11.7	3.9		
Scaled Total	21.1	6.7		

Results

- EPO was significantly higher at day 1, 2 and 3 of life in infants with abnormal cognitive scores compared to those with normal scores (p = 0.001, p=0.0002 and p=0.012). Higher Epo on day 1 was positively correlated with language scores <85 at 2 years (R= 0.8365 p = 0.0302). Higher concentrations of EPO on D1 correlated negatively with >85 language scores (R = -0.5259 p= 0.0048) and negatively with >85 day 1 cognitive scores (R = -0.5259 p = 0.0048)
- There were no significant differences between serum GM-CSF, IL-8 and VEGF in infants with normal versus abnormal composite BSID-III scores
- However, higher GM-CSF on day 1 was positively correlated with language scores <85 (R = 0.9274 p =0.0079). Higher GM-CSF correlated negatively with >85 language scores at day 2 (R= -0.3975, p = 0.0327), negatively with >85 cognitive scores at day 2 (R =-0.3975 p = 0.0327) and negatively with >85 motor score on day 7 (R = -0.4995 p =0.0348)

Conclusion

- Serum cytokines are a useful biomarkers that may predict both short and long term patient outcomes in the context of neonatal encephalopathy
- Differences in perinatal GM-CSF and EPO exist in those who at 2 years are developmentally normal and those who are delayed.
- Serum EPO and GM-CSF concentrations in the first few days of life may represent predictive biomarkers of abnormal neurodevelopment following NE.

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