**NEAR INFRARED SPECTROSCOPY AND GUT BIOMARKERS IN PRETERM INFANTS – CAN THEY PREDICT NEC?**

**Background**

We previously established normal ranges of regional tissue oxygenation in preterm infants using Near Infrared Spectroscopy (NIRS). Survival of very preterm infants has improved but the incidence of NEC has not changed. Progress in the prevention of Necrotising Enterocolitis (NEC) has been limited by difficulties in clearly defining high risk groups of preterm infants and because there are no routinely used eﬀective gut biomarkers. There is an unmet need to identify prospective biomarkers to create a window of opportunity for prevention.

We aimed to establish if gut biomarkers of tissue injury and splanchnic NIRS measurements differed in infants with NEC compared to those without NEC.

**Methods**

We examined 48 infants <30w gestation admitted to our tertiary level NICU (after ethical approval and informed consent) from Oct 2016 to May 2018. Exclusion criteria: birthweight ≤2nd centile, abnormal antenatal dopplers, major congenital anomalies or Twin to Twin Transfusion Syndrome.

For 60 minutes each week splanchnic (sTOI) and cerebral (cTOI) Tissue Oxygenation Index (TOI) was measured simultaneously using NIRO-300 (Hamamatsu KK, Japan). Subsequently splanchnic Fractional Tissue Oxygen Extraction (sFTOE) and Splanchnic Cerebral Oxygenation Ratio (SCOR) were calculated.

Weekly urinary intestinal and liver fatty acid binding proteins (I- FABP, L-FABP), Trefoil Factor 3 (TTF3) and stool Calprotectin were measured by ELISA and weekly clinical status recorded. NEC was defined as ≥ Bells stage 2.

**Results**

Median birthweight was 884g (460-1600), median gestational age 26+3 weeks (23+0-29+6) and 52% female. 7 infants developed NEC.

Over the first 7 weeks of life none of the biomarkers were affected by presence of PDA, enteric feed volumes or haemoglobin level. There were no statistically significant differences in I- FABP, L-FABP, TFF3 and Calprotectin levels between those infants with and without NEC.

sTOI was significantly lower and sFTOE was significantly higher in those infants who developed NEC compared to those without NEC. The SCOR was lower in infants who developed NEC (Table 1). sTOI, and sFTOE were significantly associated with NEC even after adjusting for confounding factors such as gender, PDA, enteral feed, ethnicity and haemoglobin.

Table 1: Splanchnic NIRS measurements in those infants with NEC compared with infants without NEC (excluding those infants who developed Haemorrhagic Parenchymal Infarcts).

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| --- | --- | --- | --- | --- | --- | --- |
|  | **Mean for Infants without NEC** | **Mean for Infants with NEC** | **Mean difference** | **LCI** | **UCI** | **P value** |
| **sTOI** | 42.8 | 34.6 | -8.15 | -15.3 | -0.96 | 0.026 |
| **sFTOE** | 0.54 | 0.63 | 0.09 | 0.01 | 0.17 | 0.023 |
| **Ln(SCOR)** | 4.34 | 3.97 | -0.37 | -0.74 | 0.00 | 0.051 |

**Conclusion**

Infants who developed NEC had significantly lower splanchnic oxygenation. If preterm infants at highest risk of NEC had continuous NIRS measurements and individual trends examined, then a reduction in sTOI and corresponding increase in sFTOE could herald the onset of NEC.

This novel finding could help clinicians diagnose NEC sooner. In the future an algorithm may provide more sophisticated information than a single biomarker alone.