Correlation Between Decreased Vagal Activity and Necrotizing Enterocolitis

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Abstract:
In the preterm, neonatal intensive care unit, NEC is the most prevalent and devastating bowel disease affecting 6-10% of infants with a mortality rate of 15-25%. Success of treatment depends on early diagnosis, however, there are no predictive measures for NEC yet. Heart rate variability (HRV) is a non-invasive measurement that provides information on vagal activity (high frequency, HF, range in the spectral analysis). Since HRV has attracted interest as an early marker of sepsis in the newborn, we hypothesized that diminished HF component of HRV spectrum would predict susceptibility to NEC. We also hypothesize that a decreased gastrointestinal (GI) motility is indicative of a decreased anti-inflammatory vagal activity which, in turn, increases the susceptibility to NEC. Vagal inputs modulate both GI motility and heart rate although the preganglionic neurons providing vagal efferents to these organs originate from different brainstem nuclei; the dorsal motor nucleus of the vagus (GI motility) and nucleus ambiguus (heart rate), respectively. It is essential, therefore, to determine whether there is a correlation between GI motility and heart rate variability. The aims of this study were to determine 1) whether preterm infants with decreased HF power measured during the first week of life develop NEC; and, 2) whether in an ICU rodent model there is a correlation between the HF power and gastric motility. We enrolled 30 preterm infants (32±1.5wks; 1878±409g at birth), exclusion criteria were congenital anomalies, central nervous system lesions or mechanical ventilation at the time of enrollment. On day 5-7 of life, postprandial resting HRV was derived from the ECG and the HF power calculated (0.2-2Hz). Infants were followed up for a month. Five chronically anesthetized and neuromuscular-blocked (NMB) rats were implanted for i.v. nutrient delivery, EKG, blood pressure and GI motility recording (strain gauge on the anterior corpus) to allow continuous measurement for 4-7 days. HF power of the HRV spectrum and GI motility were derived every other 5 minutes. Four infants (13%) developed NEC as confirmed by radiologic (pneumatosis intestinalis) and clinical findings. Seven infants were excluded because they developed non-NEC sepsis within the first 10 days of life. NEC infants had lower HF power compared to the healthy non-NEC infants (2.8±1.4 vs 45±10msec2, NEC vs non-NEC respectively; p<0.01). Interestingly, the detection of decreased HF power was obtained 0.5-9 days prior to NEC diagnosis. Four NMB rats showed a positive correlation between HF power of the HRV and GI motility (r=0.27±0.03; p<0.01); the other rat had no significant correlation. Our data suggest that preterm infants with decreased HF power measured during the first week of life develop NEC; and in an ICU rodent model there is a correlation between the HF power and gastric motility.