

Vagal Tone is a Non-Invasive Predictor of Feeding Intolerance and NEC-risk in Preterm Infants

Doheny, Kim K.¹; Gardner, Fumiyuki C.¹; Browning, Kirsteen N.², Travagli, R. Alberto²

Penn State College of Medicine, Newborn Medicine¹ and Neural and Behavioral Sciences², Hershey, PA, USA

Introduction

Preterm infants are known to have intrinsic immaturity of the enteric nervous system, which results in delayed intestinal transit. Feeding intolerance secondary to slowed gastric emptying and intestinal transit is a common problem among preterm infants in the neonatal setting and may or may not be indicative of underlying GI pathology. However, abnormalities in motility and gut transit may lead to bacterial overgrowth promoting a milieu whereby substrates and immature host defense culminate in necrotizing enterocolitis (NEC). NEC is a devastating inflammatory bowel disease that is associated with high morbidity and mortality. Given its acute onset and rapid progression, a non-invasive biomarker of gut dysmotility would be clinically useful to identify which infants are at heightened risk for NEC. The high frequency (HF) component of heart rate variability (HRV) is a non-invasive measure of parasympathetic (vagal) activity.

Objective

To test the hypothesis that diminished HF-HRV is indicative of decreased vagal activity which, in turn, leads to feeding intolerance and increased NEC-risk.

Table. Sample Characteristics

Infant Variable (N=65)	Mean \pm SD or percent
Gestational age (wks)	31.62 \pm 2.32
Birth Weight (gms)	1693.9 \pm 520.66
Male	65%
SNAP*	3.34 \pm 2.99
*SNAP = Score for Neonatal Acute Physiology, morbidity index	

Methods

Sixty-five medically stable preterm infants admitted to the neonatal intensive care unit and off mechanical ventilation by day 5 of life were enrolled in this prospective cohort study. Infant characteristics are presented in the Table.

Infants with congenital or neurological abnormality at birth were excluded from participation. Clinical outcomes were measured prospectively until hospital discharge.

Measures

Heart Rate Variability (HRV) (day 5-8): HRV measures were standardized for time of day, feeding and sleep states to control for circadian and state influences on HRV. Postprandial resting vagal tone (HF-HRV, 0.3-1.3 Hz) was measured by spectral analysis derived from the analog ECG.

Clinical Outcomes During Hospital Stay:

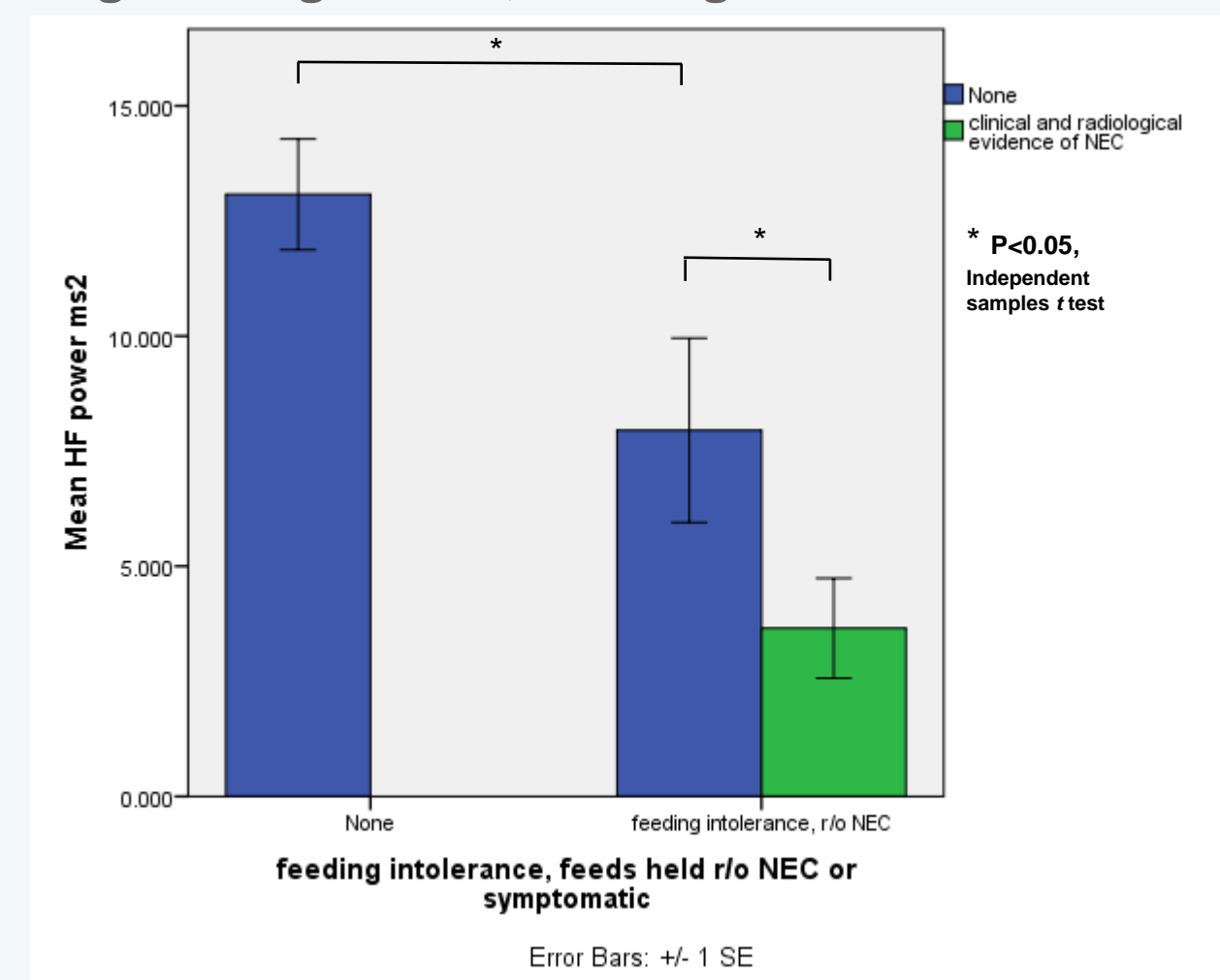
Feeding intolerance and GI dysmotility was confirmed by presence of emesis and/or large feeding residuals (>40%) with gastric distension on examination of the abdomen. Stage II+ NEC was determined using the modified Bell's staging system (radiographic confirmation of pneumatosis intestinalis and clinical findings).

Results

- Fifteen/65 infants (23%) presented with feeding intolerance and GI dysmotility by day 14 of life.
- Of those with feeding intolerance and dysmotility, 6/15 (40%) developed stage II+ NEC.

Results

Figure. Vagal Tone, Feeding Intolerance & NEC



- Vagal tone measured by HF-HRV at day 5-8 was diminished in those infants who later developed feeding intolerance (mean \pm SE, 13 \pm 1.2 vs 6.2 \pm 1.4ms², P<0.05), and markedly diminished (8 \pm 2 vs 3.7 \pm 1.1ms², P<0.05) in those infants with feeding intolerance who later developed NEC (see Figure).
- Low HF-HRV was obtained by spectral analysis 9-20 days prior to the onset of NEC symptoms.

Conclusion

Our findings suggest that vagal dysregulation measured by HF-HRV in the first week of life is a non-invasive predictive biomarker for later GI dysmotility and NEC-risk in preterm infants.

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