Heart Rate Characteristics Monitoring in the NICU: A New Tool for Clinical Care and Research

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ABSTRACT

Heart rate variability (HRV), a marker of autonomic nervous system function, is depressed in sepsis and other acute and chronic diseases. Preterm neonates with sepsis have been shown to have both depressed HRV and repetitive transient heart rate decelerations. These abnormal heart rate characteristics (HRC) of depressed variability and decelerations may precede other clinical signs and symptoms of sepsis and usually are not apparent to clinicians using conventional vital signs monitoring. In order to quantitate these changes associated with sepsis, a heart rate characteristics monitor was developed which continuously calculates an HRC index from the conventional electrocardiogram waveform tracing. This HRC index is the fold-increase in risk that a baby will experience a clinical deterioration consistent with proven or clinical sepsis in the next 24 hours. This HRC or HeRO™ (Heart Rate Observation) Monitor can alert clinicians to carefully evaluate a patient and consider antibiotic therapy or other interventions. The impact of continuous HRC monitoring on outcomes of preterm infants was the subject of a multicenter randomized clinical trial of 3003 very low birth weight infants, completed in 2010, which showed a significant reduction in mortality in neonates whose HRC index, or “HeRO Score” was displayed to clinicians in the NICU. Continuous HRC monitoring is an important new tool for both clinical care and research in the NICU.

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INTRODUCTION

Approximately a quarter of preterm very low birthweight infants (<1500 grams) develop late-onset sepsis during their stay in the Neonatal Intensive Care Unit, increasing their risk for death or neurologic morbidity, and prolonging their NICU stay (Bassler et al., 2009; Cotten et al., 2005; Stoll et al., 2002). The presentation of sepsis in NICU patients can be obvious or subtle, as illustrated in the following cases:

Case#1: Baby A, a 25 week preterm infant, was stable on nasal CPAP and advancing enteral feeds. On day 13 she is “not quite herself” according to the bedside nurse. The following day, she develops feeding intolerance, profound apnea requiring intubation, and shock. Antibiotics, fluid resuscitation, and pressors are initiated. The blood culture yields Klebsiella pneumoniae and the CSF culture (obtained after antibiotics) is negative but the CSF WBC count is elevated consistent with meningitis. The baby recovers but remains on the ventilator for 14 days after the sepsis episode.

Question: Could earlier detection of sepsis have led to improved outcomes for this patient (less time on the ventilator, less time in the hospital, or better neurodevelopmental outcome?)

Case#2: Baby B, a 25 week preterm infant, was stable on nasal CPAP and advancing enteral feeds. He has a history of mild feeding intolerance and apnea of prematurity. On day 13, he has a gastric residual of 6 ml (typical residuals had been up to 4 ml) and 8 episodes of apnea (typical apnea frequency had been 6/day). He looks well but CBC reveals a mild bandemia so he has a full sepsis workup and antibiotics are started. All cultures are negative but he receives 7 days of antibiotics for “clinical sepsis”.

Question: Could additional clinical data have reassured clinicians that this baby was not septic and reduced duration of antibiotic exposure?

These common scenarios and the resulting clinical questions led our group to develop and test use of continuous heart rate characteristics monitoring as an “early warning system” for neonatal sepsis. This research was born out of the observation by clinicians in multiple specialties that poor heart rate variability is pathologic and associated with bad outcomes. Obstetricians, for example, have long relied on recordings of heart rate to assess fetal well-being. A “non-reassuring” fetal heart rate tracing consisting of poor beat-to-beat variability and transient heart rate decelerations generally indicates diminished blood supply to the fetus, prompting clinicians to intervene to improve fetal well-being or expedite delivery (Ferrario et al., 2009). In adults with chronic illness such as congestive heart failure (Bilchick et al., 2002), diabetes (Gonzalez-Clemente et al., 2007), or renal failure (Cashion, Cowan, Milstead, Gaber, & Hathaway, 2000), decreased heart rate variability is associated with increased morbidity and mortality. Sepsis is associated with abnormal heart rate variability across the age spectrum (Ahmad et al., 2009; Chen & Kuo, 2007; Garrard, Kontoyannis, & Piepoli, 1993; Griffin & Moorman, 2001; Griffin et al., 2003; Moorman, Lake, & Griffin, 2006).

The challenge was to determine how to quantitate heart rate characteristics as they relate to neonatal sepsis and how to make this information available and useful to clinicians caring for high-risk NICU patients. To this end, hundreds of NICU patients were monitored to derive a mathematical calculation of a “heart rate characteristics index” (HRCi) which predicts clinical or blood culture-proven sepsis within the next day (Moorman et al., 2006). This research led to a commercially available device approved by the United States Food and Drug Administration for HRC monitoring that is currently in use in NICUs in the United States (HeRO™ or Heart Rate Observation Monitor, Medical Predictive Science Corporation, Charlottesville, Virginia, USA, www.MPSC.biz).

The impact of continuous non-invasive heart rate characteristics monitoring on short-term outcomes was studied in a multicenter randomized clinical trial in 3003 very low birthweight infants in 9 NICUs. The trial was completed in 2010 and...
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