

Fetal reactivity assessment during intrapartum stress by analysis of the fetal ECG signal

Akademisk avhandling

som för avläggandet av medicine doktorsexamen vid Sahlgrenska akademien vid Göteborgs universitet kommer att offentligen försvaras i hörsal Arvid Carlsson, Medicinaregatan 3, Göteborg, onsdagen den 15 juni 2011 kl. 13.00

av Sofia Blad

Fakultetsopponent: Professor Göran Lingman
Avdelningen för obstetrik och gynekologi, Skånes universitetssjukhus, Lund

Avhandlingen baseras på följande delarbeten:

- I. Blad S, Larsson D, Outram N, and Rosén KG. **Assessment of fetal reactivity biopatterns during labour by fetal ECG analysis.** *International Joint Conference on Neural Networks*, 2009. p347 – 352.
- II. Blad S, Outram N, Larsson D, Norén H, Sävman K, Mallard C and Rosén KG. **Assessment of fetal heart rate variability and reactivity during labour - a novel approach.** *In manuscript.*
- III. Blad S, Outram N, Larsson D, Norén H, Sävman K, Mallard C and Rosén KG. **Alterations in fetal heart rate variability as a measure of fetal reactivity in connection with metabolic acidosis and spontaneous vaginal delivery.** *In manuscript.*
- IV. Blad S, Welin A-K, Kjellmer I, Rosén KG and Mallard C. **ECG and heart rate variability changes in preterm and near-term fetal lamb following LPS exposure.** *Reproductive Sciences*, 2008 Jul; 15(6): 572-83.

Göteborg 2011



UNIVERSITY OF GOTHENBURG

Fetal reactivity assessment during intrapartum stress by analysis of the fetal ECG signal

Sofia Blad

Perinatal Center, Institute of Neuroscience and Physiology, University of Gothenburg, Sweden, 2011

Abstract

Fetal responses to the stress of labour and delivery are constituted by a combination of changes in neuronal, hormonal and organ based reactions. The aim of electronic fetal monitoring is to identify fetuses at risk of hypoxia during birth, thus enabling timely intervention to avoid an adverse outcome. Visual assessment of fetal heart rate (FHR) patterns is associated with substantial variation in interpretation and there is data to demonstrate the benefits of computer support decision tools. Therefore, the aims of this project were to validate computer-based methods with enhanced data analysis to monitor fetal reactivity, using alterations in RR intervals and ST waveform of the fetal ECG as signs of autonomic nervous system and myocardial metabolic reactivity changes associated with intrapartum stress. A new mathematical model was used for quantifying FHR variability (FHRV). A polynomial function was applied to a sequence of real RR data, producing an RR trend. The difference between the RR trend and the actual beat-to-beat interval at every heartbeat was calculated and a Residual value was obtained. The closer to zero the lesser the FHRV was. In the thesis, the parameters were set to allow for baseline FHR shifts. These Residual features were then tested for their ability to identify four index cases with loss of reactivity in connection with adverse outcome. The parameter settings required to identify the index cases were then tested for accuracy in a large EU database of > 7800 deliveries. The analysis showed that 2.3% of these deliveries revealed non-reactive FHR features associated with an increased risk of neonatal care. Only one of 59 cases with metabolic acidosis showed consistently reduced FHRV. In a subsequent case-controlled study of spontaneous vaginal deliveries we demonstrated that active pushing was associated with a FHRV rise in 100% of deliveries with metabolic acidosis as compared to 89% of the cases without metabolic acidosis. Metabolic acidosis was also associated with a significantly more pronounced rise in FHRV and in cases with more severe acidosis the rise was followed by a decrease in FHRV. A combined FHRV and T/QRS rise occurred in 88% of the metabolic acidosis cases as compared to 5% of controls ($p < 0.001$). The FHRV and ST parameters were also validated experimentally in an animal model of intrauterine inflammation in fetal lambs. These data showed that baseline FHRV increased with increasing maturity, while inflammation caused fetal demise particularly in preterm fetal lambs, which was associated with an increase in FHRV in connection with ST waveform depression and negative T waves. In summary, settings obtained in index cases with loss of reactivity and adverse outcome indicated increased risk of neonatal care, but could not be used to identify fetuses with metabolic acidosis *per se*. Instead, the initial pattern of reaction to develop metabolic acidosis in normal vaginal delivery was a substantial increase in FHRV followed by a decrease as the acidosis progressed. The Residual method may in the future help to identify fetuses at risk and provide additional support in decisions to intervene.

Keywords: FHR variability, fetal ECG, Asphyxia, Intrauterine infection, Residual method, STAN
ISBN: 978-91-628-8310-2