Universität Basel

Research Project

Predictive value of heart rate variability on cardiorespiratory events of preterm infants routinely immunised in the hospital

Third-party funded project

Project title Predictive value of heart rate variability on cardiorespiratory events of preterm infants routinely immunised in the hospital
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Preterm birth is a major challenge of health care systems across the globe, affecting about 10% of all infants born worldwide, resulting in almost 13 million preterm births per year. The autonomic nervous system of preterm infants is characterized by instability of heart rate and breathing, requiring continuous monitoring of vital signs over several months and long-term respiratory support. Cardiorespiratory events due to this instability, summarised under the term 'apnoea of prematurity' (AOP), affect at least 80% of very preterm infants born before 32 weeks of gestation. AOP may lead to severe hypoxaemia requiring immediate resuscitation and recent data show that repetitive episodes of AOP increase the risk of post-discharge death and long-term neurodevelopmental impairment. Most importantly, severity and frequency of AOP may drastically increase upon challenging the autonomic system by routine immunisation. It is, however, very important to provide timely immunisation and establish early immunity against typical vaccine-preventable diseases in preterm infants as they are particularly vulnerable to complications arising from those diseases. Current recommendations are to initially immunise preterm infants in the hospital under continuous monitoring of vital signs if the treating physician considers an infant to be at risk of post-immunisation AOP. However, there are no objective criteria to predict post-immunisation AOP. Although the first immunisation of very preterm infants typically takes place in the hospital under continuous monitoring of vital signs, immunisations of infants at risk of AOP are often delayed due to fear of AOP or may be initiated in non-intensive care settings (normal wards) where adequate respiratory support cannot be provided but may be needed due to post-immunisation AOP. Also, due to an international trend of early discharge home of preterm infants, immunisations may be arranged in the rooms of the family paediatrician without further monitoring of vital signs and no specific knowledge of the individual risk of post-immunisation AOP. Thus, developing of new biomarkers and objective criteria to better understand and assess the risk of post-immunisation AOP is urgently needed. We recently developed a systematic quality control algorithm for assessing heart rate variability data in a standardised manner and demonstrated that the sample entropy (SampEn) of interbeat intervals, a parameter of heart rate variability derived from nonlinear time series analysis, predicts cardiorespiratory stability in preterm infants. SampEn reflects the regularity of heart rate and the presence of spikes in a given time series of heart beats and has been validated to be a reliable predictor of incipient events such as sepsis. SampEn of heart rate can be obtained non-invasively from electrocardiogram monitors, which are routinely used to monitor preterm infants immunised in the hospital. We aim to evaluate whether real-time calculation of SampEn at a) 32 and 36 weeks corrected age, b) upon primary routine immunisation in the hospital, c) at discharge from the hospital after initial prematurity-related hospital stay, and d) on readmission for

immunisation in the hospital based on previous post-immunisation AOP or referral of the family paediatrician has prognostic utility for the risk of post-immunisation AOP in very preterm infants. We will further assess whether immunisation itself initiates a step response in SampEn and compare SampEn values from preterm infants to those of term healthy infants to study maturational effects. The biomarker SampEn provides a unique opportunity to objectively prognosticate autonomic stability with the goal of optimising risk stratification and establishing timely immunisation in preterm infants. Such real-time display of SampEn thus could become a valuable tool to better understand autonomic regulation in preterm infants and guide physicians in providing an optimal level of care for immunisation based on personalised risk assessment in order to provide an adequate setting and staffing. This approach combines both novel scientific aspects on prognostic value of nonlinear time series analysis and pragmatic utility of SampEn for decision-making on within hospital risk-stratification and necessity of readmission for immunisation.

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