Heart rate variability in low birth weight growth restricted children during sleep and wake stages

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ABSTRACT

Intrauterine growth restricted (IUGR) individuals have greater predisposition to develop a metabolic syndrome in later life manifesting itself as obesity, hypertension, type 2 diabetes or cardiovascular disease. Poor fetal growth may alter the regularity mechanism of cardiac autonomic system that is involved in the development of these diseases. The malfunctioning of the cardiac autonomic system assessed by decrease in heart rate variability (HRV) is associated with negative cardiovascular outcomes. This study is aimed at investigating the risk of development of coronary heart disease in IUGR children in later life. For that purpose HRV analysis of normal and growth restricted children was performed during sleep and wake stages. The study group consisted of 9–10 years old, 32 normal, 20 low birth weight IUGR children. The standard time domain HRV metrics (mean RR, SDNN, RMSSD, NN50 and pNN50) and Poincaré indices (SD_1 and SD_2) were used to analyse and compare the RR-interval time series of these groups. The IUGR children showed lower HRV as compared with normal children during both sleep and wake stages. The significantly decreased HRV during sleep provide an evidence of autonomic derangement that may be associated with higher risk of lethal arrhythmias in the IUGR children in later life.

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1. Introduction

Intrauterine growth restriction is the failure of the fetus to achieve his/her essential growth potential due to anatomical and/or functional disorders of the feto–placental–maternal unit [8]. The growth restricted fetus often has an estimated fetal weight less than the 10th percentile for its gestational age. The incidence of IUGR is estimated to be approximately 5–7% [6]. Recent research evidences suggested that several later life diseases including hyper-

tension, type 2 diabetes and coronary artery disease are initiated by adverse fetal growth and development [4,7,18].

Studies in animals have shown that adverse fetal growth programmes persisting changes in a range of metabolic, physiological and structural parameters [27]. An increased rate of coronary heart disease has been found in men and women who had low birth weight, who were short or thin at birth or who were small as compared with placental size [4]. The correlation between cardiovascular disease and low birth weight has been replicated among both males and females in Europe, North America and India [5,23]. The link of low birth weight to coronary heart disease in men has been verified in Helsinki [18]. In a number of studies, low birth weight has been shown to predict

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altered glucose tolerance [19]. Andersen and co-workers explored combined association of birth weight and childhood body mass index (BMI) at the age of seven with risk of coronary heart disease in adult life [2]. They found that both birth weight and BMI at the age of seven were independently associated with the risk of coronary heart disease.

The malfunctioning of the autonomic nervous system and its relation with cardiovascular mortality has been widely investigated during the last two decades [1,29,30]. In our previous study, we found reduced heart rate variability in low birth weight IUGR children with birth weight <2.5 kg as compared to normal and IUGR children having birth weight ⩾2.5 kg [3]. The reduced HRV in low birth weight IUGR may be associated with negative outcome of the cardiovascular system. This study is aimed to examine the cardiac autonomic activity of 9–10 years old normal and intrauterine growth restricted children by analysing the HRV during sleep and wake periods. The investigations showed a decrease in HRV for low birth weight IUGR children during both sleep and wake stages, however, most of the HRV parameters showed significant difference between the normal vs. low birth weight IUGR children during sleep stage.

2. Materials and methods

2.1. Data sets

This study is a collaborative research work of Child Health Department of The Leicester Royal infirmary and the Bio-Engineering group of the Department of Engineering, University of Leicester, to investigate the effect of intrauterine growth restriction (IUGR) on postnatal developmental physiology. In the original study, the researchers from Royal Infirmary Leicester UK developed a database of

69 IUGR and 127 normal children without IUGR for investigating the development of circadian rhythm in deep body temperature, heart rate and cortisol excretion [15,16]. The IUGR infants were identified either by serial ultrasound or by birth weight [14–16]. The infants whose serial abdominal girth was more than two standard deviations or birth weight below the 2nd centile were considered IUGR.

After complete medical examination, the 24 h ECG of IUGR and normal children were recorded with a Lifecard CF ambulatory ECG recorder (Delmar-Reynolds Medical Limited, Hertford, UK). The children were advised to perform normal daily routines during recording and parents were asked to keep a diary of all activities including sleep and wake timings, which were subsequently collected from them. The recordings of less than 23 h, with more than 1% of ectopic beats or with presence of heart block were excluded from the study. The ECG recording of all subjects were extracted by Pathfinder 700 series analysis system and examined for artefacts. Thirty-two normal and 36 growth restricted children participated in the current study.

The normal group comprised of 32 children (20 male and 12 female), current age 8.96 ± 0.72 years (mean ± standard deviation), birth weight 3.56 ± 0.45 kg, current weight 32.87 ± 6.13 kg, weight gain 32.87 ± 6.13 kg, current height 133.86 ± 0.86 cm and current BMI 18.21 ± 2.52 kg/m². The IUGR children having birth weight <2.5 kg ([33,11]) were included the study. The choice was motivated by the fact that birth weight is inversely related to hypertension, pulse rate and hence the risk of cardiovascular disease in adulthood. The low birth weight (LBW) IUGR group comprised of 20 children, 8 male and 12 female having birth weight 2.29 ± 0.19 kg, current weight 28.13 ± 4.74 kg, weight gain 25.83 ± 4.75, current height 131.00 ± 5.84 cm and BMI 16.38 ± 2.55 kg/m². Using the heartbeat interval time series of normal, In our study cohort, there was more
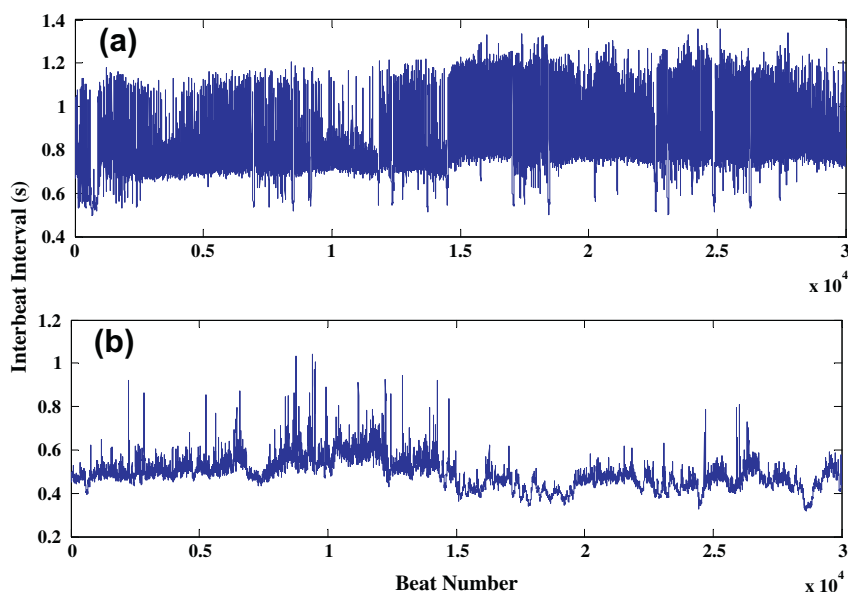

Fig. 1. The representative interbeat interval time series of normal child. (a) Sleeping period. (b) Waking period.