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QT dynamicity, microvolt T-wave alternans, and heart rate variability during 24-hour ambulatory electrocardiogram monitoring in the healthy newborn of first to fourth day of life

Leonid Makarov,[a,*] Vera Komoliatova,[a] Svetlana Zevald,[b] George Schmidt,[c] Alexander Muller,[c] Victor Serebruany[d]

[a]*Center for Syncope and Cardiac Arrhythmias in Children and Adolescents of the Federal Medical-biological Agency of Russia, Children's Clinical Hospital No. 38 of FMBA of Russia, Moscow, Russia*
[b]*Maternity Hospital No. 15 of Moscow Healthcare Department, Moscow, Russia*
[c]*Department of Noninvasive Electrophysiology of the Centre of Heart Diseases, Technological University, Munich, Germany*
[d]*Johns Hopkins University Baltimore, Maryland, USA*

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Abstract

Background: Twenty-four hour ambulatory electrocardiogram (AECG) monitoring is an established technique for integrated assessment of heart rhythm; however, comprehensive description of serial changes in cardiac electrophysiology over the first days of life in humans is lacking. The aim of this study was to determine the patterns of circadian heart rhythm based on AECG evaluation in newborns.
Methods: Twenty healthy newborns (14 boys and 6 girls) were serially examined with AECG at days 1, 2, and 4 after birth. Heart rate (HR), arrhythmias, QT dynamicity, microvolt T-wave alternans, and various indices of HR variability (HRV) including deceleration/acceleration capacity analysis were analyzed.
Results: There were no sex differences in HR. Supraventricular premature beats were noted in 35%, ventricular—in 15 % of newborns. Slope QT/RR was 0.35 (0.3-0.5); intercept QT/RR was 124 (93-148), QT/RR correlation coefficient (r) was 0.63 (0.53-0.85). Peak value of T-wave alternans was 32 ± 8 (12-55) μV. Low level of HRV was typical for all parameters of time-domain analysis compared with normal limits for older children. The overall mean values of deceleration/acceleration capacity were 3.38 ± 0.57 (2.16-4.13) and −3.58 ± 0.67 (−2.13 to −4.38) milliseconds, respectively.
Conclusion: The healthy newborns exhibit peculiarities of 24-hour cardiac rhythm with isolated premature beats, pauses of sinus rhythm less 1000 milliseconds, steep slope of QT/RR by analysis of QT dynamicity. There are low HRV, and symmetrical AC/DC capacity was typically for autonomic regulation of HR, probably due to high sympathetic activity at this age.

Keywords: Heart rhythm; Newborn; Holter monitoring

Introduction

The risk for development of life-threatening conditions in childhood is the highest among the newborns. Regardless of the underlying disease, sudden cardiac death represents a major threat for infants in general and newborns in particular. According to the US National Cardiopulmonary Resuscitation Registry, the prevalence of hospital cardiac arrest in children with noncardiac pathology is more than doubled (46% versus 18% of cases),[1] suggesting the unmet need to evaluate the risk of the development of heart rhythm (HR) abnormalities in sick children independently of whether a cardiac defect is suspected. Ventricular arrhythmias occurring during the perinatal or neonatal periods are associated with a poor prognosis and a low survival rate.[2-4] The use of 24-hour ambulatory electrocardiogram (AECG) monitoring can be very helpful in assessment of patients with suspected cardiac arrhythmias. Ambulatory ECG date enables inte-

* Corresponding author. Center for Syncope and Cardiac Arrhythmias in Children and Adolescents of the Federal Medical-biological Agency of Russia, Children's Clinical Hospital No. 38 of FMBA of Russia, Moscow, 115409 Russia.
E-mail address: leonidmakarov@yahoo.com

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grated evaluation of arrhythmias, heart rhythm parameters as well as features of autonomous nervous regulation, and signs of electrical instability of the myocardium.[5,6] Guidelines for prevention of sudden cardiac death recommend assessment of QT interval changes, T-wave alternans,[7] and heart rate (HR) turbulence[8] by ambulatory ECG[9] as the first class of indication for the risk stratification of cardiac death. Also, a new method (deceleration/acceleration capacity, or AC/DC) of HR for stratification of cardiac risk was proposed recently in adult patients.[10]

However, serial data on the dynamics of circadian cardiac rhythm in children and especially in newborns are almost entirely lacking. The cornerstone of AECG analysis in pediatric population is a precise knowledge of the normal range of analyzed parameters according to sex and age. Therefore, the objective of our study was to determine normal limits of the circadian rhythm and new noninvasive criteria of electrical stability of the heart, based on AECG data in children during the first 4 days of life.

Methods

Patients

The current study was approved by the Ethics Committee of the Maternity Hospital #15 and Pediatric Clinical Hospital #38 FMBA of Russia (Moscow, Russia). The study was performed in accordance with the revised Helsinki Declaration (World Medical Association, 2000) and the requirements of Good Clinical Practice International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH Guideline, 1996). Written informed consent was obtained from all mothers who were aware of the study protocol and strict compliance rules during feeding and nursing. Twenty apparently healthy newborn (14 boys and 6 girls) were examined at days 1, 2, and 4 after birth. The following inclusion criteria applied: normal pregnancy and delivery, healthy mother aged 18 to 28 years, gestational age of a baby at birth 38 to 40 weeks; body mass at birth 2700 or more grams, Apgar score of 8 or higher, absence of cardiovascular pathology at physical examination, and 12-lead ECG at rest. Investigators were blinded to the data, and laboratory personnel were unaware of child identity, or on which day of life the study occurred.

AECG monitoring

All participants underwent 24-hour AECG performed using digital recorders Seer MC (GE Medical Systems, Milwaukee, WI, USA) in 3 modified chest leads (V_2, V_5, aVF) at days 1 and 2 and finally at day 4 after birth. The sampling rate was 128 Hz. Analysis of the AECG date was performed with software Mars PC version 7.5 (GE Medical Systems). Nurses and mothers received detailed instructions regarding the length of wearing the recorder (24 hours) and how to keep a diary of the activities and symptoms during the test, as well as personal care/activity instructions. Cardiac rhythm abnormalities were captured and analyzed according to internationally established criteria for children.[11,12] Heart rate in beats/min, minimal HR during AECG (automated measurement from 5 RR intervals), circadian index as relation of mean HR at wake time to mean HR at sleep time, cardiac rhythm abnormalities, HR variability (HRV) by time-domain method were investigated, and the following parameters were obtained: mean-average of all normal sinus RR intervals, SD of all normal sinus RR intervals (SDNN), SD of the averaged normal sinus RR intervals for all 5-minute segments, means of the SDs of all normal sinus RR intervals for all 5-minute segments (SDNN index), root-mean-square of successive normal sinus RR interval difference (rMSSD), and finally the percentage of successive normal sinus RR intervals more than 50 milliseconds (pNN50).

Analysis of QT interval included manual measurement with evaluation of QT interval at minimal HR, an automated analysis with an evaluation of the longest QT, and estimation of the average daily corrected QT (QTc), calculated according the formulas of Bazett ($QTc = QT/\sqrt{RR^2}$) and Fridericia ($QTc = QT/\sqrt{RR^3}$), QT interval, QTpeak (QTp) interval, measured from the beginning of Q wave to the top of T wave, and corrected by Bazett formula QTp (QTpc) interval. Automatically, QT analysis was done in the lead with the beast-define T wave by threshold method. QT measurements were performed under continuous visual control with the possibility of manual editing. Editing was done in the beginning of the tape to ensure that the cursor measuring the end of the QT interval was placed in the opinion of the observer; if, for some reason, the cursor floated, it was readjusted; if this was not successful, then the beat was deleted. Rate-dependent QT interval parameters ("QT dynamicity") were measured by calculation of formula of linear regression for the definition of slope QT/RR, intercept QT/RR, and correlation between QT and RR intervals (*r* QT/RR). Detailed description of mathematical values and clinical evaluation of these parameters are outlined in detail somewhere else.[13-15] Assessment of microvolt T-wave alternans (TWA) were performed by Modified Moving Average (MMA) algorithm (time-domain TWA method) that was elaborated by Verrier for AECG monitoring.[8] Also, HR was analyzed by using new method "deceleration-acceleration capacity" (DC/AC), evaluating the ability of the heart rhythm to become slower (deceleration capacity, or DC) and faster AC. These markers were shown to be valuable predictors of sudden cardiac death in patients after myocardial infarction.[10] Deceleration-acceleration capacity parameters were calculated in the Department of Noninvasive Electrophysiology of the Centre of Heart Diseases, Technological University (Munich, Germany).

Statistics

To control for any baseline differences, analysis of variance was used. The significance of differences between different time points was calculated by Fisher exact tests for discrete variables and Wilcoxon rank-sum test for continuous variables. Normally distributed data were expressed as mean ± SD (mean ± SD) and 5‰ to 95‰. All *P* values were 2 sided. Statistical analyses were performed using SPSS/E11.5 (SPSS, Inc, Chicago, IL).