CLINICAL STUDY

Heart rate variability changes in children after cardiac transplantation

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Abstract

Background: **Heart rate variability analysis is a modern, non-invasive, precise and sensitive method of the assessment of cardiovascular systemic functions.**
Objectives: **Find out changes in parameters of time-domain analysis of heart rate variability (HRV) in children after cardiac transplantation.**
Methods: **Twenty-two subjects were enrolled and examined in this study – 2 subjects after cardiac transplantation (14 and 5 years of age) and 2 control groups of healthy subjects (10 subjects at age from 14 to 16 and 10 subjects at age from 5 to 7 y). Five parameters of HRV from 24-hour Holter monitoring have been analysed (NN intervals, SD, pNN50, rMSSD, triangular index). GiOtto ECG Holter monitor (Medatron) was used in each child.**
Time domain analysis parameters have been controlled and compared by using percentile range obtained from healthy individuals (P_{10}-P_{90}).
Results: **rMSSD, pNN50, triangular index were below 10th percentile in a 14-year-old girl. rMSSD, SD were below the 10th percentile in a 5-year-old boy.**
Conclusion: **Total heart rate variability (described by triangular index and SD parameter) and parameters describing parasympathetic activity (pNN50 and rMSSD) were decreased in both patients after cardiac transplantation. Considering the still unclear mechanism of heart innervation, it is necessary to continue in the research. Authors are planning to check the changes in the future also by means of frequency analysis of heart rate variability.** ***(Tab. 3, Ref. 22.)***
Key words: cardiac transplantation, heart rate variability, autonomic nervous system.

Human heart rate keeps changing in time in order to compensate biological needs of organism. This activity is referred to as heart rate variability (HRV) and is the result of the impacts of various factors – breathing, blood pressure changes, thermoregulation as well as central nervous system involvement. HRV analysis is a modern, non-invasive, precise and sensitive method of the assessment of cardiovascular systemic functions. Heart rate variability can be evaluated by two different methods – linear and progressing non-linear analysis (9).

The cardiac transplantation brings about a complete interruption of afferent and efferent sympathetic and parasympathetic nerve fibers, followed by axonal degeneration due to the discontinuity of nerve axon and body of nerve cell. Sinoatrial node – heart pacemaker – is totally denervated, the fact of which leads to changes in neurohumoral regulatory mechanisms. Due to the lack of extracardial stimuli, heart activity is influenced by intracardial stimuli – local regulatory mechanisms. Resting heart rate, not being influenced by external stimuli such as physical activity, postural changes, rises. This results in a decrease in heart rate variability (16, 20). Decreased heart rate variability was found in patients with diabetes mellitus (8) or juvenile hypertension (14). Decreased heart rate variability is a risk factor of cardiovascular diseases, arrhythmias, myocardial infarction or sudden death (10, 12).

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Tab. 1. Time domain analysis of heart rate variability in group of healthy children (age of 5–7 y).

	pNN50 (%)	rMSSD (ms)	NN intervals	SD (ms)	Triangular index
X	21	73	122324	158	34
SD	15	33	17617	48	9.8
SE	5,3	11	6228	17	3.4
p_{10}	3	29	87462	102	17
p_{25}	7	43	114462	123	29
p_{50}	20	73	128194	147	34
p_{75}	35	106	134190	189	41
p_{90}	39	112	137316	226	45

Values of mean (x), standard deviation (SD), standard error of mean (SE) and percentile range (P_{10}–P_{90}) of time domain analysis parameters of HRV (pNN50, rMSSD, NN intervals, SD, triangular index) in group of healthy children (age of 5–7 y).

Tab. 2. Time domain analysis of heart rate variability in group of healthy children (age of 14–16 y).

	pNN50 (%)	rMSSD (ms)	NN intervals	SD (ms)	Triangular index
X	33	95	93177	188	46
SD	4.6	32	9006	36	7.2
SE	1.5	10	3022	12	2.4
p_{10}	23	41	77313	110	32
p_{25}	32	84	88760	181	45
p_{50}	35	92	99662	188	46
p_{75}	36	102	98162	202	50
p_{90}	37	141	104487	231	54

Values of mean (x), standard deviation (SD), standard error of mean (SE) and percentile range (P_{10}–P_{90}) of time analysis parameters of HRV (pNN50, rMSSD, NN intervals, SD, triangular index) in group of healthy children (age of 14–16 y).

The aim of study was to find out changes in parameters of time domain analysis of heart rate variability (HRV) in children after cardiac transplantation.

Methods

Twenty-two subjects were enrolled and examined in this study – 2 subjects after cardiac transplantation (14 and 5 years of age) and 2 control groups of healthy subjects (10 subjects at age from 14 to 16 y and 10 subjects at age from 5 to 7 y). GiOtto ECG Holter monitor (Medatron) was used for 24-hour Holter monitoring.

Five parameters of HRV from 24-hour Holter monitoring have been analyzed: NN intervals (all intervals between adjacent QRS complexes resulting from sinus node depolarizations), SD (standard deviation of all NN intervals), pNN50 (NN50 count divided by the total number of all NN intervals), rMSSD (the square root of the mean of the sum of the squares of differences between adjacent NN intervals), triangular index (total number of all NN intervals divided by the height of the histogram of all NN intervals measured on a discrete scale with bins of 1/128 s). Time analysis parameters have been controlled and compared by using percentile range obtained from healthy individuals (P_{10}-P_{90}).

Results

Time domain analysis parameters in healthy individuals and individuals after transplantation are shown in tables as mean, standard deviation, standard error of mean and percentile range of values (Tabs 1, 2, 3).

Parameters – rMSSD, pNN50, and triangular index were below 10th percentile in a 15-year-old girl. Parameters – rMSSD, SD were below 10th percentile in a 5-year-old boy.

Discussion

First cardiac transplantation in child was performed in 1968, whereas nowadays about 300–350 transplantations are performed in children worldwide every year. 5-year survival after cardiac transplantation occurs in about 70–80 % of patients (3). Cardiac transplantation is a therapeutic method in the final stage of heart failure that is resistant to medicament treatment or in cases, where no other treatment option exists. The most frequently used methods are bicaval or biatrial anastomoses. The immunosuppressive treatment is part of post-operative management. Most frequent complications are rejection, infectious diseases, side effects of medication (hypertension, malignancies and nephrotoxicity).

Tab. 3. Time domain analysis of heart rate variability in children after cardiac transplantation.

	pNN50 (%)	rMSSD (ms)	NN intervals	SD (ms)	Triangular index
Patient 1	5	27	117502	96	18
Patient 2	7	30	111684	128	26

Values of time domain analysis parameters of HRV (pNN50, rMSSD, NN intervals, SD, triangular index) in children after cardiac transplantation. Patient 1–5 year old, patient 2–14 year old.

Most of studies correspond with the fact that an increase in norepinephrine sensitivity is the first step in heart reinnervation (11), followed by sympathetic (4, 15) and later by parasympathetic reinnervation (22), but the level and type of reinnervation varies in each individual. We can monitor and analyse changes in all components of autonomic nervous system by using the analysis of heart rate variability.

Our aim was to perform a time analysis of changes in heart rate variability in two children after cardiac transplantation. Percentile range, where values below 16th or above 84th percentile were considered as extreme (2), has been used for the comparison of the control group with examined subjects. This was applied due to the small group of patients enrolled. The percentile range method is often used in pediatrics e.g. in growth or hypertension analyses (18). The understanding of physiological mechanisms influencing the selected parameters is crucial. According

to Task Force of European Society of Cardiology and The Society of Pacing and Electrophysiology (19), such parameters as rMSSD and pNN50 correlate with the high-frequency band of heart rate variability analysis. This is mostly the effect of respiratory sinus arrhythmia (and that of parasympathetic activity), whereas triangular index and SDNN correlate with total spectral component – marker of total heart rate variability. Many other authors share the same conclusions (6, 13).

In our study, rMSSD was below 10th percentile in both patients (pNN50 also in the 14-year-old patient), thus we could expect a decreased parasympathetic control of heart in both children. Many studies describe an increase in parameters of heart rate variability after cardiac transplantation, and this reflects the dominancy of the parasympathetic component (22). On the other hand, there are studies describing no effect of parasympathetic activity on heart rate variability (5, 11). Other authors describe changes after transplantation leading also to a decrease in heart rate variability (16, 20). This corresponds with our results namely that the parameters describing total heart rate variability (triangular index and SD) are decreased in both patients.

Heart rate variability is affected also by physiological factors such as age and sex (21). When analysing HRV after cardiac transplantation we have to consider also the technique of transplantation, time since transplantation and posttranplantation complications, including the drugs. The latter facts were described in works of Bernardi et al (1998), Halpert et al (1996), Uberfuhr et al (1997), Izrailtyan et al (2000) (1, 5, 22, 7) and others.

By means of 24-hour Holter monitoring record, we detected decreased heart rate variability in patients after cardiac transplantation. Considering the still unclear mechanism of heart innervation, it is necessary to continue in the research. We are planning to check the changes in the future also by means of frequency analysis of heart rate variability.

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