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## HEART RATE VARIABILITY IN CHILDREN WITH SUPRAVENTRICULAR ARRHYTHMIAS

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### SUMMARY

#### HEART RATE VARIABILITY IN CHILDREN WITH SUPRAVENTRICULAR ARRHYTHMIAS

**Key words:** bisoprolol, heart rate variability, supraventricular arrhythmias.

The following research was made upon 50 children, age between 7 and 18 years, with supraventricular arrhythmias: the first group includes 30 children (average age  $12,93 \pm 0,52$  years) that have been administered bisoprolol with the average dose 1,25-2,5/mg/24 h and the second group, (average age  $13,55 \pm 0,60$  years) that received placebo.

The research results revealed that the arrhythmias has been associated with different symptoms as cardiac pains (90%) and palpitation (88%). The action of bisoprolol on the parameters of heart rate variability has been established by the decreased value of the statistics and spectral indexes that show the activity of the sympathetic vegetative nervous system. The bisoprolol can be recommended to children with symptomatic supraventricular premature beats while being a cardioselective drug with a high selectivity index (1:75).

### REZUMAT

#### VARIABILITATEA RITMULUI CARDIAC LA COPII CU ARITMII SUPRAVENTRICULARE

**Cuvinte-cheie:** bisoprolol, variabilitatea ritmului cardiac, aritmii supraventriculare.

Studiul a fost efectuat pe un lot de 50 de copii, cu vârsta cuprinsă între 7 și 18 ani, cu aritmii supraventriculare: lotul I, de bază a inclus 30 copii (vârsta medie  $12,93 \pm 0,52$  ani), cărora li s-a administrat bisoprolol în doza uzuală 1,25-2,5/mg/24 ore, și lotul II, martor – 20 de copii, (vârsta medie  $13,55 \pm 0,60$  ani), care au primit placebo.

Rezultatele studiului au relevat asocierea aritmiilor supraventriculare cu diverse simptome clinice cu predominarea durerilor precordiale (90%) și a palpațiilor (88%). Acțiunea bisoprololului asupra parametrilor variabilității ritmului cardiac s-a exprimat prin micșorarea indicilor statistici și spectrali caracteristici pentru activitatea sistemului nervos vegetativ simpatic. Bisoprololul poate fi recomandat în schema de tratament la copii cu aritmii supraventriculare, fiind un preparat cardioselectiv cu indicele de selectivitate înalt (1:75).

#### **Introduction.**

Supraventricular arrhythmias are common and patients are often symptomatic requiring management with drugs and electrophysiological procedures. The heart rate variability represents the measure of variation between two heart beats, that is being estimated by QRS complexes, ECG Holter evaluated in 24h by monitoring[1].

There are two methods of heart rate variability analysis: time domain analysis and frequency domain analysis, with the same importance [1, 2].

The time domain analysis is determined by measuring two normal successive QRS complexes and than calculating the average heart frequency, the difference between the shortest and the longest NN sequence, difference between night and day heart frequency.

The analysis frequency domain offers information about distribution of frequency function power. Spectrum

appreciation of RR variability sequence makes possible a qualitative evaluation of vagus impulse influence on heart rate, showing the activity of sympathetic nervous system [2]. Spectrum analysis allows us to evaluate the vegetative modulation of the heart beat. This can be achieved by a fast transform Fourier in order to separate RR sequence into frequency bands.

**Aim of study:** evaluation of selective beta-blocker (bisoprolol) on parameters of heart rate variability in children with supraventricular arrhythmias.

**Materials and methods:** the research was done upon 50 children, age between 7 and 18 years, with the following complains: heart pain, palpitation, irregular heart beat, fatigue, vegetative disturbances (sweating, cold extremities, anxiety, excitability).

The criterias of treatment where the following: sympathetic tonus and hypersympatic vegetative reactivity, supraventricular extrasistoly and ventricular on Holter ECG 24 h monitoring. Two research groups have been formed: I group of 30 children (average age  $12,93 \pm 0,52$  years) that have been administrated bisoprolol in usual dosage of 1,25-2,5/mg/24 h and II reasearch group, (average age  $13,55 \pm 0,60$  year) that received placebo. The patients have undergone a primary exam at 1 month and than 3 months. Primary and secondary visit included anamnesis, standart clinical exam, ECG, ECOCG with colored Doppler, monitoring Holter ECG 24 h with heart rate variability evaluation and home automatic monitoring of BP in 24 h. The monitoring of patients during the stage of treatment included also the secondary effect evaluation. We can mention that after a month in a patient from the I reasearch group the treatment has been changed by including amiodaron (due to the fact of heart beat disturbances that have appeared and hemodinamic changes), one patient stoped receiving the treatment of an unknown reason and

one patient didn't come at the later visits. In the I research group (children under bisoprolol) after a month 27 children have been evaluated, after 3 months – 27 children. In the placebo group after a month 19 children have been evaluated (one of patients has been taken out due to the lack of compliance), after 3 months – 19 children. So that at the end 46 children have finished the research.

The patients from the research have been divided into three groups according to the age. This way, group I with children between 7-10 years – 11 (22,0%), II group 11-14 years – 16 (32,0%) children and III group patients in late pubertary stage 15-18 years – 23 (46,0%) [Figure 1].

The analysis of children in the research group according to age division determined the prevelage of 15-18 years children in 23 (46,0%) cases, and prevalege in the II group (placebo) of 12 (60,0%) children, with no evident age difference between the groups ( $p > 0,05$ ). The research group with arrhythmias included 30 boys (60,0%) and 20 (40,0%) girls. The sex division revealed some peculiarities (Figure 2).

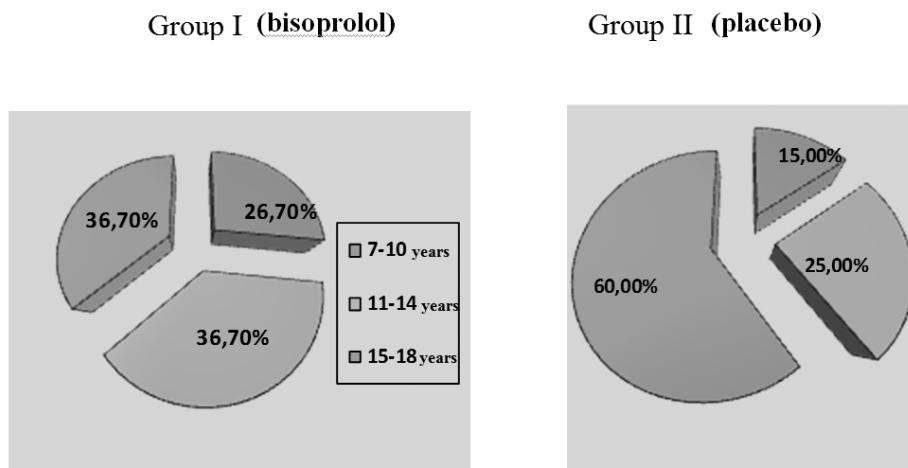


Fig. 1. Group division according to age.

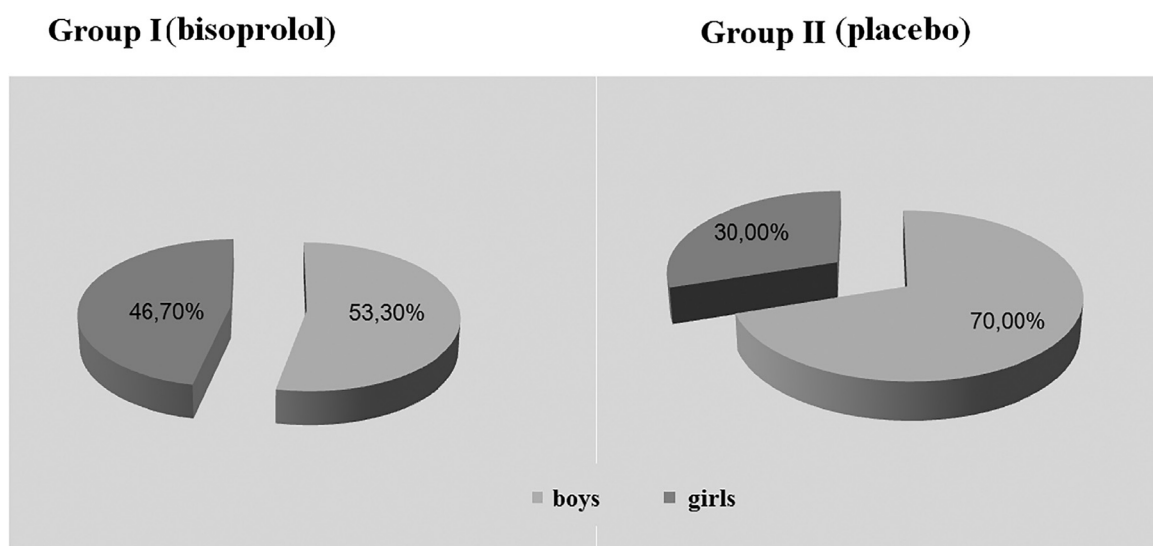


Fig. 2. Division of children by gender.

While analysing the gender of patients we may determine that there were more boys - 16 (53,3%) in the I research group (bisoprolol) and 14 (70,0%) in the II research group (placebo), with small statistic differences ( $p > 0,05$ ). From the start all the children from the research groups with arrhythmias presented heart pains (children with sympathetic tonus and hypersympathic tonus) (90,0%) The pain was of a sharp feature, with the duration of 10-20 minutes, while other factors were associated (emotion, physical effort, hyperventilation, pain without effort) in (80,0%). In 38,0% the pains were without irradiation. Also palpitations were present. So that we have detected palpitations in 88,0% case with a duration of 20-30 minutes in 43,0% cases. Also we have noticed irregularities of heart beat mostly in the morning 37 (74,0%) children.

The heart rate variability (HRV), determines the variation between two heart beats. It has been revealed by analysis of sequent QRS complexes and also by analysing the time domain with statistic parameters appreciation: SDNN = average standart deviation of normal R-R sequences in 24 h and pNN50 = % of neighbour sequences R-R that differ with more than 50 ms, in 24 h. The initial parameters of HRV is shown in the Tabel 1.

initial results from the I group (6,42; 3,87) vs a decrease at patients from the II group (-0,40; -1,28) on placebo ( $p < 0,01$ ;  $p < 0,05$ ).

This way according to the datas of time domain analysis we determined an increase of the statistic parameters in 24 h. After administarting bisoprolol in patients from the I research group PNN50, we were unable to detect decreased average level of statistic SDNN parameters comparing with the initial datas in the I research group. Long term therapy with bisoprolol showed good results upon the activities of the parasympathic vegetative nervous system and decreased activity of the symphatic system in patients with supraventricular arrhythmias [3].

We have completed the research by evaluating the heart beat rate through spectral analysis of vegetative modulation of heart beat by *Fourier* rapid changing of RR sequences in bands of high frequency (HF), low (LF), very low (VLF) and ratio LF/HF.

The spectral analysis of HRV revealed a higher incidence of low frequency (LF) and very low frequency (VLF) bands in patients with arrhythmias that explains the activity of the sympatic nevous system.

Long term therapy with bisoprolol showed better results in a month of average values of low frequency bands (LF) and very low frequency bans (VLF) with an insignificant

**Tabel 1. Statistic parameters dynamics of heart rate variability while long time treatment with bisoprolol**

Parameters		I research group			II research group			P
		N	M	m	N	M	m	
SDNN, Ms	initially	30	156,1	6,98	20	182,75	11,6	>0,05
	1 month	27	155,41	6,93	20	176,15	11,02	>0,05
	3 month	27	152,74	6,71	19	178,84	11,68	>0,05
	$\Delta$ i-1	27	-1,48	3,96	20	-6,60	5,36	>0,05
	$\Delta$ i-3	27	-4,15	5,63	19	-4,89	5,48	>0,05
PNN50, %	initially	30	20,32	2,33	20	27,01	3,0	>0,05
	1 month	27	27,31	2,79	20	26,6	2,95	>0,05
	3 month	27	24,76	2,48	19	26,14	2,98	>0,05
	$\Delta$ i-1	27	6,42**	1,85	20	-0,40	0,67	<0,01
	$\Delta$ i-3	27	3,87	2,44	19	-1,28	0,65	<0,05

Statistic parameters of time domain of HRV (SDNN și PNN 50) appreciated initially in two research groups didn't differ a lot ( $p > 0,05$ ).

The action of bisoprolol after one month and three months upon SDNN parameters, represents the world estimator of HRV shows a decrease that is more evident while comparing with the initial values of children from the II research group (-6,60; -4,89) vs children from the I research group (-1,48; -4,15), the difference between the initial level of SDNN in the research groups was quite discreat ( $p > 0,05$ ).

Evaluation of statistic parameters in real time PNN50 in dynamics after a month and 3 months by treating with bisoprolol showed a growth while comparing with the

decrease in patients of the I research group (-6502,33 ms) vs (-47,43 ms) from the II research group also results of the I group (-66334,41 ms) vs (-2291,71 ms) II group ( $p > 0,05$ ).

Evaluation of average values of spectral parameters (VLF) and (LF) in long term treatment with bisoprolol in 3 months showed an insignificant decrease in I group patients (-43652,07; -6013,42 ms) vs patients from the II group (-3077,73; -71,33 ms) [ $p > 0,05$ ], revealing a decreased activity of the symphatic nervous system in I group patients.

Ratio LF/HF considered as being a parameter of sympathetic- vagal equilibrium, presented decreased average value after a month (-1,34 $\pm$ 0,84) vs (-0,08 $\pm$ 0,11) patients from the II group ( $p > 0,05$ ). After 3 months was

established a decreased average value of LF/HF ratio in children from the I group ( $-0,44 \pm 0,78$ ) vs ( $-0,03 \pm 0,05$ ) children from the II group that represents a balance between sympathetic and parasympathic system.

The data of the spectral analysis allowed to establish an important decrease of average parameters in children with arrhythmias after a month and three. The action of bisoprolol on HRV spectral parameters has been explained by blockage of the  $\beta$  adrenergic receptors that block the action of the sympathetic nervous system and activation of the parasympathic system.

#### Conclusions:

1. The research groups were formed from patients with supraventricular arrhythmias with vegetative sympathetic tonus and hypersympathic reactivity with heart pains 90,0%, palpitations in 88,0% and irregular heart beats in 74,0% cases.
2. The analysis of statistic parameters of heart beat variability in long term treatment with bisoprolol showed a change in results in 1 and 3 months: decreased levels of SDNN ( $-6,60$ ;  $-4,89$ ) in the placebo group vs ( $-1,48$ ;  $-4,15$ ) patients on bisoprolol ( $p > 0,05$ ); increased PNN50 in the bisoprolol group ( $6,42$ ;  $3,87$ )

vs a decreased value in the ( $-0,40$ ;  $-1,28$ ) placebo group ( $p < 0,01$ ;  $p < 0,05$ ).

3. Spectral parameters appreciation of heart rate variability in a month and 3 months while bisoprolol treatment showed a decreased value of parameters LF ( $-6502,33$  ms;  $-6013,42$  ms) vs ( $-47,43$  ms;  $-71,33$  ms) comparing with placebo group ( $p > 0,05$ ) and parameters VLF levels in patients on bisoprolol ( $-66334,41$  ms;  $-43652,57$  ms) vs ( $-2291,71$  ms;  $-3077,53$  ms) the placebo group ( $p > 0,05$ ).

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