Changes in Short-Term Blood Pressure Regulation in Adolescents with Type-I Diabetes Mellitus and Essential Hypertension

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Abstract

The aim of the study was to determine the relationship between the variability in systolic blood pressure (SBP) and RR-intervals (RRI) with respect to the baroreflex sensitivity (BRS) in adolescents with diabetes mellitus type-I (DM-I) and essential hypertension (EH).

BP was recorded in 171 adolescents (130 healthy, 22 DM-I, 16 EH, 16-20 years) for 5-min (Finapres, metronome controlled breathing at a frequency of 0.33 Hz). The power spectra of SBP [mmHg^2/Hz] and RRI [ms^2/Hz] were calculated. BRS was determined by cross-spectral method. Adolescents were divided into 9 subgroups according to the RRI/SBP spectral power around the frequency of 0.1 Hz. The limits of power were estimated as percentiles (33.3% and 66.6%).

DM-I has significantly higher SBP and RRI variability but no changes in BRS in comparison to healthy; however, DM-I have in comparison with EH significantly higher BRS and RRI variability, but no significant changes in SBP variability. Significant changes in distribution of EH and DM-I in particular subgroups were found.

Adolescents with DM-I are concentrated in area with high SBP and RRI variability which corresponds to the mean values of BRS. On the other hand, EH adolescents concentrate to the areas only with high SBP variability which corresponds to the low values of BRS.

1. Introduction

Type 1 diabetes mellitus (DM-I) is a chronic endocrine and metabolic disease, frequently observed also in children, originating most often due to insufficient production of insulin. The long-term increased glycaemia results in quite a variety of afflictions significantly influencing the morbidity and mortality of adults. The EDIC study has demonstrated that a consistent salutary effect of intensive therapy [1] in DM-I patients is accompanied by a two- to threefold higher risk of premature cardiovascular complications. Further efforts are needed to accurately identify early complications, to select high-risk patients, and to treat those patients intensely [2]. Children and adolescents present another such risky group with regard to early beginning of the disease. In addition, impaired metabolic controls elicited by hormonal changes [3] during adulthood can also accelerate late complications in young patients with DM-I [4].

Complications accompany diabetes mellitus quite often and affect probably all organs: they cause except cardiopathy or vasculopathy also neuropathy.

Autoimmune reaction in connection with certain haplotypes of the major histocompatibility complex has long been thought to be responsible for the destruction of Langerhans islets. Autoimmune reaction is also one of the factors responsible for neuropathy in DM-I patients who have lymphocytic infiltration of sympathetic ganglia [5], and there were also found antibodies against adrenal medulla, and the sympathetic and parasympathetic nervous systems [6,7].

Impaired autonomous regulation is accompanied by a decreased ability of short-term blood pressure (BP) buffering. Several large studies [9,10] showed the relationship between hypertension and impaired baroreflex sensitivity and/or variability of cardiac intervals. Reduced values of these parameters have a negative effect on the prognosis of patients with heart disease and heart failure [11,12]. Also, blood pressure variability is a useful parameter in the evaluation of risk in hypertensive patients [13]. Elevated blood pressure variability was found to be associated with a higher incidence of hypertensive organ damage (e.g. left ventricular hypertrophy, thickening of the intima media thickness, with white matter lesions in the CNS etc.)

2. Aims

The aim of the study was to determine the relationship between the variability in systolic blood pressure (SBP) and RR-intervals (RRI) with respect to the baroreflex sensitivity (BRS) in adolescents with diabetes mellitus type-I (DM-I) and essential hypertension (EH).

3. Methods

The healthy participants were recruited from three secondary schools and two universities in the city of Brno, patients with essential hypertension and diabetes mellitus type I were addressed in the Children Hospital of Faculty Hospital in Brno. The informed consent to the examination was obtained from all subjects and also from parents of under-aged adolescents.

We examined 130 healthy adolescents (Co) and young adults between 16 – 20 years of age (17.62 ± 1.08 years). We examined further 16 adolescents with essential hypertension (EH) of the same age as Co (17.31 ± 1.21 years) who had repeatedly high causal blood pressure with respect to their age, sex and height and high 24-hour blood pressure (40% of values of systolic and/or diastolic blood pressure measured during day and/or night were higher than 95th percentile of values for age and height). Our research was concentrated mainly on examination of 22 adolescents (17.09 ± 1.24 years) suffering from diabetes mellitus type-I (DM-I). They have been treated with insulin pump (55%) or insulin pen (45%) for 5.88 ± 2.30 years on average.

In each subject, blood pressure was noninvasively continuously measured by photoplethysmographic method of Peňaz. The measuring cuff was placed on the second phalanx of the middle or ring finger of the subject's dominant hand. The subjects were sitting at rest for 15 min prior to the measurement; thereafter blood pressure was measured for 5 min. All participants breathed at a rate of 0.33 Hz in accordance with bar-led metronome, and they adjusted their tidal volume according to their own comfort.

The values of systolic and diastolic blood pressure, and inter-beat intervals (RRI) were detected from the recorded blood pressure signal beat-to-beat. These data sets were used for calculation of SBP and RRI power spectra in low frequency range (LF: 0.05 - 0.15 Hz) SBP_{LF} and RRI_{LF}. Baroreflex sensitivity (BRS) was calculated as the ratio between the cross spectrum (SBP x RRI) and power spectrum of SBP [14].

Examined healthy controls were divided according to systolic blood pressure variability by α quantile in 3 approximately the same numerous groups: high variability in SBP - hSBP ≥ 103 mmHg^2/Hz (α quantile 0.67-1), medium variability in SBP – 103 mmHg^2/Hz ≥ mSBP ≥ 50 mmHg^2/Hz (α quantile 0.34 to 0.66), low SBP variability - lSBP < 50 mmHg^2/Hz (α quantile 0 - 0.33). In the same way, the healthy controls were divided also according to RRI variability: hRRI ≥ 10600 ms^2/Hz (α quantile 0.67-1), medium variability in RRI – 10600 ms^2/Hz ≥ mRRI ≥ 6200 ms^2/Hz (α quantile 0.34 to 0.66), low RRI variability - lRRI < 6200 ms^2/Hz (α quantile 0-0.33). Due to this dividing, we obtained 9 different subgroups each characteristically specified by different combinations of SBP and RRI variability levels: A (hSBP, hRRI), B (mSBP, hRRI), C (lSBP, hRRI), D (hSBP, mRRI), E (mSBP, mRRI), F (lSBP, mRRI), G (hSBP, lRRI), H (mSBP, lRRI), I (lSBP, lRRI). The same border criteria were used for the classification of adolescents with diabetes mellitus and hypertension (Figure 1).

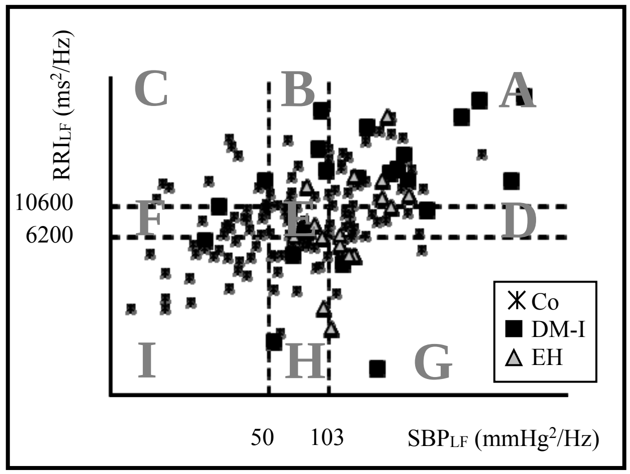

Figure 1. Graphical visualization of studied groups distribution (stars – controls, black squares – adolescents with diabetes mellitus type-I, shadow triangles – adolescents with essential hypertension. Axis in logarithmic scales).

We calculated the median and quartiles (Q25 and Q75) of each parameter for all groups of adolescents. The statistical significances of differences were evaluated using the Mann - Whitney U test. Analysis of the distribution of people in each of the subgroups was evaluated using χ^2-test.

4. Results

In this study, we have found significantly lower systolic and diastolic blood pressure in adolescents treated for diabetes mellitus type-I, and significantly higher SBP and DBP in patients with essential hypertension than in healthy controls. Group of DM-I has significantly higher SBP and RRI variability but no changes in BRS in comparison to healthy ones; however, DM-I have in comparison with EH significantly higher BRS and RRI variability, but no significant changes in SBP variability (Table 1).

Table 1. Cardiovascular parameters in studied groups adolescent with diabetes mellitus type-I and adolescents with essential hypertension in subgroups according to the heart rate and blood pressure variability

	Co	DM-I	EH
RRI	792	773	788
[ms]	(695-867)	(705-813)	(652-839)
SBP	113*	109^{+++}	129°°°
[mmHg]	(104-122)	(102-111)	(124-137)
DBP	69***	63^{+++}	71
[mmHg]	(64-74)	(55-66)	(68-77)
RRI_{LF}	8211**	16416^{+}	6888
[ms^2/Hz]	(5282-13337)	(5736-28004)	(4867-13606)
SBP_{LF}	69***	159	125°°°
[$mmHg^2$/Hz]	(38-126)	(77-267)	(97-196)
BRS	8.4	7.7^{+}	5.7°°°
[ms/mmHg]	(6.6-11.1)	(4.6-12.3)	(4.5-7.1)

Legend: median (Q25-Q75); Mann-Whitney test - Co vs. DM-I: * p<0.05, **p<0.01,***p<0.001; DM-I vs. EH: $^{+}$p<0.05; $^{+++}$p<0.001;Co vs. EH: °°°p<0.001

Table 2. The percentage distribution of healthy controls, diabetic and hypertensive adolescents

Group	Subgroup characteristic	Co	DM-I	EH
A	$hSBP_{LF}$+$hRRI_{LF}$	18.5%	45.5%	31.3%
B	$mSBP_{LF}$+$hRRI_{LF}$	10.0%	13.6%	6.2%
C	$lSBP_{LF}$+$hRRI_{LF}$	6.1%	4.5%	0.0%
D	$hSBP_{LF}$+$mRRI_{LF}$	11.5%	4.5%	12.5%
E	$mSBP_{LF}$+$mRRI_{LF}$	10.8%	4.5%	12.5%
F	$lSBP_{LF}$+$mRRI_{LF}$	10.8%	4.5%	0.0%
G	$hSBP_{LF}$+$lRRI_{LF}$	4.6%	9.2%	25.0%
H	$mSBP_{LF}$+$lRRI_{LF}$	12.3%	9.2%	12.5%
I	$lSBP_{LF}$+$lRRI_{LF}$	15.4%	4.5%	0.0%
A+B+C	$hRRI_{LF}$	34.6%	63.6%	37.5%
D+E+F	$mRRI_{LF}$	33.1%	13.5%	25.0%
G+H+I	$lRRI_{LF}$	32.3%	22.9%	37.5%
A+D+G	$hSBP_{LF}$	34.6%	59.2%	68.8%
B+E+H	$mSBP_{LF}$	33.1%	27.3%	31.2%
C+F+I	$lSBP_{LF}$	32.3%	13.5%	0.0%

Healthy controls have taken the following distribution into 9 subgroups A-I (tab. 2): the lowest number of persons were found in subgroups of G (4.6%) and C (6.1%), while the largest number of Co were in subgroups A (18, 5%) and I (15.4%). The interesting thing is that the lowest values of BRS are connected with group G (median: 4.46 ms/mmHg; quartiles: 3.91 – 4.56), the group C is on the opposite side with median value of BRS 18.94 ms/mmHg (quartiles: 16.29 – 24.88), and the values of BRS represents groups A (median: 8.60 ms/mmHg; quartiles: 7.03 – 10.82), E (median: 8.22 ms/mmHg; quartiles: 6.77 – 9.30), and I (median: 8.85 ms/mmHg; quartiles: 7.64 – 10.15).

We have found significant changes (χ^2-test) in distribution of hypertensive and diabetic adolescents: DM-I and EH have significantly higher concentration in subgroup A than Co (p<0.05); there is no significant difference in subgroup A between DM-I and EH; subgroup G contains significantly higher number of adolescents with EH (p<0.01) than Co or DM-I.

5. Discussion

We have observed in our results changes in autonomous nervous regulation of blood pressure in adolescents with type I diabetes mellitus and essential hypertension. This assumption is based on changes in distribution of studied groups of adolescent patients among particular subgroups A-I that have specific combination of sympathetic and parasympathetic activity.

Numerous animal studies focused on the understanding of sympathetic and parasympathetic activity changes and its projection into heart rate (HR) and blood pressure variability. Japundzic et al. [15] have shown dampening effect of alpha-blocker prozasin on systolic blood pressure power spectra in LF range that may indicate that alpha-adrenergic sympathetic system plays a dominant role in the normal turnover of vasomotor activity. On the other side, reflection of autonomous nervous system activity changes in the heart rate variability in the LF range is not so clear. Authors [15,16] generally agree that there is certain effect of parasympathetic nervous system in this spectral range, but some works describe also effect of beta-adrenergic nervous system on LF range power of heart rate spectrum [15].

Sympathetic over-activity in hypertensive patients is discussed often, and is supported by both invasive (e.g. microneurography and the radiotracer method of assessment of norepinephrine spillover rate) and non-invasive methods (e.g. blood pressure and heart rate variability estimation). The sympathetic over-activity in adolescents with essential hypertension is manifested by significantly increased systolic blood pressure variability due to increased concentration into the subgroups A, D and G. The reason of significant decrease of baroreflex sensitivity values may be seen in high concentration of hypertonics in subgroup G which is characterized by the lowest values of BRS.

Adolescents with diabetes mellitus type I have like the hypertonics significantly increased systolic blood pressure variability that could be mark of increased sympathetic activity. We have not found contrary to other authors [17] decreased baroreflex sensitivity that could be explained by very high concentration of young diabetics in group A which is characterized by mean values of BRS. It means that increased sympathetic activity expressed by increased short term blood pressure variability is compensated by increased parasympathetic activity. This suggestion is supported by increased short term heart rate variability.

6. Conclusion

This study could help in the future to find new parameters for early diagnosis of several diseases accompanied by autonomous dysbalance. One of these parameters could be power spectrum of systolic blood pressure in its LF part that delimited approximately 70% of hypertonics. Evaluation of early stages of autonomous dysbalance in diabetics will not be so simple. Diabetics have also increased blood pressure variability but not as reserved as observed in hypertensive patients. Further research should be focused on the effect of different treatments.

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