Photoplethysmographic assessment of the pulse wave: a blunted response to salbutamol in arterial hypertension and coronary artery disease

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Summary

Objectives: A systemic vascular effect of beta$_2$-adrenergic agonist salbutamol is partially mediated through the L-arginine–NO pathway. Therefore, the attenuation of photoplethysmographic digital volume pulse parameters under salbutamol inhalation could be used for the evaluation of endothelial function. The aim of the study was to estimate the vascular response to salbutamol in patients with arterial hypertension (AH) and coronary heart disease (CHD).

Design and Methods: Totally 71 subjects were studied: 30 patients with AH, 26 patients with CHD and 15 healthy controls (C). All the subjects underwent the detailed clinical assessment and photoplethysmographic evaluation of the pulse wave response to 400 μg salbutamol inhalation. A portable photoplethysmograph Micro Medical MP2000 (Gillingham, Kent, United Kingdom) was used for digital volume pulse analysis. The assessment was performed according to the modified protocol of Chowienczyk et al.

Results: Characteristic change in the pulse wave curve after salbutamol inhalation was observed in the controls: a decrease in the height of the inflection point (IP) (ΔIP 18.24 ± 16.42, $p < 0.05$) and the prolongation of peak-to-peak time (PPT) (ΔPPT 110.14 ± 83.01 ms, $p < 0.05$). In the patients with arterial hypertension and coronary heart disease the typical response was a minimal or absent prolongation of the PPT after salbutamol inhalation (ΔPPT 37.19 ± 47.71 ms in AH; ΔPPT 55.81 ± 56.41 ms in CHD). The difference in the change of PPT was statistically significant in the patients with AH ($p = 0.006$) and CHD ($p = 0.04$) as compared to the controls. Statistically non-significant tendency of a blunted decrease of the IP in the patients was observed (ΔIP 9.66 ± 6.79 in AH, ΔIP 10.73 ± 10.29 in CHD vs. 18.24 ± 16.42 in C, $p > 0.05$).

Conclusion: Our findings suggest that impaired vasomotor endothelial function could be responsible for a blunted response of the pulse wave parameters to salbutamol in hypertensive and coronary patients.

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Keywords: photoplethysmography, pulse wave, endothelial function, coronary heart disease, arterial hypertension

Pressure pulse waveforms are being studied more extensively than the volume pulse [1]. Nevertheless, increasingly more attention is paid to the photoplethysmographic measurements of the volume pulse parameters. Photoplethysmography (PG) is a non-invasive technique when non-visible infrared light is emitted into the skin. Light may be transmitted through a capillary bed such as it is found in the ear lobe or a finger tip. When the arterial inflow fills the capillary bed, the pulsation changes the volume of the blood vessels, and the absorption, reflection and scattering of light is modified. By detecting the non-absorbed light, changes in the blood volume can be measured [2]. The measurement of the transmitted through the finger infrared light by photoplethysmography gives a digital volume pulse (DVP) [3]. A DVP wave exhibits two peaks – "*a*" and "*b*" and a characteristic "notch" or a point of inflection (IP) in its downslope. The time interval between the first and the second peaks of a DVP is also measured (PPT) [4] (Figure 1A).

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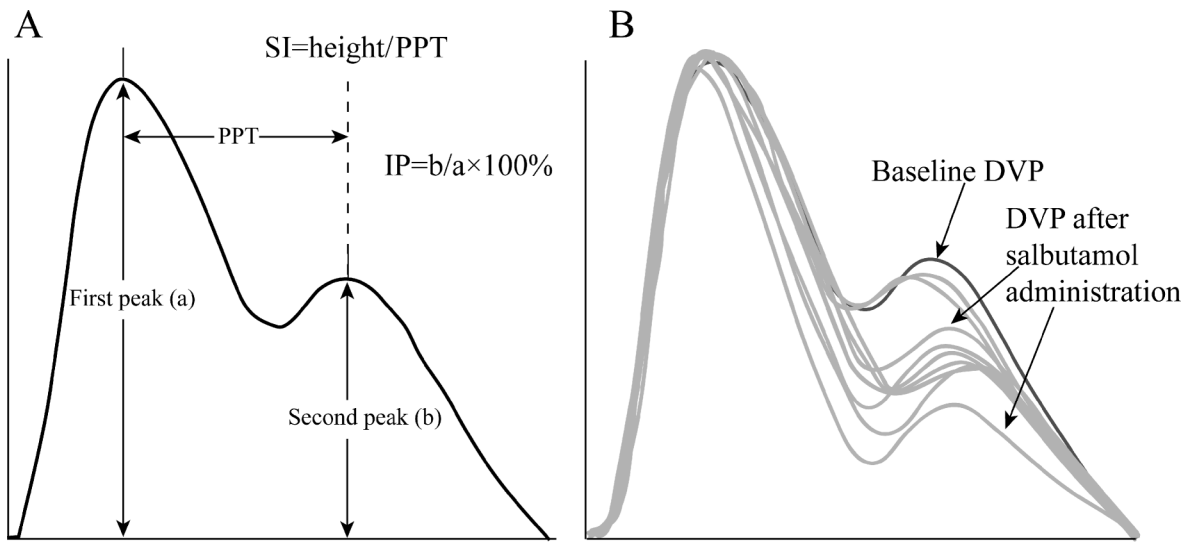

Figure 1. Examples of the photoplethysmographic digital volume pulse in healthy adults: A – parameters measured; B – a typical response of the digital volume pulse to salbutamol inhalation.

The second or the first derivatives are used to estimate the inflection point (IP) and its changes [3,4]. Previous studies have suggested that the DVP is comprised by the direct component arising from pressure waves propagating from the heart to the finger and the delayed component arising from pressure waves reflected backward from peripheral arteries mainly in the lower body, which then propagate to the finger [4]. A well-recognized fall in the IP after vasodilator drugs, such as glyceryl trinitrate (GTN), was attributed to the so-called "Windkessel effect" resulting from the increased compliance of the large arteries, and to a decreased venous return to the heart [5,6]. Changes in the DVP produced by GTN are parallel to those in the pressure pulse [7–9]. Two features of the arteries – elasticity and peripheral resistance – allow them to smooth out pulsations. The mechanism is similar to the type of the pump the Germans in the 19th century called a windkessel, so the smoothing of pulsations by the arteries is often called a windkessel effect.

Recently Chowienczyk et al [4] proposed that vascular reactivity and endothelial function could be assessed by measuring the systemic effect of beta$_2$-adrenergic agonist salbutamol on the digital volume pulse. It has been shown that vasodilator responses to beta$_2$-adrenoceptor agonists is partially mediated through the L-arginine–NO pathway [3,9–11]. This response could be attenuated during the concurrent blockade of NO synthesis by N^G-monomethyl-L-arginine (LNNMA).

The aim of this study was to assess the response of digital volume pulse parameters to salbutamol in patients with arterial hypertension and coronary heart disease and to compare them with the measurements in healthy adults.

Methods

Studies were performed with the approval of the Vilnius University Hospital Santariskiu Klinikos Research Ethics Committee and after the informed consent of the subjects was obtained.

Repeatability study

In order to evaluate the repeatability of the DVP, 23 healthy subjects (10 women and 13 men; aged 54.5 ± 12.44 years) were studied for four times by two different investigators on the same day. Each investigator performed two measurements. The DVP measurement was obtained by recording the DVP for 30 seconds. Repeatability was assessed as the inter- and intraobserver coefficients of variation and correlation.

Salbutamol study

Study population

The vascular response to salbutamol was evaluated in 56 patients (21 women and 35 men; aged 53±11 years) with coronary heart disease (n = 26) and primary arterial hypertension (n = 30). In CHD patients coronary heart disease was proven angiographically. Fifteen healthy subjects (7 men and 8 women; aged 30.72 ± 6.93 years) with no evidence of arterial hypertension (blood pressure <140/90 mm Hg), hypercholesterolemia, diabetes mellitus, cardiac or peripheral vascular disease, or any other systemic disease were included into the study as controls.

The most relevant characteristics of the coronary and hypertensive patients and the control subjects are shown in Table 1.

There was no significant difference between the patient groups regarding age, but the subjects in the control group were younger than the pa-

Table 1.
Clinical characteristics of the patient groups (AH patients and CHD patients) and the control (C) subjects

	AH, $n = 30$	CHD, $n = 26$	C, $n = 15$	p^*	p^{**}	p^{***}	All, $n = 71$
Male/female (%)	18/12 (60/40)	17/9 (65/35)	7/8 (47/53)	0.78	0.39	0.24	42/29 (59/41)
Age (years)	51.0 ± 11.5	55.3 ± 10.1	30.7 ± 6.9	0.15	<0.001	<0.001	48.3 ± 13.7
BMI (kg/m^2)	30.2 ± 7.1	28.5 ± 3.67	22.7 ± 2.8	0.27	0.02	0.03	28.5 ± 5.9
SBP (mmHg)	144.9 ± 27.2	127.3 ± 17.64	121.3 ± 11.6	0.006	0.01	0.32	133.2 ± 23.3
DBP (mmHg)	87.2 ± 14.5	76.35 ± 9.40	73.4 ± 8.0	0.002	0.007	0.36	80.5 ± 12.9
$\geq$2 RF (%)	24 (80)	22 (84)	0 (0)				46 (64)

Notes: AH – arterial hypertension; BMI – body mass index; CHD – coronary heart disease; C – control; DBP – diastolic blood pressure; RF – risk factors; SBP – systolic blood pressure; p^* – comparing AH and CHD groups; p^{**} – comparing AH and control groups; p^{***} – comparing CHD and control groups.

Table 2.
Level of lipids in the patients groups (AH and CHD groups) and in the control subjects

	AH, $n = 30$	CHD, $n = 26$	C, $n = 15$	p^*	p^{**}	p^{***}	All, $n = 71$
TCh	6.98 ± 1.9	6.48 ± 1.4	5.47 ± 0.9	0.15	<0.01	<0.05	6.75 ± 1.7
LDL-Ch	4.41 ± 1.5	4.18 ± 1.7	3.12 ± 0.8	0.66	<0.05	<0.05	4.28 ± 1.6
HDL-Ch	1.37 ± 0.3	1.19 ± 0.3	1.45 ± 1.0	0.11	<0.05	<0.05	1.29 ± 0.3
TG	2.72 ± 2.2	2.13 ± 1.1	1.8 ± 0.7	0.28	<0.01	<0.05	2.42 ± 1.7

Notes: AH – arterial hypertension; CHD – coronary heart disease; HDL-Ch – high density lipoprotein cholesterol; LDL-Ch – low density lipoprotein cholesterol; TCh – total cholesterol; TG – triglycerides; p^* – comparing AH and CHD groups; p^{**} – comparing AH and control groups; p^{***} – comparing CHD and control groups.

tients in both AH and CHD groups. Most of the patients in both groups had at least 2 cardiovascular risk factors. Subjects in the control group were without any cardiovascular risk factors.

The CHD group consisted of 26 patients (9 women and 17 men; the mean age – 55.35 ± 10.12 years). The mean arterial pressure in this group was 127.35 ± 17.64 mm Hg; there was no evidence of present or past hypertension in these patients. The AH group consisted of 30 patients with primary hypertension (12 women and 8 men; the mean age – 51.07 ± 11.56 years). The mean systolic arterial pressure in this group was 144.97 ± 27.20, the mean diastolic blood pressure – 87.27 ± 14.50 mm Hg, thus significantly higher than in the CHD group ($p < 0.05$). Blood pressure was defined as an average of 3 sitting blood pressure readings taken after 5 minutes of rest on 3 different occasions during a 3- to 4-week period. Acute coronary events were present in 20 CHD group patients (77%).

The serum lipid profile (total cholesterol, LDL-cholesterol, HDL-cholesterol and triglycerides) did not differ significantly between the CHD and AH groups but were significantly higher in both patient groups than in the control group (Table 2).

Volume pulse recording

A portable photoplethysmograph Micro Medical MP2000 (Gillingham, Kent, United Kingdom) was used for the digital volume pulse analysis. The assessment was performed using the modified protocol of Chowienczyk et al [3]. Data were collected from a patient sitting in a specially designed arm-chair with the hands comfortably placed slightly below the level of the heart, with the outstretched legs. Measurements were started after a calm-down period of 20 minutes. A probe was placed on the index finger of the right hand. In cases when the finger was cold, steady additional warming was applied and only in the absence of peripheral vasoconstriction the measurements were started.

Protocol

All the studies were performed in a quiet temperature controlled room (25 ± 1°C). All the participants were asked to refrain from drinking alcohol or beverages containing caffeine, and from smoking for at least 24 hours before the studies. All vasoactive medications were discontinued for 12 hours; if necessary the antihypertensive drugs with low probability of affecting endothelial function were given. The patients were studied in the morning after overnight fasting.

Three baseline DVP recordings were carried out for 30 seconds at 5-minute interval. Three parallel blood pressure measurements were performed using an advanced oscillometric automatic digital blood pressure monitor UA-767 (A&D Company, Limited). The results were averaged and presented as the mean basal parameter.

Salbutamol (Ventolin Inhaler, GlaxoWelcome) was given by inhalation using a spacer device (four doses of 100 μg each). Every dose was inhaled by two deep breaths in from the spacer. The repeated DVP recordings for 30 seconds were performed at 5, 10, 15, 20, 25, 40 and 60 minutes after the inhalation of Salbutamol (SLBTM).

The data were averaged by the unit and several mean parameters were calculated (Figure 1A): The *inflection point (IP)* – defined as a relative height of the inflection point expressed as a percentage of the ratio between the amplitudes of the two waves: systolic forward (a) and reflected (b) (IP = $b/a \times 100\%$); *Peak-to-peak time (PPT)* – a time interval between the peak "*a*" and the point of inflection "*b*"; *Stiffness index (SI)* – defined as a patient's height divided by the PPT (meters per second). Change of these parameters after SLBTM as well as several additional derivative parameters were calculated: maximal change of IP after SLBTM inhalation ΔIP_{max} normalized for corresponding ΔPPT ($\Delta IP_{max} \times 10/\Delta PPT$), ΔPPT_{max} normalized for corresponding ΔIP ($\Delta IP \times 10/\Delta PPT_{max}$), ΔIP_{max} normalized for ΔPPT_{max} ($\Delta IP_{max} \times 10/\Delta PPT_{max}$).

IP, PPT and SI parameters after salbutamol inhalation are presented as the mean of the measurements after 10, 15 and 20 minutes (modified protocol) and as the mean after 15 and 20 minutes (original protocol according to P. Chowienczyk). The maximal IP and maximal PPT were selected from all the recordings (at 10, 15, 20, 25, 40 and 60 minutes after salbutamol inhalation). The mean of the basal measurement was compared with those achieved after salbutamol inhalation.

Statistical analysis

Statistical analysis was performed using the GB-Stat V7.0 for Windows (Dynamic Microsystems, Inc). All measurements are presented as the mean $\pm$ standard deviation (SD). The comparison of DVP parameters before and after SLBTM inhalation was performed by means of the paired Student's *t* test. Differences between the two groups were estimated by the unpaired Student's *t* test, differences between the three groups – by the analysis of the variance (ANOVA) test; the correlation matrix was used searching for correlations between changes of parameters. All calculated probability values are 2-tailed, and $p < 0.05$ was considered to indicate statistical significance.

Results

Repeatability study

The DVP intra- and interobserver data are shown in Table 3. The best DVP repeatability, assessed as an inter- and intraobserver coefficient of variation (CV) and the coefficient of correlation (CC), was calculated for the inflection point (IP) parameter. The intarobserver coefficient of variation for the IP was 4.8%, the coefficient of correlation – 0.94. The interobserver coefficient of variation of the IP was 7.0%, the coefficient of correlation – 0.87. Thus, the high repeatability of the IP was observed. The other DVP parameters showed lower but still sufficient repeatability (Table 3).

Salbutamol test

Photoplethysmographic digital volume pulse changes in all the three studied groups after salbutamol inhalation are presented in Table 4.

The typical normal response to salbutamol inhalation showed a drop in the height of the inflection point and the prolongation of corresponding PPT (Figures 1B and 2).

The typical blunted response of the DVP to inhaled salbutamol consisted of attenuated decrease in the height of the inflection point with the absence or only a minimal prolongation of the corresponding PPT (Figure 3).

A decrease in the height of the IP after inhaled SLBTML was attenuated in most of the patients of the AH and CHD groups (ΔIP $4.8 \pm 6.2\%$ in AH, $4.8 \pm 10.0\%$ in CHD; $p > 0.05$ in both cases)

Table 3.
Interobserver and intraobserver reproducibility of the pulse wave analysis and photoplethysmography

DVP parameter	Interobserver		Intraobserver	
	Coefficient of correlation	Coefficient of variation (%)	Coefficient of correlation	Coefficient of variation (%)
IP (%)	0.87	7.0	0.94	4.8
PPT (ms)	0.79	17.7	0.85	15.2
SI (m/s)	0.84	14.4	0.90	11.9

Notes: DVP – digital volume pulse; IP – inflection point; PPT – peak-to-peak time; SI – stiffness index; *p* – value of coefficient of correlation in all cases <0.001; total number of subjects investigated $n = 23$, hence totally 92 measurements performed.

Table 4.
Photoplethysmographic digital volume pulse parameters in the patients (arterial hypertension patients and coronary heart disease patients) and in the control subjects

PG DVP parameters	AH, $n = 30$	CHD, $n = 26$	C, $n = 15$	p^*	p^{**}	p^{***}	All, $n = 71$
Mean ΔIP at 10, 15, 20 min after S.	4.8 ± 6.2	4.8 ± 10.0	10.2 ± 13.9	0.99	0.17	0.22	5.9 ± 9.8
Mean ΔIP at 15, 20 min after S.	4.7 ± 7.2	4.4 ± 10.9	11.3 ± 14.3	0.90	0.11	0.14	6.0 ± 10.6
Mean ΔPPT at 10, 15, 20 min after S.	9.0 ± 44.9	16.8 ± 40.6	45.9 ± 48.9	0.50	**0.03**	0.07	19.2 ± 45.8
Mean ΔPPT at 15, 20 min after S.	5.4 ± 37.4	15.4 ± 47.7	48.9 ± 51.1	0.39	**0.01**	**0.04**	18.3 ± 46.8
Mean ΔSI at 10, 15, 20 min after S.	0.4 ± 1.8	0.5 ± 3.7	2.2 ± 2.8	0.88	**0.04**	0.12	0.8 ± 2.9
Mean ΔSI at 15, 20 min after S.	0.5 ± 1.9	0.8 ± 2.2	2.0 ± 2.9	0.59	0.11	0.22	0.9 ± 2.3
Maximal ΔIP	9.6 ± 6.7	10.7 ± 10.2	18.2 ± 16.4	0.66	0.09	0.13	11.8 ± 11.0
Maximal ΔPPT	37.1 ± 47.7	55.8 ± 56.4	110.1 ± 83.0	0.19	**0.006**	**0.04**	59.4 ± 65.0
Maximal ΔSI	2.00 ± 2.22	2.6 ± 1.8	3.9 ± 3.5	0.24	0.07	0.22	2.6 ± 2.5
$\Delta IP_{max} \times 10/\Delta PPT$	1.1 ± 10.2	2.8 ± 3.6	2.9 ± 5.3	0.41	0.44	0.93	2.1 ± 7.3
$\Delta IP \times 10/\Delta PPT_{max}$	0.7 ± 3.2	2.1 ± 3.5	1.6 ± 1.7	0.14	0.24	0.57	1.4 ± 3.1
$\Delta IP_{max} \times 10/\Delta PPT_{max}$	1.3 ± 3.2	2.6 ± 3.4	0.2 ± 0.1	0.14	0.07	**0.001**	1.6 ± 3.0

Notes: AH – arterial hypertension; CHD – coronary heart disease; DVP – digital volume pulse; PG – photoplethysmography; IP – inflection point; PPT – peak-to-peak time; S. – salbutamol; SI – stiffness index; p^* – comparing AH and CHD groups; p^{**} – comparing AH and control groups; p^{***} – comparing CHD and control groups; $\Delta IP_{max} \times 10/\Delta PPT$ – ΔIP_{max} normalized for corresponding ΔPPT; $\Delta IP \times 10/\Delta PPT_{max}$ – ΔPPT_{max} normalized for corresponding ΔIP; $\Delta IP_{max} \times 10/\Delta PPT_{max}$ – ΔIP_{max} normalized for ΔPPT_{max}.

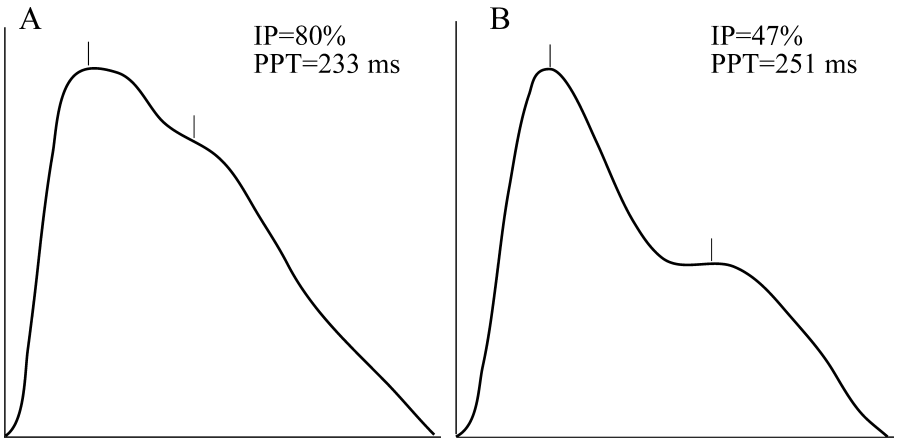

Figure 2. Typical response of the digital volume pulse (DVP) to salbutamol (SLBTM) in one of the control subjects: at a 25 minute ΔIP = 33%, the corresponding ΔPPT = 18 ms. A – DVP before SLBTM; B – DVP after inhaled SLBTM.

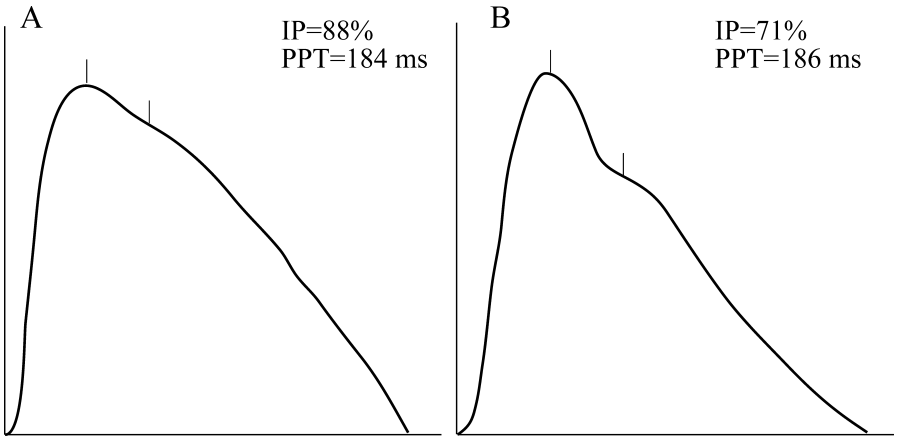

Figure 3. Characteristic response of a hypertensive patient: at the 20 minute ΔIP is only 17% and corresponding ΔPPT = 2 ms; A – the digital volume pulse (DVP) before salbutamol (SLBTM) inhalation; B – the DVP after inhaled SLBTM.

as compared to the statistically significant drop of the IP observed in the control group ((ΔIP 10.2 ± 13.9%, $p < 0.05$). Unfortunately, the difference between ΔIP in all three groups did not reach statistical significance in the present study.

The changes in the PPT parameter after inhaled SLBTML significantly differed in the AH and CHD groups as compared to the control group. The mean ΔPPT at 15 and 20 minutes after SLBTM inhalation was found to be significantly longer in the controls (48.9 ± 51.15 ms) as compared to the AH (4 ± 37.4 ms, $p = 0.01$) and CHD patients (15.4 ± 47.7, $p = 0.04$). Maximal PPT was also significantly shorter in both AH and CHD groups compared with the control group (37.1 ± 47.7 ms, 55.8 ± 56.4 ms and 110.1 ± 83.0 ms respectively, ANOVA $p < 0.01$). The mean ΔPPT at 10, 15 and 20 minutes after SLBTM inhalation was significantly shorter in the AH group than in the control group; the same tendency was observed in the CHD group but it did not reach statistical significance.

The mean ΔSI at 10, 15 and 20 minutes after SLBTM inhalation was found to be significantly smaller in the AH group than in the controls (0.4 ± 1.8 m/s in AH and 2.2 ± 2.8 m/s in C, $p = 0.04$) and had the same tendency in the CHD group although it did not reach statistical significance.

The derivative parameter ΔIP_{max} normalized for ΔPPT_{max} had a tendency to be greater in both patient groups as compared to the control group (1.3 ± 3.2 in AH, 2.6 ± 3.4 in CHD and 0.2 ± 0.1 in C, ANOVA $p < 0.05$). Nevertheless, it reached statistical significance only due to the comparison of the controls and the CHD patients ($p = 0.001$).

The inhalation of salbutamol had no accompanying alteration of the heart rate or the mean blood pressure at 10, 15, 20, 25, 40 and 60 minutes after salbutamol inhalation when the DVP was recorded. We also explored the possible influence of the heart rate on the DVP parameters after the inhalation of SLBTM and did not find any strong correlation (Table 5). Only the mean ΔIP at 10, 15 and 20 minutes ($r = 0.303$) as well as the maximal ΔIP ($r = 0.305$) after SLBTML inhalation showed statistically significant but not strong correlation with the changes in the heart rate (Table 5).

Since the methodology of PG still needs further development, in order to find out how long after the inhaled SLBTM measurements must be performed, we investigated the cumulative rate of time when a maximal decrease in the IP was present. When this time interval was only 15 minutes, the cumulative rate of the decrease in ΔIP_{max} was only 41%; it increased to 86 % when the period was prolonged to 25 min (Table 6). The same tendencies were found after the cumulative rate of the maximal PPT prolongation analysis was performed (Table 7). On the basis of these results, we recommend to measure the DVP response to salbutamol inhalation after 15, 20 and 25 minutes and to monitor DVP parameters after 40 and 60 minutes in order to observe returning to the baseline of DVP parameters.

Table 5.
Correlation coefficients (*R*) between changes of the inflection point, peak-to-peak time, stiffness index parameters and the heart rate occurring after salbutamol inhalation

Parameters	*R* value	*P* value
Mean ΔIP at 10, 15, 20 min after SLBTM	**0.303**	**<0.05**
Mean ΔIP at 15, 20 min after SLBTM	0.241	n.s.
Mean ΔPPT at 10, 15, 20 min after SLBTM	–0.155	n.s.
Mean ΔPPT at 15, 20 min after SLBTM	–0.213	n.s.
Mean ΔSI at 10, 15, 20 min after SLBTM	0.203	n.s.
Mean ΔSI at 15, 20 min after SLBTM	0.168	n.s.
Maximal ΔIP	**0.305**	**<0.05**
Maximal ΔPPT	–0.204	n.s.
Maximal ΔSI	0.197	n.s.
$\Delta IP_{max} \times 10/\Delta PPT$	–0.059	n.s.
$\Delta IP \times 10/\Delta PPT_{max}$	0.142	n.s.
$\Delta IP_{max} \times 10/\Delta PPT_{max}$	0.116	n.s.

Notes: IP – inflection point; n.s. – not significant; PPT – peak-to-peak time; *R* – correlation coefficient; SI – stiffness index.

Table 6.
Cumulative frequency of the distribution of ΔIPmax decrease time

T (minutes)	*F* (number)	*C* (number)	*C* (%)
5	8	8	14.28
10	7	15	26.78
15	8	23	41.07
20	14	37	66.07
25	11	48	85.71
40	6	54	96.42
60	2	56	100

Notes: *C* – cumulative frequency; *F* – frequency; *T* – time interval.

Table 7.
Cumulative rate of maximal prolongation of the peak-to-peak time interval

T (minutes)	*F* (number)	*C* (number)	*C* (%)
5	3	3	5.35
10	7	10	17.85
15	8	18	32.14
20	14	32	57.14
25	11	43	76.78
40	9	52	92.85
60	4	56	100

Notes: *C* – cumulative frequency; *F* – frequency; *T* – time interval.

Discussion

The currently accepted method for the non-invasive clinical assessment of vasomotor endothelial function is based on the analysis of flow-mediated vasodilatation in the brachial artery [13]. The reason why it cannot be used very widely is the necessity of a sophisticated, expensive ultrasound unit and special skills of an investigator [14]. The photoplethysmographic method proposed by Chowienczyk et al in 1999 [4] could be a suitable alternative of non-invasive assessment of endothelial function. The authors have demonstrated that beta$_2$-adrenergic agonist albuterol (salbutamol) reduces the wave reflection in the DVP partly by the activation of the L-arginine–NO pathway. Vasodilation is mediated through the combination of endothelial and smooth muscle mechanisms because salbutamol induces direct smooth muscle relaxation and NO release from endothelial cells [9,10]. The method was applied only in patients with type II diabetes mellitus and revealed a disturbed endothelial function in these patients [4,15].

Since numerous studies have demonstrated endothelial dysfunction in most patients with coronary heart disease and primary arterial hypertension [16,17], we have chosen to estimate the characteristic influences of inhaled beta$_2$-adrenergic agonist salbutamol on photoplethysmographic digital volume pulse parameters in AH, CHD patients and healthy control subjects. The typical response of PG DVP parameters to SLBTM in controls was a distinct decrease in the height of the IP with the corresponding prolongation of the PPT interval. In both groups of patients (AH and CHD) the characteristic response to inhaled SLBTM was a blunted decrease of the IP with a minimal or absent prolongation of the PPT interval. The heterogeneity of vascular response to salbutamol within the groups (evidenced by wide SD intervals of the IP, PPT and SI) could be responsible for the statistical significance of the differences was not always reached. Perhaps further studies on the genetics of beta$_2$-receptor polymorphism will explain this phenomenon in the future.

The derivative parameter $\Delta IP_{max} \times 10/\Delta PPT_{max}$ was added in order to test whether the combination of the IP and PPT changes could be a more sensitive index of endothelial function. We believe that the significant difference in the change of this parameter in the CHD patients as compared to the controls should be taken into account when continuing investigation of the method.

Changes in PG DVP parameters after the inhalation of SLBTM, observed in the present study of the patients with arterial hypertension and coronary heart disease are in concordance with the results of Chowienczyk et al [4] and Gopaul et al [15] who were able to show similar changes in patients with type II diabetes. In previous studies it has been shown [4,12] that the blunted response of digital pulse volume and pulse wave parameters to inhaled salbutamol is NO related. Hence, we could speculate that the mechanism responsible for the changes in the PPT and IP parameters of the photoplethysmographic DVP under SLBTM found in the present study in patients with AH and CHD could be attributed to possible endothelial vasomotor dysfunction of the patients.

We estimated that the response to SLBTM could not have been contributed to merely heart rate and blood pressure changes. We were not able to discover strong correlations between the heart rate and ΔPPT changes under SLBTM. This could be explained partly by the timing of the recordings – the greatest change in the heart rate was observed during the first 10 minutes after inhalation and diminished thereafter.

Several technical details of the study must be discussed. The protocol used in the present study slightly differs from that, originally described by Chowienczyk et al [4]. The data in our study were collected from a patient sitting in a specially designed arm-chair with the hands comfortably placed only slightly below the level of the heart with the outstretched legs but not in the supine position as it was described in the original protocol. We propose that the sitting measurements are better because the DVP waveform depends upon the venous return.

In order to minimize the erratic absorption of inhaled salbutamol a spacer device was used. In the present study salbutamol was given by inhalation using a spacer device (four doses of 100 μg each). We recommended a patient to inhale a dose of SLBTM (100 μg) from the spacer two times for more complete appropriation of the drug.

Repeated potoplethysmographic digital volume pulse recordings for 30 seconds were performed at 5, 10, 15, 20, 25, 40 and 60 minutes after the inhalation of SLBTM. Although Wilkinson et al [12] have shown that the plasma salbutamol concentration is stable between 5 and 20 minutes after inhalation and then declines, the extension of measurements to 25 minutes and the averaging of the measurements at 15, 20 and 25 minutes allowed to increase the cumulative frequency of the maximal DVP response. Measurements after 40 and 60 minutes were performed in order to demonstrate a return to the baseline of the DVP parameters. This has confirmed that changes in

the DVP are salbutamol-related but are not determined by physiological relaxation of a patient.

Among the limitations of the present study, a relatively small number of subjects in the control group must be mentioned. The possibility that within the AH and CHD groups there could have been patients with and without endothelial dysfunction and it could weaken the statistical significance of the results, should also be considered. Therefore, larger studies including the comparison of photoplethysmographic data to the results of the other methods used to assess endothelial function are required.

Conclusions

In conclusion, the present study has demonstrated that patients with essential hypertension and coronary heart disease have a blunted response to inhaled salbutamol with the attenuation of the drop in the inflection point and a minimal or absent prolongation of the corresponding peak-to-peak time on the photoplethysmographic digital volume pulse. Hence, taken in conjunction with the results of the previous investigations, the findings of the present study suggest that the impaired vasomotor endothelial function could be responsible for a blunted response of digital volume pulse parameters to salbutamol in hypertensive and coronary patients.

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