Research Paper

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Observations on the arterial baroreflex in neurally mediated vasodepressor syncope

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THE arterial baroreflex was studied in subjects who had recently had an episode of vasodepressor syncope. This was determined using 2–3 mcg/kg intravenous boluses of phenylephrine and assessing the bradycardic response. The values were measured in ms/mmHg and expressed as the angular coefficient of the regression line between the increase in R–R interval on the electrocardiograph and the systolic arterial pressure. In subjects examined immediately after the vasodepressor syncope episode the bradycardic response was much more marked than in controls ($p < 0.01$) and in the subjects themselves 6 months after the episode, provided that they were symptom-free ($p < 0.01$). It is concluded that in vasodepressor syncope there is a phase in which the baroreflex is highly sensitive and that this is due not to a lowering of the stimulation threshold but to a gain in the efferent arc, which explains a 'vagotonic' response.

Key words: Syncope, Autonomic function, Cardiovascular reflexes

Introduction

Vasodepressor syncope (VDS) is a reflex event in which orthosympathetic activity is temporarily reduced and hypotension and bradycardia ensue.[1–5] The arterial baroreflex serves to keep the arterial pressure (Pa) constant at a set point or operating point, which is determined by the mean arterial pressure and by the arterial pulse. In resting man, when there are no obvious internal or external stresses, it is a change in Pa that triggers the baroreceptor reflex. The set point may vary with state, such as in exercise or in emotional stress.[6] Efferent pathways act on the cardiac (heart rate, myocardial contractility, atrioventricular conduction, cardiac output) and arterial (vascular resistance) targets and modulate the pressure values.[7] In the neurogenic arc, that represents the anatomical pathway of the arterial baroreflex, parasympathetic afferents and sympathetic and parasympathetic efferents operate. The cardiac reflex that follows a rise in Pa and the one that operates in an episode of VDS utilize vagal efferent pathways.[8]

The aim of the study was to evaluate the sensitivity of the baroreceptor–cardiac reflex and particularly the bradycardic response in subjects with VDS.

Patients and Method

Twelve patients (five women) prone to VDS on prolonged standing were studied. Their mean age was 22 ± 4.3 years (range 17–33 years). Twelve healthy symptom-free subjects matched for age and sex formed the control group. All participants gave their informed consent and the study was approved by the ethics committee of the hospital. The inclusion criteria were at least one previous episode of transient loss of consciousness attributable to VDS (in fact, from one to four) and freedom from any other disease, past or present. The diagnosis was established on the following criteria: loss of consciousness lasting a few seconds, spontaneous resolution and no confusional state following the episode, negative cardiological and neurological examinations and blood chemistry tests (physical examination with normal standing Pa values, baseline and 24-h dynamic electrocardiograph, echocolorcardiogram, electroencephalograph, magnetic resonance imaging of the head, blood counts and haemoglobin, blood glucose, K^+ and Na^+). In all subjects the syncopal or presyncopal symptoms were reproduced by the tilt test without the use of isoprenaline (hypotension and bradycardia with R–R intervals under 2 800 ms). In accordance with the protocol, the study was conducted within 24 h of the spontaneous transient loss of consciousness. In seven of the patients (four men and three women) the study was repeated after a symptom-free period of 6 months.

Both patients and controls, in quiet respiration and lying down, received intravenous boluses of phenylephrine 2–3 mcg/kg until a SBP rise of at least 30 mmHg was obtained.[9]

Continuous online electrocardiograph (Spacelabs Inc.) and arterial pressure (Finapres-Ohmeda) recording were taken. The analogic signals were converted into digital signals by means of analogic-to-digital conversion cards (MIO16F-5 National Instruments) with a frequency of 250 samples per second.

The test in which there was a SBP increment equal or greater than 30 mmHg was the only test considered valid: the values used to calculate the baroreflex were those between the starting value and the maximum obtained (≥ 30 mmHg) of SBP after phenylephrine injection: thus the regression line

between variation of SBP and that of R–R interval (ms/mmHg) for every point (beat-by-beat) recorded during the test between the starting systolic blood pressure (SBP) value and those maximum was calculated. The coefficient of regression (α angle) of the line of the correlation between increase of R–R interval and increase of SBP, expressed in ms/mmHg, gives the gain in the baroreflex.

The α angle values of the VDS patients, close to and distant from episode, were compared with those of the controls by means of variance analysis.

Results

Table 1 gives the values of the angular coefficient of the regression line (α angle) and the index of correlation (r) for each of the VDS patients and of the controls. Table 2 lists the α angle values in the patients retested 6 months after the last episode of loss of consciousness. The mean value of the coefficient of regression of the VDS patients differs significantly ($p < 0.01$) from that of the controls (Table 1). The mean value of the α angle of the seven patients, seen 6 months after the previous VDS episode, differs significantly from that found in the test done immediately after the episode, whereas it was statistically indistinguishable from that of seven normal controls (I.A., F.S., D.G.P., C.I., B.S., T.A., C.L.) comparable for age (Table 2). The data is illustrated in Fig. 1.

Discussion

In the present study the patients who suffered from VDS had a greater bradycardic response than controls to the hypertensive stimulus indicating that the arterial baroreflex responded in a different way to the controls. The study also showed that the baroreflex does not have a lower threshold but a higher gain in efferent response: this idea is sustained because the value of regression coefficient (α angle) which shows the baroreflex sensitivity, was modified more than 6 months later (Table 2).

These data support the hypothesis put forward by several authors that there is an abnormal baroreceptor reflex in VDS,[2,10–12] although they offer no suggestions as to the immediate mechanisms or to the anatomical site that influences the behaviour of the baroreflex.

In the critical phase of the VDS a period of intense activation is followed by a sudden fall of sympathetic tone, as demonstrated by the decreased vascular resistance,[2,3] the increased flow of blood to the forearm,[4,5] the reduction of sympathetic bursts in the periphery[1] and the changes in the spectra of frequency of the R–R signal on the electrocardiograph.[13] If, therefore, a strong sympathetic activation precedes the critical phase of VDS, which is reflected in a sudden loss of sympathetic tone and the entry of a vagal component, it means that the autonomic nervous system is ready to cope and can do so

Table 1. Values of coefficient of regression (α angle) of the line correlating variation in R–R time (ms) and variations in SAP in patients with VDS in the postcritical phase and in normal controls. The coefficient of correlation (r) attained a very high significance level ($p < 0.001$) in all patients except one (#), in whom the level was $p < 0.01$

VDS patients	α angle	r	Normal controls	α angle	r
P.G.	21.2	0.878	R.E.	5.4	0.866
M.G.	16.6	0.969	I.A.	9.8	0.659
T.M.	45.4	0.767	F.S.	10.2	(#)0.585
S.L.	21.5	0.807	D.G.P.	9.1	0.718
M.A.	17.8	0.937	C.I.	7.3	0.654
C.G.	18.3	0.923	S.A.	6.2	0.863
I.G.	38.7	0.962	B.S.	8.8	0.921
D.A.M.	27.2	0.956	N.L.	5.9	0.783
B.A.	18.7	0.976	D.A.G.	9.9	0.822
C.V.	29.2	0.833	B.M.	6.7	0.795
M.D.	14.5	0.725	T.D.	10.8	0.854
R.V.	13.4	0.721	C.L.	8.5	0.766
Mean ± SD*	23.55 ± 9.93			8.22 ± 1.85	

*F = 27.677, D.F. 1/22, $p < 0.01$.

Table 2. Values of coefficient of regression (α angle) of the line correlating variation in time R–R (ms) and variations in systolic blood pressure (SBP) (mmHg) in patients with VDS in postcritical phase (column A) and 6 months after the last episode of syncope (column B)

VDS patients	A	B
P.G.	21.2	13.3
T.M.	45.4	13.0
C.G.	18.3	9.3
I.G.	38.7	14.8
D.A.M.	27.2	13.4
C.V.	29.2	10.2
M.D.	14.5	5.8
Mean ± SD*	27.8 ± 11.12	11.4 ± 3.13

*Seven controls: mean of α angle = 9.21 ± 1.17.
A vs. B: F = 14.09, D.F. 1/12, $p < 0.01$.
A vs. Controls: F = 19.32, D.F. 1/12, $p < 0.01$.
B vs. Controls: F = 2.99, D.F. 1/12, p = N.S.

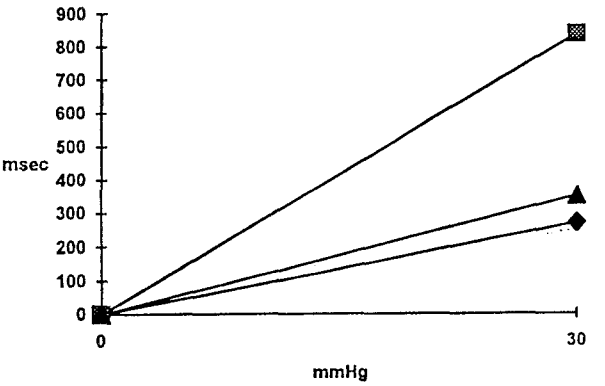

FIG. 1. Cumulative graph of the relationship between increase of systolic blood pressure (SBP) (mmHg) and R–R interval (ms) in the subjects with vasodepressor syncope, in critical (■), post-critical (▲) (after a symptom-free period of 6 months), and in the controls (◆).

whenever it is suitably stressed. It must be emphasized that only the bradycardic component of the efferent arc becomes evident, since the pressure component is used as stimulus; it is, however, sufficient to indicate the way in which the system works. Other authors[14,15] have reported a behaviour of other autonomic reflexes (deep breathing, bradycardia at standing up) in subjects with VDS which is different from controls.

A further aspect that emerges from this study is the modification of the response to the hypertensive stimulus months later: this signifies a modification of the system's ability to respond. This phenomenon might indicate a reduction of the ability of the autonomic nervous system to express a vagotonic response and might thus not have symptoms.

In conclusion, this study shows that the arterial baroreflex in patients shortly after an episode of VDS is abnormal and recovers when the patients are symptom free.

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