Baroreceptor Reflex Sensitivity Index Derived from Phase 4 of the Valsalva Maneuver

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SUMMARY The purpose of this study was to find a method to assess the sensitivity of the baroreceptor reflex avoiding the use of a pressor amine. Following the release of the Valsalva maneuver (VM), there is usually a pressor rise similar to the one obtained by phenylephrine administration. We were able to assess the baroreceptor reflex sensitivity index (BRSI) using this phase of the VM. Included in this study were nine healthy subjects, 25 patients with chronic Chagas' disease, and 10 hypertensive patients. The brachial artery and the antecubital vein were cannulated. VM was then performed during 20 seconds, and later 50 to 200 μg of phenylephrine were administered intravenously (i.v.). During Phase 4 of the VM, multiple correlations between systolic pressure and cycle length were obtained. The best correlations were observed when initial beats after the release were disregarded. During this period, changes in pressure were not followed by changes in cycle length. The following results were obtained: rise in systolic pressure by VM: 60 ± 28 mm Hg and by phenylephrine: 30 ± 26 mm Hg. The Valsalva BRSI (BRSI val) was 9.52 ± 5.4 msec/mm Hg, with a mean r of 0.92 ± 0.08; the phenylephrine BRSI (BRSI ph) was 9.91 ± 5.4 msec/mm Hg, with a mean r of 0.86 ± 0.11. The correlation between both BRSI was: Y = 0.06 + 0.94X; r = 0.91. These results indicate that the BRSI obtained by both methods is similar. We conclude that during the initial beats following the release of the VM there is a total inhibition of the baroreceptor reflex; and that following this brief inhibition period it is possible to measure the BRSI without use of a pressor amine such as phenylephrine.

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KEY WORDS baroreceptor reflex • Valsalva maneuver • phenylephrine • hypertension • Chagas' disease

BRISTOW et al.\(^1\) and Gribbin et al.\(^1\) have described a method to assess the sensitivity of the baroreceptor reflex (BRS), which is based on the degree of heart rate slowing induced by an acute elevation of systemic arterial pressure. This method, although accurate and sensitive, requires use of an alpha-adrenergic agent (phenylephrine) to increase the peripheral vascular resistance and blood pressure and has the disadvantage that these drugs could change the viscoelastic properties of the aorta and therefore eventually modify the BRS.\(^8\)

The following study was undertaken to measure the BRS through beat to beat changes of systemic arterial pressure and heart rate during phase 4 of the Valsalva maneuver (VM) in normal subjects, in patients with Chagas' disease, and patients with arterial hypertension. The reason for including in this study hypertensives and patients with Chagas' disease was to assess the accuracy of the indexes under a wide range of values, the latter two groups of patients providing us with conditions that show abnormal baroreflex sensitivity.\(^1\)\(^4\) This investigation was therefore done to verify the possibility of using the VM to assess the BRS.

Methods

Subjects

Included in this study were nine healthy subjects (mean age, 35 ± 12 SD years), 25 patients with chronic Chagas' disease (38 ± 9.2 years), and 10 hypertensive patients (42 ± 12 years). The normal subjects had a normal cardiovascular and respiratory history, a normal physical examination, and a normal electrocardiogram and chest X-ray. The diagnostic criteria of Chagas' disease was based on the epidemiology and serologic tests previously reported.\(^4\)\(^*\) Seven of this group of patients had heart failure. The hypertensive group included cases of different degrees of severity: labile, moderate, and severe. The day of the procedure the subjects lay supine, and the antecubital vein and the brachial artery were cannulated percutaneously. Intraarterial blood pressure and lead II of the ECG were simultaneously recorded in a Mingograph 34 polygraph. Five minutes later, the VM was per-
formed by blowing a mercury column and maintaining it at the level of 40 mm Hg for about 20 seconds. Later, 50–200 μg of phenylephrine was injected intravenously.

Baroreceptor Sensitivity Determination

Phenylephrine Method

The protocol of Bristow et al. was followed, in which systolic arterial pressures and R-R intervals (in msec) were measured from the time of the injection of the pressor agent until just after the peak of the pressure rise. Each systolic pressure was plotted against the second R-R interval following it. Linear relationships between systolic pressure and R-R interval were calculated where the regression coefficient corresponded to the index of BRS (BRS\text{ph}). The correlation coefficient was also calculated for each linear regression, and when the $r$ value was smaller than 0.65, the case was not included.

Valsalva Method

We usually did a first VM at a lower paper speed (fig. 1) to evaluate the hemodynamic response; later, a second one at 50 mm/sec was done, at which time the measurements were made. During phase 4, two periods could be distinguished: a first one in which increments in blood pressure were not followed by changes in cycle length; and a second, in which a progressive slowing of the heart rate followed the increase in pressure. During this second period, starting with the first beat with lengthened R-R interval and finishing with the beat with the highest systolic blood pressure, linear regressions were obtained in the same way as with the phenylephrine method by calculating the regression coefficient (BRS\text{val}) and correlation coefficients (figs. 1 and 2).

When all the beats of phase 4 are included, the BRSI is generally half of what is obtained by the proposed method.

Results

Phenylephrine Method

The mean rise in systolic arterial pressure induced by phenylephrine injection was 30.2 ± 26 mm HG ($\overline{X}$ and sd), and the average BRSI ph was 9.91 ± 5.4 msec/mm Hg. The highest value of BRSI ph (30.6 msec/mm Hg) was obtained in a normal subject, and the lowest (0.96 msec/mm Hg) in a Chagasic patient with heart failure (fig. 3). The $r$ value of this method was 0.86 ± 0.11.

Valsalva Method

The mean rise in systolic arterial pressure during phase 4 of the VM was 60.8 ± 28 mm Hg. The average BRSI val was 9.42 ± 5.4 msec/mm Hg. The highest BRSI val (27 msec/mm Hg) was obtained in another normal subject, and the lowest (0.91 msec/mm Hg) in the same Chagasic patient with

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<td>FIGURE 1. Upper Panel: 5 mm/sec recording of blood pressure (BP) and electrocardiogram (ECG) during Valsalva maneuver. The first and second arrows indicate strain (S) and release (R) respectively. Arrows and dots indicate the second period of phase 4 of the Valsalva maneuver, used for baroreceptor sensitivity calculation. Lower Panel: 50 mm/sec recording of cycle length (RR) and systolic blood pressure (BP) during Valsalva maneuver. The first arrow indicates the time of release (R). The beats between the second and third arrows correspond to those used for baroreceptor sensitivity calculation.</td>
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<td>FIGURE 2. Correlation between cycle length (RR) and systolic blood pressure (BP) in several beats following the release of Valsalva maneuver. The last five beats were used for baroreceptor reflex sensitivity index calculation. The regression coefficient (RC) of the correlation corresponds to the baroreceptor reflex sensitivity index (BRSI val).</td>
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heart failure as with the phenylephrine method (fig. 3). This latter patient had a VM with very little pressure rise and almost no change in cycle length. The mean \( r \) value of this method was 0.92 ± 0.08.

Both BRSI (val and ph) were plotted (fig. 3), and a linear regression was obtained: \( Y = 0.06 + 0.94 X \), and an \( r \) value of 0.91. This high correlation between both methods indicate that the BRSI can be calculated by the VM with accuracy.

**Discussion**

Baroreceptor reflexes tend to keep arterial blood pressure constant, but their sensitivity varies with physiological, pharmacological, and pathological conditions.

Sleep, exercise, body posture,\(^{16-11}\) neurological disorders,\(^{12-13}\) arterial hypertension,\(^3\) idiopathic orthostatic hypotension,\(^{14-15}\) congestive heart failure,\(^{14, 18}\) and many other disorders have been reported to affect the baroreflex sensitivity. Cardiac slowing after systemic arterial pressure rise induced by phenylephrine injection indicates that both afferent autonomic fibers from the baroreceptor areas and efferent cardiac vagal fibers are intact;\(^{2, 4-14, 18}\) the VM, on the other hand, can be used to test the overall integrity of the reflex circuit (sympathetic and parasympathetic).\(^{12, 13, 16}\) Moreover, more accurate information about the autonomic nervous system function can be obtained from the VM when we calculate the BRS and get an index of quantification. Experimental data\(^6\) have shown that noradrenaline and other pressor amines change the viscoelastic properties, distensibility and elastic modulus of the aorta and the carotid sinus, and could therefore alter the BRS. Yet our results show both indexes as being almost identical, suggesting that phenylephrine does not significantly alter the sensitivity of the baroreceptor reflex. The advantage of the Valsalva method, however, is that the rise in blood pressure induced during phase 4 is purely physiological. Furthermore, the injection of phenylephrine in a patient with severe hypertension or denervation hypersensitivity may not be desirable and repeated injections should also be avoided. Our technique obviates these difficulties. The BRSI obtained by both techniques was very similar, as can be seen in figure 3, with good correlation between both indexes (\( r = 0.91 \)).

The presence of square wave Valsalva maneuver would not allow calculation of the BRS by this technique. Fortunately in this study, the square wave Valsalva was not found even in patients with congestive heart failure. To our knowledge, the square wave response is a late phenomenon in the course of congestive heart failure. Patients with respiratory diseases and increased intrapleural pressures would also be disqualified. We did not have patients with idiopathic orthostatic hypotension with blocked response and absence of overshoot, but this technique could probably not be used in these cases either.

The practical consequences of our findings is that the BRSI val, being an easy, accurate, and safe procedure, can be carried out as many times as needed in the cardiac catheterization laboratory or in a clinical physiology laboratory without the need of cannulating a peripheral vein or injecting adrenergic drugs. Another interesting finding in our study was the demonstration of an inhibition of the BRS during the initial seconds after the release of the VM. It was not the aim of this study to investigate such phenomenon. Several investigators\(^{16-18, 20}\) have also described this inhibition during phase 4, but they do not offer an explanation. It has been suggested that this inhibition be the consequence of persistent activation of the adrenergic system that normally occurs during phase 2 of the VM.\(^6\) Attenuation of the vagally mediated BRS has been described during circulatory stress or increased adrenergic activity.\(^16\)

**References**

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