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Normative Data on Phases of the Valsalva Maneuver

Jong-Chyou Denq, *Peter C. O'Brien, and †Phillip A. Low

*Department of Neurology, National Defense Medical Center, Tri-Service General Hospital, Taipei, Republic of China; and *Health Sciences Research and †Department of Neurology, Mayo Clinic, Rochester, Minnesota, U.S.A.*

Summary: The phases of the Valsalva maneuver have well-known pathophysiology, and are used in the evaluation of adrenergic function. Because scant normative data is available, we have evaluated normative data for the Valsalva maneuver in control subjects. The patient, supine, performed the Valsalva maneuver maintaining an expiratory pressure of 40 mm Hg for 15 seconds. We reviewed 188 Valsalva maneuver recordings of normal control subjects, and recordings were excluded if two reproducible recordings were not obtained, or if expiratory pressure was <30 mm Hg or <10 seconds. One hundred and three recordings were acceptable for analysis; 47 female and 56 male subjects, age in years (mean ± SD) was 52.2 ± 17.3 and 44.8 ± 17.3, respectively. The association of expiratory pressure with age ($P < 0.001$) and gender ($P < 0.001$) was complex, expressed as a parabola in both men and women, but resulted in phases I and III that were not significantly different. An increase in age resulted in a progressively more negative phase II_E ($P < 0.05$) and attenuation of phase II_L ($P < 0.01$). An increase in supine blood pressure resulted in a significantly more negative phase II_E ($P < 0.001$) and a lower phase IV. Phase IV is unaffected by age and gender. **Key Words:** Valsalva maneuver—Phases—Blood pressure—Normative data—Autonomic.

In contrast to the availability of tests of cardiovagal and sudomotor functions (Low, 1993*a,c*), adrenergic function is more difficult to evaluate. Tests of adrenergic function include the measurement of plasma norepinephrine, evaluation of orthostatic blood pressure (BP) reduction, BP response to sustained handgrip, and dose-response studies of directly and indirectly acting alpha agonists (Low, 1993*b,c*). Whereas these tests are clearly useful and important, some are insensitive (plasma norepinephrine and orthostatic BP recordings), are uncomfortable, invasive (infusion studies), or lack reproducibility (Low, 1993*a,c*). The Valsalva maneuver is widely used in the assessment of adrenergic function and provides valuable information about sympathetic vasomotor and cardiomotor adrenergic function. With availability of noninvasive instruments, beat-to-beat BP monitoring during the Valsalva maneuver becomes possible and reliable. The aim of our study is to provide normative data and to examine the effect of age and gender on BP responses to Valsalva maneuver.

METHODS AND SUBJECTS

Subjects were free of disorders known to affect the autonomic nervous system and were not on any medications known to affect autonomic function (Low, 1993*a,c*). No coffee, food, or nicotine were permitted for 3 hours before the study. Prior to the study, the patients were asked to empty their bladder, and lay comfortably supine for 20 minutes. Beat-to-beat BP was monitored using a Finapres Monitor (Ohmeda, Englewood, CO) and input into a computer console that displays systolic, diastolic, and mean blood pressures (SBP, DBP, and

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Address correspondence and reprint requests to Phillip A. Low, M.D., Department of Neurology, Mayo Clinic, 811 Guggenheim Building, 200 First Street SW, Rochester, MN 55905.

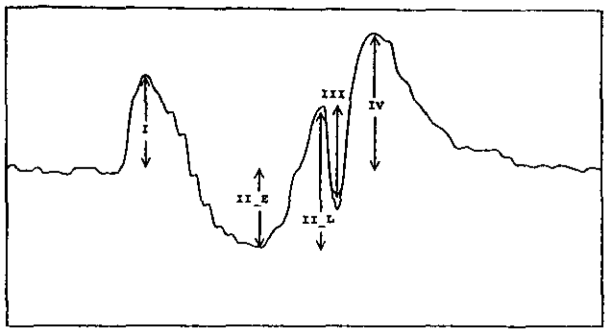

FIG. 1. Representative Valsalva maneuver. The amplitude of phase I was measured from baseline to peak. Phase II_E was measured from baseline to the trough of phase II. Phase II_L was determined from end of phase II_E to the beginning of phase III. Phase III was measured from the end of phase II_L to the trough of phase III. Phase IV was determined as its height above baseline.

MBP) continuously. The patients, supine, performed the Valsalva Maneuver, maintaining an expiratory pressure of 40 mm Hg for 15 seconds. Inclusion criteria for an acceptable recording were the following:

1. Expiratory pressure at least 30 mm Hg and 10 seconds.
2. Reproducible Valsalva maneuver BP curve, defined as maximal and minimal SBP that differed by <10 mm Hg. We also required that the configuration of phase by similar qualitatively.
3. Absence of a flat-top BP curve. This refers to a BP curve that resembled the expiratory wave form.

Recordings were made from 188 normal control subjects. Of these, 103 recordings (56 male and 47 female) satisfied the inclusion criteria and were accepted for analysis. The age in years (mean ± SD) for the male and female subjects was 52.2 ± 17.3 and 44.8 ± 17.3 respectively and were evenly distributed from ages 10 to 83 years.

Data Analysis and Statistics

The baseline values of BP (SBP, MBP and DBP) were derived from the average of 30 stable seconds before the Valsalva maneuver. The amplitude of phase I was measured from baseline to peak (Fig. 1). The reduction of early phase II (II_E) was measured from baseline to the trough of phase II. The magnitude of late phase II (II_L) was determined from end of phase II_E to the beginning of phase III. The amplitude of phase III was measured from the end of late phase II to the trough of phase III. The magnitude of phase IV was determined as its height above baseline. For the responses, the one that results from the most satisfactory expiratory pressure was accepted. If both expiratory pressure recordings were identical, we accepted the largest of the values.

We evaluated associations with age and gender using stepwise (stepping up) regression. Where gender was significant, differences in the nature of the associations and in variability were of sufficient magnitude that regressions were performed separately for male and female subjects. Using the resulting regression models, residuals from the models were used for nonparametric estimation of percentiles (O'Brien and Dyck, 1995). Because negative values do not exist for phase II_L, a default value of 0 was used when the lowest model-based percentile was 0 or less. Tests for paired data were compared using the paired t test. Data was expressed as mean ± SD (standard deviation) and significance was accepted at $P < 0.05$.

RESULTS

Expiratory Pressure and Phases I and III

Expiratory pressure varied with age ($P = 0.001$), fitted in both men and women by a parabolic model, and men had larger expiratory pressures (peaking at approximately 45 years old) than women ($P = 0.001$), whose expiratory pressure peaked at approximately 58 years old. The association was somewhat complex, because there was also an age-gender interaction ($P = 0.01$) and an age squared term ($P = 0.005$). For women:

$$\text{Expiratory pressure} = 15.001 + (0.824*X) - (0.007*X^2); \quad (1)$$

For men:

$$\text{Expiratory pressure} = 28.795 + 0.631X - 0.007X^2, \text{where X is age in years.} \quad (2)$$

However, none of associations between expiratory pressure and age and gender resulted in a significant difference in amplitude of either phase I or III, indicating that men and women of different ages generated the same standard BP perturbation.

The equations relating the clinically relevant phases of the Valsalva maneuver (phases II_E, II_L, and IV) are shown in Table 1. Where a gender effect was present the equations were provided separately.

Early Phase II

Phase II_E alterations for SBP and MBP (but not DBP) increased with age ($P < 0.001$). There was no

TABLE 1. *Table of regressions on blood pressure: effects of age and gender*

Y	Intercept	Age
Phase II_E		
MBP	−3.65	−0.13†
SBP	−3.83	−0.54†
DBP	−2.87	NS
Phase II_L (women)		
MBP	20.62	NS
SBP	26.51	NS
DBP	26.22	−0.16*
Phase II_L (men)		
MBP	34.37	−0.37†
SBP	47.85	−0.51†
DBP	26.94	−0.27†
Phase IV		
MBP	23.72	NS
SBP	38.13	NS
DBP	15.84	NS

DBP, diastolic blood pressure; MBP, mean blood pressures; NS, not significant; SBP, systolic blood pressure.

For Phase II_L, a significant gender effect was observed for MBP (P = 0.028), SBP (P = 0.045), and DBP (P = 0.025). Statistical significance: *$P < 0.05$; †$P < 0.001$.

gender difference for any of the blood pressures (Table 2). Percentiles for subjects of different ages are shown in Table 2. There is also a regression of phase II_E with supine SBP and MBP, an increase in resting BP resulting in more negative phase II_E. The relevant equations are as follows:

$$1.\ \text{Phase II\_E\_SBP} = 56.8 - 0.64 * \text{baseline SBP}. \quad (3)$$

$$2.\ \text{Phase II\_E\_MBP} = 14.2 - 0.26 * \text{baseline MBP}. \quad (4)$$

Late Phase II

Phase II_L was significantly larger in men than women (Table 1), and became progressively smaller with age in men (SBP, DBP, MBP). There was no age effect in women for MBP or SBP, and a modest slope for DBP (0.16, $P < 0.05$). The clinically relevant percentiles for phase II_L for subjects of different ages are shown in Table 3.

Phase IV

Phase IV did not vary with either age or gender (Table 4). The mean change in phase IV was 23.7 mm Hg. The 2.5th, 5th, 95th, and 97.5th percentile for MBP for phase IV were 0, 2.4, 43.3, and 47 mm Hg respectively. Phase IV was affected by resting BP, the relevant equations being:

$$1.\ \text{Phase IV\_DBP} = 45.2 - 0.40 * \text{baseline DBP}. \quad (5)$$

(6)

$$2.\ \text{Phase IV\_MBP} = 68.9 - 0.49 * \text{baseline MBP}. \quad (6)$$

DISCUSSION

The dynamic alterations during head-up tilt and the Valsalva maneuver are particularly important in detecting adrenergic failure. There are four main phases in the Valsalva maneuver. In phase I, there is a transient increase in BP caused by increased intrathoracic and intra-abdominal pressures, causing mechanical compression of the aorta (Brooker et al., 1974; Booth et al., 1962). In phase II_E, the reduced preload (venous return) (Brooker

TABLE 2. *Clinically relevant percentiles during early phase II (II_E) of the Valsalva maneuver*

Age, years	10–29	30–39	40–49	50–59	60–69	70–79	≥80
MBP; Men = Women							
Mean	−6.3	−7.6	−8.9	−10.2	−11.5	−12.8	−14.1
95th	−23.2	−24.5	−25.8	−27.1	−28.4	−29.7	−31.0
97.5th	−25.6	−26.9	−28.2	−29.5	−30.8	−32.1	−33.4
DBP; Men = Women							
Mean	−2.9	−2.9	−2.9	−2.9	−2.9	−2.9	−2.9
95th	−13.5	−13.5	−13.5	−13.5	−13.5	−13.5	−13.5
97.5th	−16.2	−16.2	−16.2	−16.2	−16.2	−16.2	−16.2
SBP; M = F							
Mean	−14.7	−20.1	−25.5	−30.9	−36.4	−41.8	−47.2
95th	−42.3	−47.8	−53.2	−58.6	−64.0	−69.5	−74.9
97.5th	−48.7	−54.1	−59.6	−65.0	−70.4	−75.8	−81.3

DBP, diastolic blood pressure; MBP, mean blood pressure; SBP, systolic blood pressure.

TABLE 3. *Clinically relevant percentiles during late phase II (II_L) of the Valsalva maneuver*

Age, years	10–29	30–39	40–49	50–59	60–69	70–79	≥80
MBP							
Men; mean	27.0	23.3	19.6	15.9	12.2	8.5	4.8
95th	13.9	10.2	6.5	2.8	0.0	0.0	0.0
97.5th	13.3	9.6	5.9	2.2	0.0	0.0	0.0
Women; mean	20.6	19.5	19.5	19.5	19.5	19.5	19.5
95th	6.0	6.0	6.0	6.0	6.0	6.0	6.0
97.5th	6.0	6.0	6.0	6.0	6.0	6.0	6.0
DBP							
Men; mean	21.6	18.8	16.1	13.4	10.7	8.0	5.3
95th	7.3	4.6	1.9	0.0	0.0	0.0	0.0
97.5th	7.2	4.5	1.8	0.0	0.0	0.0	0.0
Women; mean	23.0	21.4	19.8	18.2	16.6	15.0	13.5
95th	4.5	4.8	5.1	5.4	5.7	6.0	6.2
97.5th	4.4	4.7	5.0	5.3	5.6	5.9	6.2
SBP							
Men; mean	37.7	32.6	27.6	22.5	17.4	12.4	7.3
95th	15.6	10.5	5.5	0.4	0.0	0.0	0.0
97.5th	15.1	9.9	4.9	0.0	0.0	0.0	0.0
Women; mean	26.5	26.5	26.5	26.5	26.5	26.5	26.5
95th	8.0	8.0	8.0	8.0	8.0	8.0	8.0
97.5th	5.0	5.0	5.0	5.0	5.0	5.0	5.0

DBP, diastolic blood pressure; MBP, mean blood pressure; SBP, systolic blood pressure.

et al., 1974) and reduced stroke volume (Brooker et al., 1974) lead to a decrease in cardiac output in spite of compensatory tachycardia (Corbett, 1969) from withdrawal of cardiovagal tone (Candel and Ehrlich, 1953). Total peripheral resistance increases (Korner et al., 1976) as a result of efferent sympathetic discharge to muscle (Delius et al., 1972), and within 4 seconds after the increase in sympathetic discharge, the decrease in BP is arrested (Delius et al., 1972). This is phase II_L. In healthy subjects phase II_L is so efficient that by the beginning of phase III, MBP is at the resting MBP level or above. Phase III, like phase I, is mechanical, lasting 1 to 2 seconds, during which BP decreases (Brooker et al., 1974; Booth et al., 1962). The major mechanism is the sudden decrease in intrathoracic pressure. Additional factors may be an increase in left ventricular afterload (Buda et al., 1979), and sudden expansion of intrathoracic vessels (Eckberg, 1980). There is a further burst of sympathetic activity during this phase (Wallin and Eckberg, 1982). Phase IV, in the clinical autonomic labora-

TABLE 4. *Clinically relevant percentiles during phase IV of the Valsalva maneuver*

Age, years	10–29	30–39	40–49	50–59	60–69	70–79	≥80
MBP; M = F							
Mean	23.7	23.7	23.7	23.7	23.7	23.7	23.7
97.5th	47.0	47.0	47.0	47.0	47.0	47.0	47.0
95th	43.3	43.3	43.3	43.3	43.3	43.3	43.3
5th	2.4	2.4	2.4	2.4	2.4	2.4	2.4
2.5th	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DBP; M = F							
Mean	15.8	15.8	15.8	15.8	15.8	15.8	15.8
97.5th	37.9	37.9	37.9	37.9	37.9	37.9	37.9
95th	32.9	32.9	32.9	32.9	32.9	32.9	32.9
5th	0.0	0.0	0.0	0.0	0.0	0.0	0.0
2.5th	0.0	0.0	0.0	0.0	0.0	0.0	0.0
SBP; M = F							
Mean	38.1	38.1	38.1	38.1	38.1	38.1	38.1
97.5th	78.3	78.3	78.3	78.3	78.3	78.3	78.3
95th	74.3	74.3	74.3	74.3	74.3	74.3	74.3
5th	3.6	3.6	3.6	3.6	3.6	3.6	3.6
2.5th	0.0	0.0	0.0	0.0	0.0	0.0	0.0

DBP, diastolic blood pressure; MBP, mean blood pressure; SBP, systolic blood pressure.

tory setting, with the patient lying supine, is primarily dependent of cardiac adrenergic tone (Sandroni et al., 1991). Intravenous phentolamine 10 mg resulted in the expected elimination of late phase II, but *augmented* rather than blocked phase IV. In contrast, the intravenous administration of 10 mg propranolol completely blocked phase IV (Sandroni et al., 1991). Peripheral adrenergic tone could contribute by maintaining arteriolar vasoconstriction when cardiac output has returned to normal.

There were differences in expiratory pressure by age and gender, men having slightly larger expiratory pressures than women, with the highest pressures attained at women at an older age. The magnitude of expiratory pressure should not be confused with expiratory capacity or power. These were the pressures generated when patients were requested to attain and maintain an expiratory pressure of 40 mm Hg for 15 seconds. The reasons for the age and gender effects are speculative. Of greater pragmatic importance is the fact that these differences did not translate into any differences in either phase I or III, suggesting that these differences in expiratory pressure resulted in equivalent mechanically induced BP changes responsible for phases I and III. Perhaps there is an equivalency of effort; the smaller woman generated a smaller expiratory pressure but the effort was relatively greater, resulting in the same BP changes as a man.

We should address the issue for the large number of patients that have been excluded from analysis. Because normative data on the phases of the Valsalva maneuver for a large group of controls does not seem to be available, we accepted for analysis only those subjects who fulfilled strict entry criteria. These subjects had Valsalva maneuver waveforms, whose peak and minimal SBP varied by < 10 mm Hg, and had similar morphology of the phases. We excluded subjects who had arterial pressures that increased and decreased with the expiratory pressure ("flat-top" response). These excluded subjects performed adequate expiratory pressures and their data is interpretable in a semiquantitative way in the clinical laboratory. Because the quantitative measurements of the phases are less accurate, they have been excluded from this study.

The selection of parameters measured has been confined to those with a proven physiologic basis and has been found to be useful in the clinical autonomic laboratories. Other approaches have been recommended. Approaches relating baroreflexes to latencies of BP and heart rate responses can be increased in autonomic neuropathies (Ferrer et al., 1991), but because the physiologic basis has not been validated, we have not adopted the approach. Changes in heart period in response to corresponding changes in BP could reflect alterations in baroreflex gain. We are currently evaluating the relationship of baroreflex gain determined using standardized methods and microneurography of a limb nerve with BP–heart period changes during the Valsalva maneuver. Once the quantitative relationship between the methods is established, it might be necessary to analyze the quantitative relationship between heart period and BP for the maneuver.

Our findings that phase II_E varies with baseline BP is consonant with a recent report (Piha, 1995). We recommend that evaluation of BP responses should be based on MBP (Low, 1993*c*) which is less variable than SBP and DBP as has been used by other investigators (Braune et al., 1996). There is a progressive attenuation of II_E and a reduction in II_L with increasing age, a finding that was found in an earlier study (Piha, 1995). These data indicate that changes in II_E should be interpreted with caution in hypertensive patients. Early phase II depends on preload and cardiomotor function. The increase with age could be related to the known impairment with age of cardiovagal function and peripheral adrenergic function. The regression equation of age-related normal limits of MBP in II_E, II_L and IV were: $-47 + 0.3x$, $2.4 - 0.02x$, and $1.7+0.01x$. The lower 95th percentile at age of 60 was -29 and 1.2 mm Hg for II_E and II_L (Piha, 1995). These reference limits are similar with our results. The range of ages was 25 to 60 years.

Phase II_L attenuates with increasing age, so that an absent response is not abnormal in patients older than 60 years. Although this phase results from baroreceptor unloading with consequent peripheral adrenergic activation (Ebert et al., 1992), these findings should be reconciled with the known increase in plasma norepinephrine (Roberts and Turner, 1987; Ziegler et al., 1976) with aging, and the reports that muscle sympathetic nerve activity to the peroneal nerve remains unchanged (Ebert et al., 1992) or becomes mildly attenuated (Iwase et al., 1991) with age. Adrenoreceptors show reduced potency with aging (Elliott et al., 1982; Hyland and Docherty, 1985). There is an increase in supine BP with age in this group of controls (Low et al., 1997), and the decreased in BP on standing is significantly dependent on supine BP (Gert van Dijk et al., 1994). There are also structural and functional changes in the circulation itself, and to an impaired skeletal muscle pump (Smith et al., 1994), which declines with aging (Booth et al., 1994; Rogers and Evans, 1993). In sum, these data are best interpreted as indicating that phase II_L represent vasomotor tone and that the major contributor is sympathetic adrenergic activity, modulated significantly by a number of factors.

The phase IV BP response of the Valsalva maneuver, measured intra-arterially, was found to be reduced with increasing age (Ingall et al., 1990). Our data indicate that phase IV has no age or gender effects and these findings also noted in other reports. Other investigators have noted that the initial decrease of SBP and DBP in passive head-up tilt and the decrease of SBP during phase II of Valsalva maneuver correlated significant with their baseline values (Piha, 1995; Braune et al., 1996). Phase IV, with the patient supine is mainly caused by cardiac adrenergic activation (Sandroni et al., 1991) and is unimpaired with increasing age, but is affected negatively by an increase in BP.

In conclusion, the use of phases of the Valsalva maneuver should incorporate the effects of age and gender. A loss of phase II_L is abnormal at any age for women, and for men below the age of 60 years. Men over the age of 60 years can have absence of II_L but likely have peripheral adrenergic failure if this is associated with II_E in excess of 30 mm Hg MBP. Phase IV can be negligible with the maneuver performed in the supine position. It is affected by antecedent BP. If the preceding decrease in BP in phase II_E is large (> 30 mm Hg MBP), then an absent IV is abnormal.

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