

*LETTER TO THE EDITOR*

**GENDER DIFFERENCES IN VASOCONSTRICTOR RESERVE**

Sir,

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The incidence of neurally mediated syncope is known to be greater in women (1). Vasoconstrictor reserve (VCR), i.e. the extent to which total peripheral vascular resistance can be increased from baseline conditions, has been suggested to be an important determinant of orthostatic tolerance (2). A decrease in VCR assessed in terms of changes in forearm vascular resistance during lower body negative pressure (2), head-up tilt (3) and dynamic exercise (4) has been reported in patients with syncope. Studies have shown gender differences in autonomic regulation (5, 6). It has been shown that women have lower autonomic support of blood pressure (6). Whether there are gender differences in VCR is not known. Therefore, in the present study, we tested the hypothesis that there are gender differences in VCR.

In principle, VCR should be determined by maximal activation of sympathetic drive to resistance. Fu et al (2) tested the hypothesis that VCR is a determinant of orthostatic tolerance; orthostatic tolerance was assessed using lower body negative pressure, and VCR was assessed using the cold pressor test during 60 degrees head-up tilt. However, in the present study, we determined VCR by measuring the pressor response (specifically, the increment in diastolic pressure) to sustained isometric handgrip (rather than cold pressor test)

during 70 degrees head-up tilt, i.e. when the sympathetic nervous system is already activated. That is why the term 'reserve' is used. We used isometric handgrip rather than the cold pressor test to activate the sympathetic drive to blood vessels instead of cold pressor test because in a previous study from our laboratory, we found the diastolic pressure response to isometric handgrip to be greater than the response to cold pressor test in healthy normotensives (7). Furthermore, since isometric contractions of antigravity muscles help maintain upright posture, and muscle tensing has been shown to be useful in aborting impending syncopal attacks (8, 9), the use of isometric handgrip to elicit vasoconstrictor reserve seems more logical.

Tests were done in the morning 2-3 hours after a light breakfast. None of the subjects were taking any medication and none had a significant medical history. To control for age and body mass index, two important factors influencing pressor responses, we studied age and body mass index matched healthy volunteers. Maximal voluntary contraction (MVC) was noted as the maximum pressure (in mm Hg) sustained during three seconds of handgrip using a handgrip dynamometer. Resting heart rate and blood pressure were recorded after five minutes rest in the supine position. Blood pressure was measured with an

automated noninvasive BP monitor (Colins Press-Mate Inc., Japan). VCR was determined by asking the subject to sustain isometric handgrip at 1/3rd of MVC for at least 2 minutes using a handgrip dynamometer after 5 minutes of 70 degrees head-up tilt, i.e. when blood pressure, and heart rate attained steady state (data not shown), while the subject remained tilted. VCR was noted as the difference between maximum diastolic pressure at the end of 2 minutes sustained isometric handgrip during head-up tilt minus baseline diastolic pressure in the supine position. The study protocol was approved by the Institute Research Committee of Jawaharlal Institute of Postgraduate Medical Education and Research, Pondicherry, and the local ethics committee, and all subjects gave informed consent. Gender differences were tested using unpaired *t*-test. The null hypothesis was rejected if the two-tailed P value was less than 0.05.

All data are presented in Table I. Both MVC and VCR were significantly higher in males ( $P < 0.0001$  and  $0.0002$  respectively). However, there were no gender differences in VCR after correcting for differences in MVC ( $P = 0.94$ ). It is worth noting that whereas differences in baseline heart rate and blood pressure were insignificant ( $P > 0.1$  for all), gender differences in VCR were highly significant ( $P = 0.0002$ ).

First, the study provides evidence that VCR is lower in females. The fact that there is no gender difference in VCR after correcting for differences in MVC suggests that MVC is a major determinant of VCR. This may partly explain the increased predilection of females to neurally mediated

TABLE I: Subjects' baseline characteristics, maximal voluntary contraction and vasoconstrictor reserve. Data are the means  $\pm$  SD.

<i>Parameter</i>	<i>Males (n=11)</i>	<i>Females (n=9)</i>	<i>P value</i>
Age (yr)	20.5 $\pm$ 0.9	20 $\pm$ 0.5	0.21
Body mass index (kg/m <sup>2</sup> )	21.2 $\pm$ 1.6	21.9 $\pm$ 3.2	0.49
Systolic pressure (mm Hg)	114 $\pm$ 7	111 $\pm$ 10	0.44
Diastolic pressure (mm Hg)	62 $\pm$ 4	62 $\pm$ 7	0.93
Heart rate (beats per minute)	75 $\pm$ 14	84 $\pm$ 10	0.13
Maximum voluntary contraction (kg)	36 $\pm$ 5	23 $\pm$ 3	<0.001
Vasoconstrictor reserve (mm Hg)	45 $\pm$ 8	28 $\pm$ 7	0.0002

syncope; however, this hypothesis needs to be tested in patients with syncope. Further, it must be noted that the subjects examined in this small study were aged between 19 and 23 years, and the magnitude of gender differences in VCR also needs to be tested across other age groups. Second, this study establishes the use of sustained isometric handgrip during head-up tilt as a simple laboratory model for evaluating VCR, and this will serve as a prelude to studies on patients (for example, syncope) in whom it is likely to be diminished.

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definition of VCR used here and its significance; Prakash wrote the first draft of the manuscript. All contributors read and

approved the final form of the manuscript. Prakash acts as guarantor for the research reported here.

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