National Journal of Physiology, Pharmacy and Pharmacology

RESEARCH ARTICLE

A cross-sectional study of gender differences in cardiovascular responses to orthostatic tolerance test in adolescents

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Received: May 21, 2019; **Accepted:** June 21, 2019

ABSTRACT

Background: Clinical data show higher incidence of postural hypotension in women than men. Clinicians make use of orthostatic tolerance test (OTT) to investigate such a situation and also in other varieties of clinical disorders ranging from most common disorders such as diabetes, hypertension leading to autonomic neuropathy to very rare disorders such as Shy-Drager syndrome and dysautonomias. This study will help to assess gender differences in cardiovascular response to orthostatic challenge. **Aims and Objectives:** The objective of the study was to evaluate the gender differences in cardiovascular responses such as change in systolic blood pressure (BP), diastolic BP, heart rate (HR), and mean arterial pressure (MAP) during OTT in 16–20 years of age group. **Materials and Methods:** The present cross-sectional study was conducted in 34 males and 36 female students of the age group of 16–20 years. The autonomic test used to assess orthostatic tolerance was OTT which is widely used for routine clinical evaluation of autonomic dysfunction. HR and BP changes during the orthostatic challenge were recorded, and 30:15 ratio was calculated from R-R interval of electrocardiogram ECG recording during the challenge. **Results:** Among the baseline parameters of males and females only HR, diastolic BP, and MAP were comparable. BP response during orthostatic challenge showed that MAP was significantly lower for females than males ($P < 0.05$). HR response was not statistically significant. **Conclusion:** The values being significantly lower for females than males this study helped to support the fact that women have less responsiveness to BP regulation during an orthostatic challenge in adolescents.

KEY WORDS: Gender; Orthostatic Challenge; Orthostatic Tolerance Test, Autonomic Dysfunction

INTRODUCTION

Orthostatic hypotension and fainting are much more common in young women than in young men. By their early 20s, survey research indicates that almost 50% of young women report at least one episode of orthostatic intolerance or fainting, whereas only 25% of young men report similar symptoms.[1] In addition, clinically documented hypotensive disorders of blood pressure (BP) regulation are far more common in women than in men.[2] Study done to evaluate the effect of gender on autonomic regulation have shown that males have higher sympathetic control on cardiovascular regulatory mechanisms than females as reflected by high systolic BP (SBP), diastolic BP, and cardiac output in men during the stress.[3] Other study was done to assess the effect of gender on different parameters of sympathetic activity such as vascular tone, cardiac ejection, and arterial pressure suggest that men have predominant control of sympathetic vascular regulation.[4] This study also suggests that women show dominant parasympathetic influence on heart rate (HR)

Access this article online	
Website: www.njppp.com	Quick Response code
DOI: 10.5455/njppp.2019.9.0519121062019	

regulation.[4] Women have a lower central sympathetic neural output to the periphery and also demonstrate an attenuated vasoconstrictor effect of efferent sympathetic nerve activity during the autonomic challenge.[5]

Regarding orthostatic tolerance, women have less responsiveness in mechanisms that underlie BP regulation under orthostatic challenge.[6] Studies done in this regard show that women have a less sympathetic influence on BP and greater parasympathetic influence on R-R interval during orthostatic stress than men.[7] Frequency domain analysis of HR variability in supine and standing position in males and females shows significantly higher values of low frequency (LF) for males than women and that high frequency (HF) power in normalized units (HFn) was larger in females.[8,9] Another study done in the same context shown that HF/LF ratio was significantly higher in the adolescent and adult females compared to male of these age groups.[10] In the same study finding that gender differences are limited to adolescent and adult age groups may indicate a role for female sex hormones in cardiac autonomic modulation.[10]

Clinical data show higher incidence of postural hypotension in women than men.[1,2] Study conducted to investigate these clinical finding shows that women have a more active parasympathetic system, higher estrogen levels, and a lower center of gravity.[11] Thus, women compensate for the drop of BP in response to positional change less effectively.[11] Therefore, considering above studies it can be stated that women have more dominant parasympathetic and men have dominant sympathetic regulation of cardiac activity and this fact is supported by a study conducted to assess gender differences in the neural control of HR.[12] However, certain studies fail to support such findings or rather contradict the findings.[13,14]

Thus, the above-mentioned findings suggest the differential role of gender on cardiovascular regulation. Although men and women have different cardiovascular regulation, conclusive data are lacking about the effect of gender on differences in cardiovascular responses to autonomic stressor tests in Indian adolescent population; hence, this study is conducted to evaluate the influence of gender on autonomic responses during orthostatic tolerance test (OTT) in Indian adolescent population.

MATERIALS AND METHODS

The present cross-sectional study was conducted under the auspices of the Department of Physiology. In the present study, the data were collected from healthy adolescent male and female students of age group of 16–20 years. A total of 70 subjects (34 males and 36 female) volunteers were recruited as study participants.

Inclusion Criteria

Healthy males and female students of the age group 16–20 years who are free from any medical disorders were included in the study.

Exclusion Criteria

The following criteria were excluded from the study:

1. Students with neurological impairment or any other disease including respiratory, cardiac, and neurological disorders
2. Students on any medication
3. Students practicing yoga and regular exercises including isometric hand grip exercises
4. Students having H/O substance abuse such as smoking and alcohol.

The study was approved by Institutional Ethics Committee on human subject research. After the selection students were briefed about the nature of the study and written informed consent was obtained.

Personal details as name, age, sex, occupation, contact number, and history of any medical illness were obtained. The anthropometrical data measured were height in cm, weight in kg, and body mass index was calculated.

Baseline parameters of participants such as HR and BP were recorded after complete rest of 15 min, with the help of automatic BP monitor OMRON model – HEM-7111 Manufactured by OMRON HEALTH CARE Co., Ltd. 24, Yamanouchi Yamanoshita-cho, Ukyo-ku, Kyoto, 615-0084 Japan. Electrocardiogram (ECG) is recorded with the help of INCO II channel Digital Physiograph model: EPR – 2 manufactured by NIVIQURE, Bengaluru and Instruments and Chemicals Pvt. Ltd., Model Town, Ambala City – 134003, Haryana.

General precautions followed before conducting autonomic function tests,

1. Before autonomic function testing, participants were advised not to be on fasting
2. Not to take tea/coffee or other beverages which are likely to affect autonomic function
3. Participants were advised to remain relaxed throughout the test.

OTT and 30:15 ratio – in this test, autonomic stress is induced by changing the position from lying down to standing actively. The normal response seen is initially increase in HR followed by a decrease in HR. Fall in BP is observed. Standing up from a lying or sitting position creates a gravitational gradient with blood accumulation in the lower body parts, decrease in central blood volume, and BP. Compensatory effects including, among others, the baroreflex-mediated

BP regulation (parasympathetic withdrawal and sympathetic activation) maintain an adequate BP.

The subject is instructed about the test. With the subject lying quietly in the supine position baseline BP, HR is recorded. The subject is then asked to attain a standing position within 3 sec unaided for 2 min and after that to again come back to the supine position. BP and HR are recorded at an interval of 30 s for 2 min and also during the recovery phase. 30:15 ratio is calculated from ECG recording obtained during standing [Figure 1].

In this test after standing shortest R-R interval at or around the 15th beat and the longest R-R interval at or around 30th beatare measured, and the HR response is expressed as the 30:15 ratio.

Statistical analysis was performed with SPSS software version 16.0 and involved quantitative variables summarized through mean and standard deviation. Difference between the mean of the two groups was tested using Student's unpaired *t*-test, where the significance of $P < 0.05$.

RESULTS

Table 1 shows the baseline values of males and females. Among all only HR, DBP, and mean arterial pressure (MAP) were comparable.

Table 1: Baseline values of males and females

Gender	Heart rate	SBP	DBP	MAP
Males	69.7±7.9	119.2±10	63.5±5.8	82±6.4
Female	71.7±9.5	109.5±9.3	65.6±7.9	80.2±7.9
P value	0.344	< 0.001*	0.22	0.292

(*) $P<0.05$. SBP: Systolic blood pressure, DBP: Diastolic blood pressure, MAP: Mean arterial pressure

Table 2 shows the MAP values of males and females during OTT. The baseline values of MAP during OTT were not different for males and females ($P > 0.05$). MAP response during OTT shows an initial increase and followed by fall. The absolute MAP values during standing show a significant difference in both the groups. The values were lower for females than males, and the difference was statistically significant ($P < 0.05$).

Table 3 shows that baseline values of SBP were higher for males than females ($P < 0.05$). Absolute SBP values show a significant difference in males and females both during and after the test. DBP values during the test show no significant difference in males and females.

HR response and 30:15 ratio – Table 4 shows HR values of males and females during OTT. The baseline values of HR during OTT were not different for males and females ($P > 0.05$). HR changes during and after the test show no significant difference in males and females; the values were not statistically significant ($P > 0.05$). 30:15 ratio was also not significantly different in males and females ($P > 0.05$).

DISCUSSION

This study was done to evaluate gender differences in cardiovascular responses to OTT in adolescents. In OTT, the mean baseline values of MAP, DBP, and HR did not differ significantly between males and females, but baseline values of SBP were different in males and females. Thus, the outcomes of MAP, DBP, and HR were compared during OTT. BP responses during OTT show that MAP values of females were significantly lower than males during the test; SBP was also higher for males than females during OTT but was not comparable due to differences in baseline values. DBP during the OTT did not show any significant difference

Table 2: MAP change during OTT of male and female

Gender	MAP Baseline	MAP during test				MAP after test		
		30 s	1 min	1 ½ min	2 min	1 min	2 min	3 min
Males	82±6.4	92.7±7	89.6±6.5	89.6±5.9	88.5±5.64	80.9±7.2	80.4±6.4	79.4±5.8
Female	80.2±7.9	87.5±9	86.1±9.3	85.5±9.5	84.6±8.08	79.5±8	78.5±7.8	78.5±8.2
P value	0.292	0.009*	0.082	0.034*	0.024*	0.458	0.286	0.612

(*) $P<0.05$. MAP: Mean arterial pressure, OTT: Orthostatic tolerance test

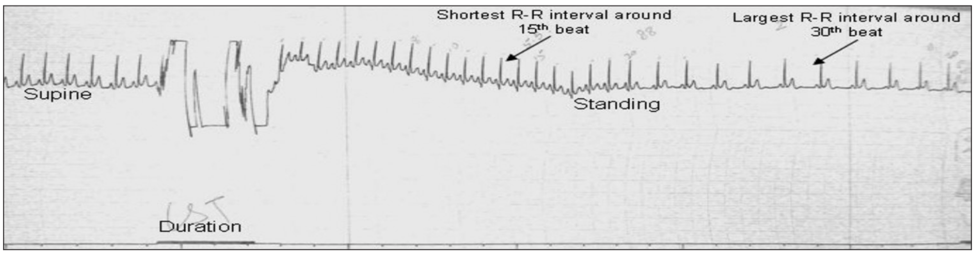

Figure 1: Electrocardiogram recording during test

Table 3: SBP change during OTT of male and female

Gender	Baseline SBP	SBP during test				SBP after test		
		30 s	1 min	1 ½ min	2 min	1 min	2 min	3 min
Males	119.2±10	128.3±11.5	120.2±10.4	120.5±8.2	120.2±7.4	118.7±9.3	118.3±8.7	117.7±8.6
Female	109.5±9.3	115.4±12	111.7±12.3	111.5±11.8	109.2±9.6	109.1±9.7	108.6±10.1	108.7±10.2
P value	<0.001	<0.001	0.003	<0.001	<0.001	<0.001	<0.001	<0.001

SBP: Systolic blood pressure, OTT: Orthostatic tolerance test

Table 4: HR values and 30:15 ratio during OTT of male and female

Gender	Baseline HR	During test				After test			30:15 ratio
		30 s	1 min	1 ½ min	2 min	1 min	2 min	3 min	
Males	69.7±7.9	83±11.3	89.5±12.1	90.2±11.5	89.1±10.7	71.4±8.4	70.2±7.6	69.1±7.2	1.52±0.216
Female	71.7±9.5	85.1±12.1	89.1±13.1	88.6±12.6	90.1±11	72.1±9.5	70.2±9.6	69.4±9.2	1.51±0.171
P value	0.344	0.456	0.875	0.591	0.731	0.747	0.984	0.893	0.708

(*) $P<0.05$. HR: Heart rate, OTT: Orthostatic tolerance test

in males and females. HR response during OTT did not show any significant difference in males and females. 30:15 ratio was also not statistically significant for males and females. Thus, this result supports the findings of an earlier study that females have less responsiveness in mechanisms that underlie BP regulation during orthostatic challenge than males.[6]

Barnett *et al.* showed that healthy women have a less sympathetic influence on BP and greater parasympathetic influence on R-R interval than men during orthostatic stress induced by head-up tilt (HUT) test.[7] Regarding the studies done in concern to establish the mechanism of gender differences in cardiovascular response to orthostatic stress by Fu *et al.* concluded that lower orthostatic tolerance in women is associated with decreased cardiac filling rather than reduced responsiveness of vascular resistance during orthostatic challenges.[15] Fu *et al.* showed that women have blunted sympathetic neural responses to orthostatic stress compared with men which are probably due to smaller stroke volume, presumably due to less cardiac filling during orthostasis.[16]

Few studies also incorporate various different methods to induce orthostatic stress to assess the gender difference. These methods are lower body negative pressure (LBNP) wherein orthostatic stress is induced by subjecting the lower body to negative pressure which creates negative pressure in legs and pelvic region which simulates the orthostasis, and a 2nd method called as HUT using tilt table. Studies conducted by (1) White *et al.*, (2) Gotshall and Montgomery *et al.* showed that women compensate less effectively to orthostatic stress induced by LBNP.[15,17-19] However, studies conducted by Mellingsæter *et al.* and Brunetto *et al.* fail to support such findings or rather contradict the findings.[13,14] Probably because in the earlier study was conducted in elderly individual and in the later study, subjects were subdivided according to aerobic fitness, which could be the cause of different findings.

Thus, these studies show that women compensate to orthostatic stress less effectively than men. In the present study also MAP shows significantly lower values in females than males. MAP is a major important determinant of baroreceptor sensitivity in various cardiovascular reflexes, including BP regulation. In our study also showed lower SBP values in females than males. Thus, our study supports similar findings in BP responses to orthostatic stress induced by active standing. Clinicians make use of OTT more commonly to evaluate the cases of orthostatic hypotension in adolescents. Hence, it is suggested that gender differences should be taken into account while performing these tests in adolescent patients suffering from orthostatic hypotension.

Strength

1. This pilot study could be a good basis for future full-scale studies with a larger sample size it would be possible to uncover gender difference in adolescent population more conclusively, which remained possibly undetected in the present study in Indian adolescents
2. In present study supine to standing test was used to provide orthostatic challenge, whereas many other investigators used head-up tilt test or application of LBNP, which makes our results not fully applicable to theirs and could also contribute to the differences in our findings.[13,14] However, standing up from a sitting position is an everyday challenge in the lives of every person, and therefore, a supine to standing test represents a more realistic life situation than the above-mentioned methods.

Limitations

1. A limitation of this study was the small sample size
2. The present study also does not investigate the possible mechanisms of difference observed.

CONCLUSION

The BP responses to orthostatic challenge test are different in males and females. The values were significantly lower for females than males. This study helped to support the fact that women have less responsiveness to BP regulation during the orthostatic challenge. Gender differences should be taken into account while performing OTT.

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How to cite this article: Barawade AA, Patil P. A cross-sectional study of gender differences in cardiovascular responses to orthostatic tolerance test in adolescents. Natl J Physiol Pharm Pharmacol 2019;9(9):869-873.

Source of Support: Nil, **Conflict of Interest:** None declared.