



Water ingestion affects orthostatic challenge-induced blood pressure and heart rate responses in young healthy subjects: gender implications

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Summary: Evidence exists that women have lower orthostatic tolerance than men during quiescent standing. Water ingestion has been demonstrated to improve orthostatic tolerance in patients with severe autonomic dysfunction. We therefore sought to test the hypothesis that water ingestion would improve orthostatic tolerance in healthy young women more than in aged-matched men. Thirty seven (22 men and 15 women) healthy subjects aged 22.5 ± 1.7 and 21.5 ± 1.4 (means \pm SD) respectively, ingested 50ml (control) and 500ml of water 40min before orthostatic challenge on two separate days of appointment in a randomized controlled, cross-over design. Seated and standing blood pressure and heart rate were determined. Orthostatic tolerance was assessed as the time to presyncope during standing. Ingesting 500ml of water significantly improves orthostatic tolerance by 22% (32.0 ± 5.2 vs 26.2 ± 2.4 min; $p < 0.05$) in men and by 33% (24.2 ± 2.8 vs 18.3 ± 3.2 ; $p < 0.05$) in women. Thirty minutes after ingesting 500ml of water, seated systolic blood pressure, diastolic blood pressure, pulse pressure and mean arterial pressure rose significantly in men while only systolic blood pressure and pulse pressure rose significantly in women. However ingesting 500ml of water did not have significant effect on seated heart rate in both men and women. Ingestion of 500ml of water significantly attenuated both the orthostatic challenge-induced increased heart rate and decreased pulse pressure responses especially in women. Diastolic blood pressure tended to be positively correlated with orthostatic tolerance strongly in men than in women. Pulse pressure correlated positively while heart rate correlated negatively to orthostatic tolerance in women but not in men independent of other correlates. Water ingestion is associated with orthostatic tolerance strongly in women but weakly in men independent of other correlates. In conclusion, the findings in the present study demonstrated that water ingestion caused improvement strongly in young women than in young men. This improvement is associated with increased pulse pressure and decreased tachycardiac responses during orthostatic challenge.

Keywords: Gender, Heart rate, orthostatic challenge, Pulse pressure, Water ingestion

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INTRODUCTION

When individuals assume an upright posture, blood progressively pools in the compliant veins of the lower limbs. This action decreases central blood volume and the return of venous blood to the heart is decreased, resulting in reduced stroke volume and cardiac output, subsequently elicits orthostatic challenge by challenging blood pressure (Brown and Hainsworth, 1999; Smit *et al.*, 1999). It has been reported that orthostatic challenge translocates $\frac{1}{2}$ to 1 litre of thoracic blood to the region below the diaphragm (Smit *et al.*, 1999). A reduction in arterial pressure despite the fall in cardiac output is prevented by compensatory sympathetic-mediated tachycardia and vasoconstriction that compensate for the

gravitational reduction in venous return and stroke volume (Brown and Hainsworth, 1999; Fu, *et al.*, 2005). Hence, individuals with posturally-related hypotension and syncope fail to maintain adequate arterial pressure during orthostatic challenge. Orthostatic tolerance is a measure of an individual's ability to prevent hypotension, inspite of the venous pooling and plasma transudation which occurs during standing or other simulated gravitational stress (Hainsworth, 1985; Smit *et al.*, 1999; Brown and Hainsworth, 2000). However, if the stress is too enormous or too prolonged, ability to maintain a normal level of arterial blood pressure fails, leading to hypotension and possibly syncope (Hainsworth, 1985). The inability of a person to prevent hypotension during orthostatic challenge is referred

to as orthostatic intolerance. It has been clearly demonstrated that women, primarily young women, are susceptible to orthostatic intolerance than men (Robertson, 1999; Fu, *et al.*, 2004, 2005). Studies suggested that women might have stronger chronotropic response to orthostatic challenge, where as men might have greater sympathetic-mediated vascular response to orthostatic challenge (Fu, *et al.*, 2004, 2005). This speculation was supported by the observation that women demonstrated greater tachycardiac response than men (Convertino, 1998; Shoemaker, *et al.*, 2001; Fu, *et al.*, 2004), but was not in accordance with the observation that vascular response to orthostatic challenge was comparable for both sexes (Convertino, 1998; Shoemaker, *et al.*, 2001; Fu, *et al.*, 2004).

Another factor which has been shown to influence orthostatic challenge is the plasma volume and blood volume (El-sayed and Hainsworth, 1995; Claydon *et al.*, 2004). Under circumstances such as blood donation, orthostatic intolerance has important medical or and societal relevance. Over 150,000 people experience orthostatic intolerance or syncope yearly during blood donation to the American Red Cross (Tavernier-Trend, *et al.*, 1999). Intervention that would improve orthostatic tolerance could exert a beneficial impact on donor's safety, convenience and interest to donate again. The main interventions to prevent orthostatic intolerance in blood donation facilities are focused on post-donation food and beverage with little emphasis on pre-donation factors such as water ingestion.

Most individual do not have syncope frequently and do not require aggressive treatment, however, some individuals with frequent syncopal episodes do require therapeutic approaches. Unfortunately, most pharmacological interventions do not result in significant symptomatic improvement and are expensive and associated with adverse effects (Kapoor, *et al.*, 1994; Sheldon, 2000). Alternative interventions which can increase blood volume may be helpful to improve orthostatic tolerance both for patients with autonomic dysfunction (El-sayed and Hainsworth, 1996; Mtinangi and Hainsworth, 1999; Shanon, *et al.*, 2002; Fu, *et al.*, 2005), and presumably for otherwise healthy.

Drinking water, one of the most basic human daily activities, has recently been found to have unexpected haemodynamic effects, and it seems this may be of great public health relevance especially in persons with poor orthostatic tolerance (Jordan, *et al.*, 2000; Schroeder, *et al.*, 2000; Shannon, *et al.*, 2002; Lu, *et al.*, 2003; Fu, *et al.*, 2005). However, the effectiveness of this simple, readily available, safe and cost-free intervention has not been examined in

young adults, particularly with gender implication. We therefore sought to test the hypothesis that water ingestion would improve orthostatic tolerance in healthy young women more than in age-matched men. We also sought to determine the influence of gender on pressor and chronotropic responses to water drinking during orthostatic challenge in young healthy subjects.

MATERIALS AND METHODS

Subjects

Fifteen (15) healthy young women and twenty-two (22) men matched for age and weight participated in the study. They were all normotensive individuals taking no regular medication (including steroid hormonal contraception) or had medical problems. None was a trained athlete and obese, but are physically active individuals. No woman was pregnant during the study, all had regular menstrual period of about 28 days. Subjects were screened with a careful history, physical examination and ECG to establish normal cardiovascular or neurological functions. All participants were informed of the purpose and procedure used in the study and gave their written informed consent to the protocol before participating in the study. The summary of the descriptive data for the participants in both groups is presented in Table 1.

Experimental Protocol

In a randomized, cross-over design, each participant underwent the determination of orthostatic tolerance twice on separate days of appointment between 8 am and 12 noon at room temperature in order to avoid circadian autonomic variation. Participants abstained from alcohol, caffeine-containing drinks and strenuous exercise for at least 24hr prior the study. Participants had an overnight fast for 12hr, and were asked to empty their urinary bladder before starting the study in order to avoid any effect of urinary bladder or stomach distension, which are known to affect peripheral sympathetic discharge. Baseline data were obtained during a 10min period of quiet sitting, after which participants drank either 50ml (control intervention) or 500ml of drinking water at room temperature. Participants remained seated for additional forty minutes. They were then asked to assume an upright position. The test protocol was terminated at the participants' request with associated presyncope symptoms (dizziness, lightheadedness, weakness, blurred vision, impairment of concentration). Orthostatic tolerance was determined as the time (min) the participant cannot continue the orthostatic challenge. Cardiovascular responses that

lead to early termination of the postural challenge were graded by two blinded investigators.

Subjects were asked to be in an upright posture after 40min in seated position on the 1st day of appointment with the before ingestion of 50ml or 500ml of water at room temperature. This procedure was repeated on the 2nd day of appointment with the ingestion of alternative volume of water at room temperature. Subjects were made to sit in a chair in a relaxed position and not to talk. Supervision of the subjects was continuous to avoid any manoeuvres, such as postural sway (crossing of legs or calf contractions) (Ten-Harkel *et al.*, 1994; Claydon and Hainsworth, 2005). Study sessions took place in a quiet, dimly lit laboratory at a comfortable ambient temperature (28±2°C).

Measurements

The recordings were taken at 0, 10, 20, 30 and 40min in seated position and during standing at 1, 5, 10min and at termination/presyncope. Heart rate was determined from R-R interval obtained from a standard electrocardiogram. Systolic and diastolic pressures were measured using electrophygmomanometry (Seinex, SE-7000, Belfast, BT153HN, UK). Pulse pressure was determined by deducting diastolic pressure from systolic pressure while mean arterial pressure was estimated by diastolic blood pressure + 1/3 pulse pressure.

Statistical analysis

All data were expressed as means±SD. Intra-individual and inter-individual differences were compared by paired and unpaired t-tests, respectively. Correlational analysis was assessed by Pearson's test. Probability values of $p < 0.05$ were considered statistically significant for all tests. Statistical analysis was performed with statistical package for social sciences for windows (SPSS® Chicago IL., version 14.0).

RESULTS

Clinical characteristics

Table 1 summarizes the descriptive data for both groups. Both groups did not differ in age, body mass index, weight, hip/waist ratio, hip and waist circumference but differ in height ($p < 0.001$). Pre-ingestion means of systolic blood pressure (SBP), diastolic blood pressure (DBP), pulse pressure (PP) and heart rate (HR) were not significantly different between men and women, and within the groups (Tables 2 and 3).

Effect of water ingestion on orthostatic tolerance

Men receiving 500ml of water tolerated orthostatic challenge 23% longer (13.3±4.4 vs 15.1±5.2min,

$p < 0.05$; Fig. 1), whereas women receiving 500ml of water tolerated orthostatic challenge 33% longer (8.34±3.2 vs 11.2±2.8min $p < 0.01$; Fig. 1). Tolerance time to orthostatic challenge was significantly associated with water ingestion ($r = 0.30$, $p = 0.018$, $n = 37$). Although the relationship was significant in women ($r = 0.46$, $p < 0.01$) but not in men ($r = 0.23$, $p > 0.05$). Pulse pressure correlated positively ($r = 0.42$, $p < 0.01$) while heart rate correlated negatively ($r = -0.32$, $p < 0.05$) to orthostatic tolerance in women but not in men. However, DBP correlated positively with orthostatic tolerance strongly in men ($r = 0.45$, $p < 0.01$) but not in women.

Table 1.
Participants characteristics

Variable	Men (n=22)	Women (n=15)
Age, yr	22.5±2.1	21.5±1.9
Height, m	1.7±0.1	1.6±0.1***
Weight, kg	58.5±5.7	54.5±6.5
Body mass index, kg/m ²	20.3±1.5	20.9±2.5
Hip, inch	34.8±1.0	35.6±2.4
Waist, inch	29.6±1.6	28.8±2.2
Waist/Hip ratio	0.80±0.01	0.79±0.01

Values are expressed as means ± SD, n; number of subjects, *** $p < 0.001$ vs men.

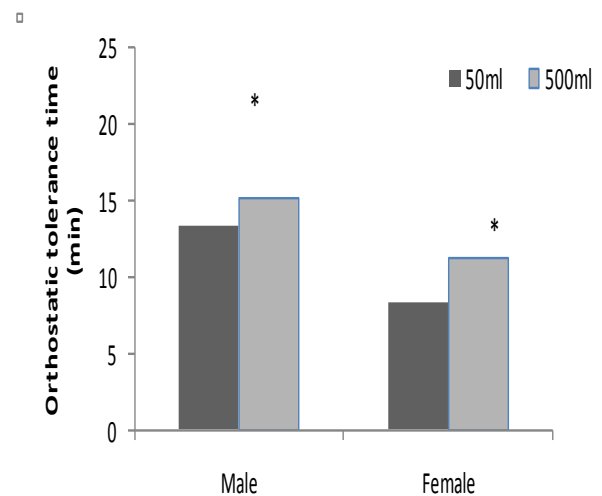


Figure 1. Effect of ingestion of 500ml of water on orthostatic tolerance. Values are expressed as means ± SD for 15 women and 22 men. * $p < 0.05$ vs 50ml.

Cardiovascular responses to water ingestion in sitting position

Thirty minutes after ingesting 500ml of water, SBP ($p < 0.001$; Table 2), DBP ($p < 0.05$; Table 2) and PP ($p < 0.001$; Table 2), rose significantly in men. On the other hand, thirty minutes after ingesting 500ml of water, SBP ($p < 0.05$; Table 3) and PP ($p < 0.001$; Table 3) rose significantly, while DBP was not affected significantly in women ($p < 0.001$; Table 3). Thirty

minutes after ingestion of 500ml of water, HR increased ($p < 0.001$; Table 2) significantly in men whereas there was a significant decrease ($p < 0.001$; Table 3) in women.

Drinking 50ml of water did not cause any significant change in cardiovascular responses during sitting

Table 2.
Cardiovascular responses to water ingestion in sitting position in men

	Ingestion (50 ml)			Ingestion (500 ml)		
	Pre	Post	Δ	Pre	Post	Δ
SBP (mmHg)	121.2 \pm 9.7	124.5 \pm 11.7	3.3 \pm 2.0	119.6 \pm 6.6	128.8 \pm 7.9	9.2 \pm 1.3*
DBP (mmHg)	73.7 \pm 8.5	76.9 \pm 6.4	3.2 \pm 2.1	73.4 \pm 11.1	77.7 \pm 8.7	4.3 \pm 2.4*
MAP (mmHg)	89.5 \pm 8.1	90.7 \pm 4.3	1.2 \pm 3.8	88.8 \pm 10.4	94.8 \pm 6.7	6.0 \pm 3.7*
PP (mmHg)	47.5 \pm 7.8	48.8 \pm 6.6	1.3 \pm 1.2	46.2 \pm 10.4	51.0 \pm 10.8	4.8 \pm 0.4*
HR (beats/min)	73.4 \pm 10.7	74.8 \pm 8.9	1.4 \pm 1.8	73.9 \pm 10.8	76.0 \pm 10.7	2.1 \pm 0.1*

Values are expressed as means \pm SD for 22 men before (Pre-) and 30 min after (Post-) water ingestion. Systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), pulse pressure (PP) and heart rate (HR). * $p < 0.05$, Δ , change from pre ingestion values.

Table 3.
Cardiovascular responses to water ingestion in sitting position in women

	Ingestion (50 ml)			Ingestion (500 ml)		
	Pre	Post	Δ	Pre	Post	Δ
SBP (mmHg)	117.4 \pm 13.9	119.7 \pm 11.6	2.3 \pm 2.3	113.1 \pm 11.0	121.5 \pm 10.0	8.4 \pm 1.0*
DBP (mmHg)	74.8 \pm 12.2	78.1 \pm 9.3	3.3 \pm 2.9	74.5 \pm 8.4	75.5 \pm 13.1	1.1 \pm 4.7
MAP (mmHg)	89.0 \pm 11.7	91.1 \pm 7.1	2.1 \pm 4.6	87.4 \pm 8.1	90.8 \pm 11.3	3.4 \pm 3.2
PP (mmHg)	42.6 \pm 10.6	44.1 \pm 12.8	1.5 \pm 2.2	38.7 \pm 9.7	45.9 \pm 9.3	7.2 \pm 0.4*
HR (beats/min)	79.4 \pm 10.3	78.3 \pm 8.9	-1.1 \pm 1.4	81.0 \pm 10.4	79.0 \pm 9.5	-2.0 \pm 0.9*

Values are expressed as means \pm SD for 15 women before (Pre-) and 30 min after (Post-) water ingestion. Systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), pulse pressure (PP) and heart rate (HR). * $p < 0.05$, Δ , change from pre ingestion values.

Table 4:
Cardiovascular responses to water ingestion in standing position

	Ingestion (50 ml)		Ingestion (500 ml)	
	Δ in men	Δ in women	Δ in men	Δ in women
SBP (mmHg)	0.4 \pm 2.8	-5.0 \pm 0.8*	3.3 \pm 1.3*#	-1.2 \pm 0.6*#
DBP (mmHg)	-1 \pm 4.8	0.4 \pm 0.7	2.1 \pm 1.2*	1.8 \pm 5.8n
MAP (mmHg)	0.6 \pm 3.6	-2.6 \pm 0.2*	-1.2 \pm 1.0*	0.8 \pm 4.1n
PP (mmHg)	1.4 \pm 4.4	-5.4 \pm 0.1*	0.8 \pm 1.8	-3.2 \pm 1.9*#
HR (beats/min)	9.3 \pm 0.6*	17.4 \pm 0.2*	9.4 \pm 0.8*	5.2 \pm 1.2*#

Values are expressed as means \pm SD for 15 women and 22 men before (Pre-) and 5min after (Post-) water ingestion. Systolic blood pressure (SBP), diastolic blood pressure (DBP), pulse pressure (PP) and heart rate (HR). * $p < 0.05$, # $p < 0.05$ vs 50ml, Δ , change from seated values.

Table 5.
Cardiovascular responses to orthostatic challenge during water ingestion at termination

	Ingestion (50 ml)		Ingestion (500 ml)	
	Δ in men	Δ in women	Δ in men	Δ in women
SBP (mmHg)	-11.1 \pm 8.1*	-11.1 \pm 10.1*	-10.9 \pm 10.3*	-3.5 \pm 8.9#
DBP (mmHg)	-3.7 \pm 11.6	-0.3 \pm 9.3	-8.1 \pm 9.8*	-4.1 \pm 6.1*
MAP (mmHg)	-6.2 \pm 8.0	-3.9 \pm 8.4	-9.0 \pm 7.3	3.9 \pm 6.5
PP (mmHg)	-7.4 \pm 14.7*	-10.8 \pm 9.6*	-2.7 \pm 14.3	0.5 \pm 6.6#
HR (beats/min)	15.9 \pm 9.3*	17.7 \pm 10.2*	11.5 \pm 8.4*	6.4 \pm 9.5*#

Values are expressed as means \pm SD for 15 women and 22 men. Systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), pulse pressure (PP) and heart rate (HR). * $p < 0.05$, # $p < 0.05$ vs 50ml, Δ , change from seated values.

Effects of water ingestion on cardiovascular responses to standing

Table 4 summarizes cardiovascular responses induced by 5min of standing in men and women with ingestion of 50ml and 500ml. After 5min of standing, SBP did not increase significantly in men while there was a significant decrease in women before ingestion of 500ml of water. However, following ingestion of 500ml of water in men, 5min standing led to a significant increase in SBP. Ingestion of 500ml of water in women significantly attenuated the decrease in SBP after 5min of standing. Standing did not cause any significant effect in DBP in both men and women before ingestion of 500ml of water. The increase induced by 5min standing in DBP was significant in men while that of women was not significant after ingestion of 500ml of water. 5min of standing led to insignificant increase in PP in men while it resulted in a significant decrease in women before ingestion of 500ml of water. Ingesting 500ml of water did not affect PP in men. However, in women, ingesting 500ml of water significantly attenuated the decrease in PP induced by standing. 5min of standing induced significant increase in HR in both men and women. However, ingestion of 500ml of water led to significant attenuation of increased HR during standing in women but not in men.

Before ingestion of 500ml of water, standing induced significant reductions in SBP in men and women at termination of the orthostatic challenge (Table 5). The reduction in SBP in men was not significantly affected by ingestion of 500ml of water in men; whereas, the reduction in women was significantly attenuated (Table 5). At termination of orthostatic stress, DBP was not significantly altered in both men and women before ingestion of 500ml of water. However, ingestion of 500ml of water led to significant fall in DBP (Table 5). At termination of orthostatic stress, there was a significant decrease in PP in men and women before ingestion of 500ml of water. However, following ingestion of 500ml water, the decrease in PP was significantly abolished in women whereas the decrease observed in men was not significantly different (Table 5). At termination, postural stress induced a significant tachycardia response in men and women before ingestion of 500ml. ingestion of 500ml of water significantly attenuated the tachycardia response in women but not in men (Table 5).

DISCUSSION

The main finding from the present study is that drinking 500ml of water significantly increased orthostatic tolerance during standing in healthy young adult men and women. In addition, the improvement exerted by water ingestion was stronger in women

than in men. Water ingestion increased tolerance time to orthostatic challenge by 23% in men and by 33% in women (Fig 1). Both men and women were able to withstand the orthostatic challenge to postural stress for an average of 6 additional minutes. Improvement of this degree in patients with impaired orthostatic tolerance is associated with appreciable symptomatic improvement (El-sayed and Hainsworth, 1996; Shannon *et al.*, 2002).

Our results demonstrated that ingestion of a moderate volume of water elicited a pressor response in normal young individuals. There was no significant change in chronotropic response, a finding that is in accordance with previous studies in normal young Caucasians (Faguis and Berne, 1994; Schroeder *et al.*, 2002), normal old (Jordan *et al.*, 2000), patients with autonomic failure (Jordan *et al.*, 2000; Shannon *et al.*, 2002) but some reports (Schroeder *et al.*, 2001; Routledge *et al.*, 2002) are not in consonance with the observations in normal subjects. There had not been any study to show whether or not gender difference occurs in cardiovascular response to water ingestion. The current study seems to be the first to show that drinking half a litre of water elicits significant stronger seated pressor response in men than in women. Previous studies have suggested that the pressor response of water ingestion is mediated through sympathoadrenal activation (Jordan *et al.*, 2000; Scott, *et al.*, 2001; Lu *et al.*, 2003). It is interesting to note that, despite the increases in seated systolic blood pressure and pulse pressure, diastolic blood pressure (an index of vascular resistance) was not increased in women in this study. The lack of diastolic blood pressure response in women might be as a result of the vasodilatory effect of estrogens, presumably by enhancing the basal nitric oxide biosynthesis/bioavailability (Christou *et al.*, 2005).

Water drinking itself elicits large pressor response in patients with orthostatic intolerance, such as patients with autonomic failure, tetraplegics and in older normal subjects (Jordan *et al.*, 2000). It has also been reported that water ingestion in individuals that had lower orthostatic tolerance had the greatest improvement in orthostatic tolerance (Jacob *et al.*, 1998; Jordan *et al.*, 2000). Most reports (Robertson, 1999; Fu *et al.*, 2004, 2005) but not all (Brown and Hainsworth 1999), demonstrated that susceptibility to orthostatic intolerance is more common in young women than in men, and this difference is especially dramatic after space flight (Waters *et al.*, 2002) or bed rest (Custaud *et al.*, 2002) in which dehydration or hypovolaemia occurs.

However, what is unclear is whether, water ingestion would exert greater protection against poor orthostatic tolerance in young women when

compared to men (Troven-Trend *et al.*, 1999; Shoemaker *et al.*, 2001; Custaud *et al.*, 2002; Fu *et al.*, 2004). Previous studies have concentrated on the pressor effect of water ingestion in patients with autonomic failure, idiopathic orthostatic tachycardia and this effect of water ingestion on orthostatic challenge in normal young men and women are not known. We therefore hypothesized that water drinking might exert stronger beneficial effect in young healthy women than in young aged-matched men during orthostatic challenge. The results from multiple regression analyses showed that orthostatic tolerance correlated strongly with water ingestion in women but weakly in men independent of other correlates (age, weight, height, BMI, waist circumference) support the hypothesis that water drinking would exert greater protection against impaired orthostatic tolerance in women than in men.

This study also supports the observations that women might have stronger tachycardiac response whereas men might have stronger pressor response to orthostatic challenge (Fu *et al.*, 2004, 2005). On the other hand, the diastolic blood pressure response in both genders was comparable, despite the fact that women had lower tolerance to orthostatic challenge in this study. This observation is consistent with those in the previous study (Fu, *et al.*, 2005). This finding provides strong evidence that women and men may have comparable adrenergic vasoconstrictor response during orthostatic challenge. The improvement in orthostatic tolerance with water ingestion in both men and women might be due to enhanced pressor and attenuation of tachycardiac responses induced by orthostatic challenge. Although, the effect of water ingestion on pressor and chronotropic responses in women were stronger. The enhancement of pulse pressor and attenuation of the positive chronotropic response by water ingestion during exposure to orthostatic challenge in women than those in men may explain a better improvement in orthostatic tolerance in women impacted by water ingestion.

This finding further indicate that water drinking may be more effective in preventing orthostatic hypotension and/or orthostatic tachycardia in women than in men. The mechanism responsible for this heart rate reduction with water ingestion is yet to be elucidated, although Routledge *et al.*, suggested enhanced cardiac vagal outflow. This result therefore suggests that the cardiovascular response to water ingestion in healthy young subjects especially women may be an integrated responses consisting of an enhanced pressor response that may be sympathetically mediated coupled with a parallel attenuated tachycardia response possibly mediated by an increase cardiac vagal activity. The enhancement of the diastolic blood pressure response might suggest

that water somehow abate the vasodilator response or possibly enhances vasoconstrictor responses. Baroreceptors exert important control over reflex-mediated changes in vagal outflow to regulate heart rate, thereby maintain blood pressure during standing. The ability to rapidly adjust this adaptive response is related to cardiac baroreceptor sensitivity which primarily reflects reduced vagal outflow during standing (Cooper and Hainsworth, 2002). Therefore, this finding support the hypothesis that baroreceptor sensitivity for control of cardiac vagal outflow may be enhanced by water ingestion probably more in women than in men. Moreover, previous studies suggested that baroreflex heart rate regulation tends to decrease in women compared to men (Shoemaker *et al.*, 2001). The fact that water drinking attenuated orthostatic-induced tachycardia more in women than in men, further provides explanation for the improvement of orthostatic tolerance better in women than in men.

Patients with orthostatic-induced hypotension and tachycardia are difficult to treat because no available intervention can replicate the ability of baroreceptors to rapidly adjust the cardiovascular responses. Pharmacological intervention, even short acting pressor agents take about 90min to reach a peak effect and once the effect is evident, the supine posture must be avoided for several hours to prevent possibly increases in arterial pressure. Regardless of the time of dosing, long acting pressor agents such as a mineralocorticoid, fludrocortisone that expands fluid volume and promote vasoconstriction by increase peripheral α -adrenoceptor sensitivity, have been associated with electrolyte disturbance (hypokalaemia, hypomagnesium), peripheral oedema, weight gain, and elevation of supine blood pressure or congestive heart failure (Grubb, 2005). Hence, non-pharmacological intervention such as water ingestion would be a preferred alternative because water ingestion enhanced blood pressor and blunted chronotropic responses.

In conclusion, water ingestion elicited pressor response in healthy young individuals and this simple, readily available, no-cost intervention, could exert a considerable improvement on orthostatic tolerance. The result of this study also demonstrate that water drinking attenuated orthostatic challenge-induced tachycardia and decreased stress-induced pulse pressure strongly in women than in men. Therefore this finding indicate that water ingestion could be an alternative or adjunct intervention in individuals that are susceptible to orthostatic intolerance or in individuals with predisposing factors (such as prolonged standing or heat exposure) for orthostatic intolerance. The improvement of orthostatic tolerance by water ingestion is better in

women than in men, possibly due to significant attenuation of orthostatic challenge-induced tachycardia and enhanced pulse pressure responses observed, particularly in women. Furthermore, the findings in this study implies that water ingestion should not be considered as cardiovascular-inert activity, hence there is a need for caution to control for oral water intake in investigations involving agents/drugs administration with water ingestion.

REFERENCES

- Brown C.M and Hainsworth R. 2000. Foreign Vascular responses during orthostatic challenge in normal subjects and patients with posturally related syncope. *Clin. Auton Res.* 10:53-55
- Brown C.M, Hainsworth R, (1999). Assessment of capillary fluid shifts during orthostatic challenge in normal subject and subjects with orthostatic intolerance. *Clin Auton Res.* 9:69-73
- Christou D.D, Jones P.P, Jordan J., Diedrich A., Robertson D., Seals D.R (2005). Women have lower tonic autonomic support of arterial blood pressure and less effective baroreflex buffering than men. *Circulation* 111:494-498.
- Claydon V.E, Norcliffe L.J, Moore J.P, Riverach M. Leon-velarde E, Apenzener O, Hainsworth R, (2004). Orthostatic tolerance and blood volume in Andean high altitude dwellers. *Exp physiol* 89(5): 565-571.
- Convertino V.A (1998). Gender differences in autonomic function associated with blood pressure regulation. *Am J physiol* 275:R1909-R1920
- Cooper V.L and Hainsworth R., 2002. Effect of head-up tilting on baroreceptor control in subjects with different tolerances to orthostatic challenge. *Clin Sci (London)* 103: 221 –226
- Custaud M.A, de Souza Neto E.P, Abry P, Flandrin P, Millets C, Duraille M, Fortrat J.O, Gharib C. (2002). Orthostatic tolerance and spontaneous baroreflex sensitivity in men versus women after 7days of head-down bed rest. *Auton Neuro Sci* 100:66-76
- El-Sayed H, Hainsworth R, (1995). Relationship between plasma volume, carotid baroreceptor sensitivity and orthostatic tolerance. *Clin Sci* 88:463-470.
- El-Sayed H, Hainsworth R, (1996). Slat supplementation increases plasma volume and orthostatic tolerance in patient with unexplained syncope. *Heart* 75:134-160
- Fagius J, Berne C. (1994). Increase in muscle nerve sympathetic activity in humans after food intake. *Clin Sci.* 86:159-167
- Fu Q, Arbab-Zadeh A, Perhonen M.A, Zhang R, Zuckerman J.H, Levine B.D (2004). Haemodynamic of orthostatic intolerance: implications for gender differences. *Am J physiol* 286:H449-H457
- Fu Q, Witkowski S, Okazaki K, Levine B.D (2005). Effects of gender and hypovolemia on sympathetic neural responses to orthostatic challenge. *Am J physiol* 289:R109-R116.
- Grubb B.P (2005). Neurocardiogenic syncope and related disorders of orthostatic intolerance. *Circulation* 111:2997-3006.
- Hainsworth R, (1985). *Arterial blood pressure in hypotensive Anaesthesia* ed. Enderby, G.F.H, pp.3 Churchill Living stone, London.
- Jacob G, Shannon J.R, Black B, Binaggioni I, Mosqueda- Garcia R, Robertson R.M, Robertson D. (1997). Effect of volume loading and pressor agents in idiopathic orthostatic tachycardia. *Circulation* 96:575-580.
- Kapoor W.N, Smith M.A, Miller N.L (1994). Upright tilt testing in evaluating syncope: a comprehensive literature review. *Am J Med* 97:78-88.
- Lu C, Diedrich A, Tung C, Paranjape S.Y, Harris P.A, Byrne D.W, Jordan J, Robertson D, (2003). Water ingestion as prophylaxis against syncope. *Circulation* 108:2660-2665.
- Mtinangi B.L, Hainsworth R, (1999). Effects of moderate exercise training on plasma volume, baroreceptor sensitivity and orthostatic tolerance in healthy subjects. *Exp physiol* 84: 121-130
- Robertson D, (1999). The epidemic of orthostatic tachycardia and orthostatic intolerance. *Am J Med Sci* 317:75-77.
- Routledge, H.C, Chowdhary S, Coote J.H, Townend J.N (2002). Cardiac vagal response water ingestion in normal human subjects. *Clin Sci.* 103:157-162.
- Schroeder C, Bush V.E, Nordifte L.J, Luft F.C, Tank J, Jordan J, Hainsworth R. (2002). Water drinking acutely improves orthostatic tolerance in healthy subjects. *Circulation* 106:2806-2811.
- Scott E.M, Greenwood J.P, Gillbey S.G, Stoker J.B and Mary A.S.G (2001). Water ingestion increases sympathetic vasoconstrictor discharge in normal subjects. *Clin sci* 100:335-342.
- Shannon J.R, Diedrich A, Biaggioni I, Tank J, Robertson R.M, Jordan J. (2002). Water drinking as a treatment for orthostatic syndromes. *Am J. Med* 112:355-360
- Sheldon R, (2000) Pacing to prevent vasovagal syncope *cardiol Clin* 18:81-93.
- Shoemaker J.K, Hogeman C.S, Khan M, Kimmephy D.S, Sinoway L.I (2001). Gender effects sympathetic and haemodynamic response to postural stress. *Am J physiol* H2028-H2035
- Smit A.A.J, Halliwill J.R, Low P.A, Wieling W, (1999). Pathophysiological basis of orthostatic

- hypotension in autonomic failure *J. physiol* 519(1): 1-10.
- Ten-Harkel A.D, Van Lieshout J.J and Wieling W. (1994). Effects of leg muscle pumping and tensing on orthostatic arterial pressure: a study in normal subjects and patients with autonomic failure. *Clin sci.* 87:553-558
- Trover-Trend J.J, Cable R.G, Badon S.J (1999). A case controlled multicenter study of vasovagal reactions in blood donors: influence of sex, age, donation status, weight, blood pressure and pulse. *Transfusion* 39:316-320.
- Waters W.W, Ziegler M.G, Meck J.V (2002). Post-spaceflight orthostatic hypotension occurs mostly in women and is predicted by low vascular resistance. *J Appl. Physiol* 92:586-594.