Hyper-hydration with a Carbohydrate-Electrolyte Solution Does Not Improve Orthostatic Tolerance in Healthy Young Individuals

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A potential risk factor for astronauts is post-spaceflight orthostatic intolerance, which may be due to losses of plasma volume during spaceflight. One way to offset and minimize plasma volume loss is through a proper hydration strategy. The effects of hyper-hydration with Gatorade on orthostatic intolerance are unknown. Twenty-two individuals (12 men, 10 women) underwent a tilt table test [70° head up tilt (HUT)] during two conditions: euhydrated and hyper-hydrated. Heart rate (HR) and blood pressure (systolic, SBP; diastolic, DBP) were measured at baseline (BL), HUT, and recovery (REC). SBP did not change with HUT and was similar between groups. DBP was higher during HUT compared to BL (men: 63±7 to 80±10 mmHg, women: 72±7 to 80±7 mmHg, P=0.039) and overall higher in women (69±10 vs. 74±10 mmHg, for men vs. women, respectively, P=0.003). HR was higher during HUT and higher in women (men: 61±8 to 88±15, women: 71±11 to 104±16, for BL to HUT, respectively, P<0.001). Men had longer tilt times (33±15 vs. 18±12 min, euhydrated for men vs. women, respectively, P<0.001). Tilt times were similar between the two hydration conditions (men: 33±15 and 31±18, women: 19±12 and 16±7 min, for euhydration and hyper-hydration, respectively, P=0.442). In summary, men were more orthostatically tolerant than women. Gatorade did not improve orthostatic intolerance.
A potential risk factor for astronauts is post-spaceflight orthostatic intolerance, or the inability to maintain blood pressure in the upright posture (9). This is a very common crisis in returning astronauts on landing day (9). For example, about 20% of all astronauts experience symptoms of orthostatic intolerance upon returning from 5-16 days of spaceflight (9). This is likely due to insufficient cardiovascular responses during an orthostatic challenge that can cause symptoms including lightheadedness, loss of peripheral vision, a sudden drop in systolic blood pressure, or even passing out (9, 17). During an orthostatic challenge, such as standing up, about 300-800 ml of blood will pool in the dependent regions, such as the legs and splanchnic circulation, lowering venous return, which decreases stroke volume and cardiac output (2, 18). Ohm’s Law, as it pertains to the cardiovascular system, states that mean arterial pressure is directly related to cardiac output ($Q_c$) and total peripheral resistance (TPR). $Q_c$ is the product of stroke volume (SV) and heart rate (HR). The reduction in SV, related to an orthostatic challenge, must be compensated for (by increases in HR and/or TPR) in order to maintain blood pressure. If these responses are insufficient, this may pose a potential risk in the case of an emergency egress, specifically on landing day.

The causes of orthostatic intolerance are likely multifactorial and may include: changes in the baroreceptor reflex, muscle wasting and reduced aerobic fitness, increase in venous compliance, and a change in the circulating levels of catecholamines that can result in alterations in the sensitivity of β-adrenoreceptors in the smooth muscles of arterioles (26). This has been shown by Convertino et al. (1996) as increases in beta 2-adrenergic responsiveness post 14 days simulated microgravity. It has been shown that muscle sympathetic nerve activity actually increases during spaceflight, however very few astronauts have been studied and many limitations arise to determine if the responses are specific to microgravity exposure or secondary to other physiological effects (27). Although it is hard to draw conclusions from spaceflight, it has been shown that head-down bed rest will reduce muscle sympathetic nerve activity (27). These changes that decrease this nerve activity may contribute to the inability to maintain blood pressure in the upright posture. An increase in sympathetic activity will increase peripheral vasoconstriction, increasing preload, and in turn blood pressure. Even though few studies have shown increases in sympathetic nerve activity during spaceflight, there are many other physiological changes that occur during such period, including changes in plasma volume.
These changes will also affect blood pressure and blood pressure regulation because the human body is a closed system and therefore distribution of blood is important.

**Plasma volume and orthostatic intolerance**

During spaceflight, astronauts will experience a loss of plasma volume, which may be one contributing factor to orthostatic intolerance (9). Plasma volume loss occurs quickly during exposure to microgravity, and most likely occurs because of the headward fluid redistribution, which distends the heart and stimulates baroreceptors (8). This can lead to increased urine and sodium output, decreasing plasma volume (8). With a loss of plasma volume, the volume of blood in the central circulation is reduced. Consequently, decreasing the volume of blood to the heart reduces the heart’s ability to supply oxygen to vital organs such as the brain. This loss presents a higher risk for orthostatic intolerance on landing day, when individuals are re-exposed to Earth’s gravitational forces because stroke volume is reduced.

When an individual undergoes bed rest, he/she experiences many of the same physiological changes that occur during spaceflight (7). Thus, bed rest can be used as a ground-based surrogate for space travel. Waters et al. (2004) was able to restore plasma volume loss after bed rest in men, which resulted in all subjects completing 30 minutes of 70⁰ tilt and ameliorated orthostatic intolerance (7). On the last day of bed rest, the subjects consumed a one 1.0 gram salt tablet per 125 ml of water, with a total volume of 15 ml/kg of body weight (e.g.: 8.7 ± 0.3 g salt with 1084.5 ± 43.5 mL water) (7). The fluid loading protocol used in Waters et al.’s (2004) study is the same protocol currently used in astronauts (7). However, astronauts returning from space travel still experience symptoms of orthostatic intolerance when using this hydration strategy. One potential for the differences between a ground-based study and space travel may be that space travel induces higher plasma volume losses than does bed rest (7). Another confounding factor may be that the ground-based hydration protocol was only administered on the last day of bed rest. Perhaps successful strategies need to incorporate hydration over a longer period of time. Additionally, a restoration of plasma volume may not be sufficient enough to see improvements in orthostatic intolerance, and increasing plasma volume may be necessary. Increasing plasma volume (and therefore blood volume) has the potential to increase venous return, and therefore, cardiac preload, stroke volume, and blood pressure.

**Hydration strategies**
Water alone to hyper-hydrate has not been successful for long-term treatment of orthostatic intolerance because the excess fluid is excreted by the kidneys (2). There is a risk of developing hyponatremia if water intake is in excess of the renal capacity to excrete water (21,22). While this risk of hyponatremia is small because it would require consuming excessive amounts of water (10-15 L/day)(21), it can result in neurological symptoms, swelling, headache, lethargy, confusion, nausea, vomiting, muscle cramps, seizures, coma, brain damage, and possibly death (21,22).

Supplementation with products other than just water alone may provide a safer and more effective alternative. For example, Easton et al. (2009) evaluated the effects of hyper-hydration in men, showing that supplementation with creatine and glycerol increased plasma volume by 3.2 ± 2.4%, improved blood pressure, and decreased presyncope. Glycerol alone has been reported to increase plasma volumes by 7.5% compared to euhydration (restoration of plasma volume) and dehydration, which decreased plasma volumes (4). Previous studies have shown that salt supplementation over the course of 8 weeks has shown increases in body weight, plasma volume, and time to syncope (10,11). It has been shown that hydrating with a carbohydrate electrolyte solution (CES) was slightly better at maintaining plasma volume compared to water (-3.0 ± 1.6% loss with water vs. -1.1 ± 1.6% with CES) (1). Moreover, Moreno et al. (2013) examined the effects of hydrating with Gatorade after exercise induced dehydration, reporting that Gatorade hydration promoted a faster recovery of heart rate (6).

The purpose of this investigation was to determine the effects of euhydration vs. hyper-hydration with Gatorade on orthostatic intolerance in both women and men during normal daily routine. Hyper-hydration may be an important countermeasure for orthostatic intolerance; however, the effect of hyper-hydration in women exposed to an orthostatic challenge has not been studied. The comparison of hyper-hydration between men and women has also not been studied. We hypothesize both groups (women and men) will demonstrate decreased orthostatic intolerance and increases in time to presyncope during the hyper-hydration trial. We also hypothesize that the relative improvements will be comparable between the sexes.

**Methods**

**Subjects**

Twenty-two healthy men and women (Table 1) ages 21±4 yrs (mean ± SD) gave their written informed consent before participating in the present study, which was approved by the
Northern Arizona University’s Institutional Review Board. We excluded people with history of neurological disorders, cardiovascular disease, respiratory disease, hypertension, diabetes, kidney disorders, sleep apnea, body mass indexes (BMI) greater than or equal to 30 kg·m⁻², and a history of fainting and orthostatic intolerance.

**Experimental design**

The subjects reported to the lab for two testing sessions (randomly assigned): once in a euhydration state and once in a hyper-hydration state. The sessions were separated by approximately 1 month where women, were testing during the same phase of their menstrual cycle. For the euhydration trial, subjects carried out their normal routine in regards to food and drink. During the hyper-hydration trial, subjects consumed 2 liters of Gatorade per day (1 L each in the morning and afternoon) on top of normal intake for 6 days before the study, and 1 liter the morning of the study. The subject was weighed at the beginning of the six days, as well as after the hydration protocol to assess changes in mass.

**Procedure**

Subjects arrived at the laboratory following a 4-hr fast, having refrained from caffeine and alcohol for 48-hrs prior to testing, and having limited physical activity for 12-hrs prior. Subjects were instructed to empty their bladders, and a pregnancy test was administered to females. A negative test was required before testing. Weight was measured before the subjects were instructed to lay supine on an electronic tilt table. A standard 3-lead electrocardiogram (ECG Module, Finapres Medical Systems) was placed on the subject’s chest, a blood pressure cuff (SunTech Tango Plus) was attached over the brachial artery of the left arm, a beat-by-beat blood pressure cuff (Finometer) was placed on the middle finger on the right arm, and a piezoelectric respiratory belt transducer (ADInstruments) was placed on the subject’s chest to monitor breathing rate. Subjects were secured to the tilt table using a thick Velcro strap placed on the subject’s waist. Subjects remained supine for instrumentation (20 min) prior to baseline. The subjects then remained supine for a 5 min baseline (BL), after which the subject was tilted to 70⁰ head up (HUT) for 45 min or until presyncope. Subjects were instructed to relax and keep their knees locked. The test was immediately terminated if the subjects complained of symptoms of presyncope (dizziness, light-headedness, nausea, difficulty breathing, feeling hot/sweaty) and the subjects remained supine for a 5 min recovery. Presyncope was defined as a decline in blood pressure of >20/10 mmHg or a rapid decline in heart rate of >25 bts·min⁻¹. We monitored heart
rate (HR), blood pressure (systolic, SBP; diastolic, DBP), and assessed tilt time during the tilt table test. All sessions were conducted in the afternoon in dimmed light with an ambient temperature of 22±2°C.

**Data analysis**

Data are reported as means ± SD. For analysis, the 3 min preceding presyncope was removed for subjects who did not last the full 45 minutes. Statistical analysis was carried out using three way repeated measures ANOVA [hydration status × sex × stage] to compare SBP, DBP, and HR at the last time point for each subject. All statistical analyses were performed using Sigma Plot (San Jose, CA). T-tests and paired t-tests were used to compare baseline measurements. Statistical significance was declared as P < 0.05.

**Results**

**Baseline Measurements**

Subjects were well matched for baseline characteristics; there was no significant difference between men vs. women in age, height, weight, BMI, SBP, DBP, and HR (Table 1). There was no difference in weight between the euhydrated vs. hyper-hydrated trials (P=0.776)

<table>
<thead>
<tr>
<th>Table 1. Baseline subject characteristics</th>
<th>Men (n=12)</th>
<th>Women (n=10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>22±6</td>
<td>21±1</td>
</tr>
<tr>
<td>Height (meters)</td>
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<td>1.7</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>67.3±7.3</td>
<td>61.6±8.6</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>22.2±2.7</td>
<td>21.5±2.3</td>
</tr>
<tr>
<td>Resting SBP (mmHg)</td>
<td>116±10</td>
<td>113±8</td>
</tr>
<tr>
<td>Resting DBP (mmHg)</td>
<td>70±8</td>
<td>74±6</td>
</tr>
<tr>
<td>Resting HR (bts/min)</td>
<td>71±17</td>
<td>73±15</td>
</tr>
<tr>
<td>Euhydration Weight (kg)</td>
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<td>60±8</td>
</tr>
<tr>
<td>Hyper-hydration Weight (kg)</td>
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<td>62±8</td>
</tr>
</tbody>
</table>

Values are means ± SD
Blood pressure

SBP did not change with HUT and was similar between groups. DBP was higher during HUT in both groups (men: 63±7 to 80±10 mmHg, women: 72±7 to 80±7 mmHg, P=0.039) and overall higher in women (69±10 vs. 74±10 mmHg, for men vs. women, respectively, P=0.003)(Figures 1 and 2).

![Figure 1: Systolic (top) and diastolic (bottom) blood pressure during each tilt phase of the hyper-hydration and euhdration trials for men. Data presented as the mean ± SD. * Significant difference during HUT.](image1)

![Figure 2: Systolic (top) and diastolic (bottom) blood pressure during each tilt phase of the hyper-hydration and euhdration trials for women. Data presented as the mean ± SD. * Significant difference during HUT.](image2)
HR

HR was higher during HUT and higher in women (men: 61±8 to 88±15, women: 71±11 to 104±16, for BL to HUT, respectively, P<0.001) (Figure 3).

Figure 3: Heart rate during each tilt phase of the euhydration trial for men and women. Data presented as the mean ± SD. *Significant difference during HUT. † Significant difference between sexes.

Figure 4: Heart rate during each tilt phase of the euhydration trial for men and women. Data presented as the mean ± SD. *Significant difference during HUT. † Significant difference between sexes.
Presyncope/Tilt times

Men had longer tilt times (33±15 vs. 18±12 min, euhydrated for men vs. women, respectively, P<0.001) (Figure 4). Tilt times were similar between euhydration status and hyperhydration status within each group (men: 33±15 and 31±18, women: 19±12 and 16±7 min, for euhydration and hyper-hydration, respectively, P=0.442).

Discussion

The primary findings from this study are 1) DBP and HR were higher during HUT compared to BL in both groups, 2) DBP and HR were higher in women compared to men, 3) Men had greater orthostatic tolerance than women, 4) Hyper-hydration with Gatorade did not improve orthostatic intolerance.

During an orthostatic challenge, Qc and SV will immediately decrease due to pooling of the blood in the dependent regions (2,18). The normal compensatory mechanisms will be seen as increases in HR, small reductions in SBP, and large increase in DBP (2). These responses are seen in the current study as shown in the increases in HR and DBP during HUT compared to BL. These cardiovascular responses can be explained by reflex sympathetic stimulation, which will stimulate β1 adrenergic receptors to stimulate an increase in HR and α1-adrenergic receptors to stimulate the vasoconstrictor response in order to increase TPR (23).
We found that 90% of women experienced symptoms of orthostatic intolerance and/or presyncope during their normal hydration state, while only 50% of men did. Women also had higher HR’s during HUT compared to men. The overall higher DBP seen in women takes into account the fact that women had higher resting and recovery DBP’s compared to men. These findings are mainly supported by previous studies (9,15,24). For example, Waters et al. (2002) showed that 100% of women experienced symptoms of orthostatic intolerance, while they were only present in 25% of men. Convertino (1998) found that women had decreased tolerance compared to men when exposed to lower body negative pressure, which is another form of an orthostatic challenge (19). He also found that the rate in elevation in HR was greater in females versus males during LBNP (19). Shoemaker et al. (2001) also demonstrated an increased HR during HUT in women compared to men (18). The prevalence of orthostatic intolerance is significantly higher in female astronauts compared to male astronauts (9).

Potential explanations for the lower tolerance in women could include: pelvic blood pooling (15), body composition (5), attenuated sympathetic nerve activity (18), reduced peripheral resistance (5), and/or differences in $\alpha_1$ adrenergic or $\beta_2$ adrenergic receptor sensitivities and/or densities (5, 20). For example, Fu et al. (2005) found that men and women have similar vasomotor sympathetic (muscle sympathetic nerve activity and plasma norepinephrine concentration) and vasoconstrictor responses (TPR and DBP) during orthostatic stress. They also showed that women had lower SBP than men, possibly because of a smaller stroke volume during orthostatic stress. This could be due to the fact that women have smaller and less distensible hearts (15). In contrast, it has been shown that women have smaller increases in total peripheral resistance and greater heart rate responses than men in response to orthostatic stress (8, 9,18,19,24). The decreased resistance can be partially explained by estrogen, which increases vasodilation via the nitric oxide pathway (9). Westby et al. (2012) showed that female astronauts had increased lower limb venous compliance post 60 days bed rest compared to decreases in men, which may contribute to blood pooling upon upright posture. However, it has been also shown that women have reduced calf venous compliance compared to men (5). For example, during LBNP women had greater decreases in thoracic fluid volume and less increases in calf circumference (28), indicating that women have a greater fluid shift from the thoracic region than men, but this shift is not to the legs and rather to other regions of the lower body. Women have demonstrated increased compliance in capacitance vessels in the
pelvic area, which creates more pooling of blood in the pelvic region, leading to reduced preload during orthostatic stress (15). For example, White and Montgomery (1996) showed that women had significantly greater increases in pelvic blood volume during exposure to LBNP compared to men (28). These differences in responses in women compared to men may translate into a less effective strategy in maintaining blood pressure during an orthostatic challenge. It has been hypothesized that women may rely more heavily on vagal withdrawal (which increases HR), whereas men have a greater sympathetic stimulation to the peripheral vasculature (19). It is critical to have adequate restrictor responses in order to maintain blood pressure during an orthostatic challenge (24).

Bed rest and exposure to microgravity has been shown to shift fluid from the extracellular space to the intracellular space (2). Gatorade is rich in sucrose, which will stimulate fluid absorption in the small intestine, while the sodium in Gatorade will help retain water in the extracellular space (14). Therefore, Gatorade (a carbohydrate-electrolyte solution) may be a more effective and efficient tool than water or sodium alone for hyper-hydrating individuals. However, there are several candidate reasons we did not find an improvement in tilt table times with the supplementation of Gatorade. First, salt supplementation has been shown to increase mean arterial pressure, plasma volume and tilt time (10,11,16). For example, Sayed et al. (1996) supplemented subjects 7g of sodium chloride for eight weeks, while Claydon et al. (2004) used 6 g of slow-release sodium chloride per day for 8 months. Our subjects only drank 0.9 g of sodium per day for 6 days. This may have not been adequate salt supplementation to see improvements, and a solution with greater sodium content over a longer period of time may be needed to produce the desired results. Claydon et al. (2004) also showed that salt supplementation increased forearm vascular resistance, which can be related to total peripheral resistance. The improvements in tilt time in the salt supplementation studies may not have stemmed from an increase in plasma volume but rather may have been due to an effect of enhancing sympathetic control of vasculature. This line of reasoning is supported by increased forearm vasoconstriction and higher heart rates at the point of tilt termination in Claydon et al’s. (2004) study.

Second, it has been shown that ingestion of carbohydrates before tilt will predispose an individual to postural related syncope (12). When glucose water is ingested prior to tilt, it has been shown to lead to greater increases in heart rate, plasma osmolality, and an attenuation of the increased peripheral resistance relative to water (12). For example, Lu et al. (2008) gave their
subjects 500 ml of 10% glucose water 5 minutes prior to tilt. Glucose water ingestion reduced the percentage of subjects tolerating tilt from 87% to 47% compared to water ingestion (12). As expected, HR and TPR increased with tilt in both groups; however, the glucose water group showed increased HR but decreased TPR compared to the water group (12). The decrease in TPR may be due to an increased vasodilation in the splanchnic circulation from glucose (the increase in HR may also be to compensate for this). Insulin concentration increases, which occur about 30 minutes after carbohydrate ingestion (13), may be an explanation for the contrasting effects of carbohydrates and water. Insulin concentration will cause a rise in cardiac output, but will cause vasodilation and, therefore, a subsequent reduction in total peripheral resistance (12). Glucose causes a fall in BP soon after mealtime, with a max response at 30-60 minutes, however intravenous infusion of glucose has little effect on BP, which indicates that the gastrointestinal tract is likely responsible for these effects (12). The rate of delivery of glucose into the small intestine determines the fall in BP and increase in HR after mealtime. This is why the absorption rate of glucose is very important in determining cardiovascular responses to carbohydrate ingestion; however, the mechanisms behind these effects are unclear (12). Gatorade is rich in sucrose, which provides a faster gastric emptying rate and an energy source (14). Sucrose will also stimulate fluid absorption in the small intestine, while the sodium in Gatorade will help retain water in the extracellular space (14). It is difficult to make a comparison with the current study because the Gatorade we gave the subjects was 6.7% sugar/liter and was given over a period of time. The subjects were instructed to finish their last liter of Gatorade 4 hours prior to the tilt table test, which should be enough time to negate the syncopal effects of sugar after ingestion.

Limitations

We did not directly assess plasma volume, rather took a crude measurement of euhydration and hyper-hydration weights. There was no difference between the two trials in terms of weight, but it is possible that plasma volume did not increase due to hyper-hydration.

Conclusion

In summary, consistent with previous work, women were more orthostatically intolerant than men. Orthostatic intolerance is a common crisis of returning astronauts and is highly dependent on losses of plasma volume during space. Proper hydration is needed to help prevent plasma volume loss during spaceflight. Hyper-hydration with Gatorade did not increase tilt time.
or improve orthostatic intolerance, and would not be an appropriate hydration strategy in populations that are particularly susceptible to orthostatic intolerance, such as returning astronauts. A solution with greater sodium content and less carbohydrates, as well as hyper-hydrating over a longer period of time, may be needed to adequately hyper-hydrate and increase plasma volumes to see increases in orthostatic intolerance, but further research is required.

**Grants**

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**References**


