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NARRATIVE REVIEW

A Practical Review of Acute Orthostatic Intolerance

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Abstract

Orthostatic intolerance generally develops when an individual is unable to adequately maintain blood pressure during an orthostatic challenge, and symptoms of presyncope or syncope develop. Triggers of orthostatic intolerance may include postural changes, prolonged standing, rapid cessation of exercise, warm environments, inadequate fluid intake or an emotionally stressful event. Focused on healthy, young individuals, this review examines the various methods used to test acute orthostatic intolerance. These include: head-upright tilt, lower body negative pressure, and rapid standing. Finally, the major factors thought to influence orthostatic intolerance are discussed, highlighting areas requiring further research. **Health & Fitness Journal of Canada 2010; 3(2):44-51.**

Keywords: orthostatic intolerance, lower body negative pressure, haemodynamics, stroke volume

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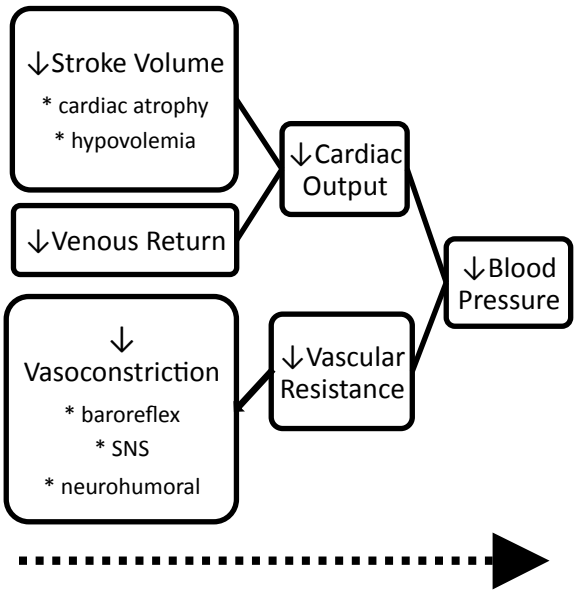
Background

Orthostatic intolerance refers to the inadequate physiological compensation to maintain blood pressure during orthostasis, where rapid and substantial decreases in central blood volume challenge cardiovascular control (Buckey et al., 1996). The mechanisms of this phenomenon have yet to be completely elucidated; however, it is thought that rapid central hypovolemia may overwhelm the vasomotor reserve available for vasoconstriction (Fu et al., 2005), leading to a reduction in brain perfusion, triggering a neurocardiogenic reflex response. Traditional physiological signs include a sudden reduction in heart rate, cardiac output and blood pressure (Mosqueda-Garcia et al., 2000). Figure 1 illustrates the relationship of cardiac output and vascular resistance on blood pressure. Individual differences in the haemodynamic response to orthostasis, including those of homozygous twins, are striking despite similar orthostatic tolerance (Goswami et al., 2009; O'Leary et al., 2007). Symptoms of presyncope such as nausea, blurred vision, sweating and dizziness represent the onset of orthostatic intolerance (Rickards et al., 2008).

Unlike chronic orthostatic intolerance, which is the result of cardiovascular abnormalities or autonomic nervous system dysfunction, acute orthostatic intolerance occurs in healthy individuals as the result of hypovolemia due to sudden postural shifts or other environmental stressors (Mukai and Lipsitz, 2002). This review will focus on the factors affecting acute orthostatic intolerance in young adults owing to the various age-related maladaptations that may increase the incidence of orthostatic intolerance in the elderly. Further, this review is not an

exhaustive review of the literature, but rather includes selections from prominent research in the areas that will best provide an overview of the suspected aetiology of this phenomenon.

Figure 1: Potential mechanisms responsible for blood pressure reductions in response to an orthostatic challenge.



Common Methodologies / Tests of Orthostatic Tolerance

Orthostatic stress testing in the clinic or lab may involve one or more of the following methods: active standing, head-upright tilt (HUT) tilt-table testing, lower body negative pressure (LBNP), and combined HUT and LBNP. Continuous beat by beat blood pressure (i.e., finger plethysmography, or arterial tonometry) and ECG is ideally required. Respiration, end-tidal carbon dioxide or peripheral, thoracic, and cerebral blood flow may also be assessed.

Standing

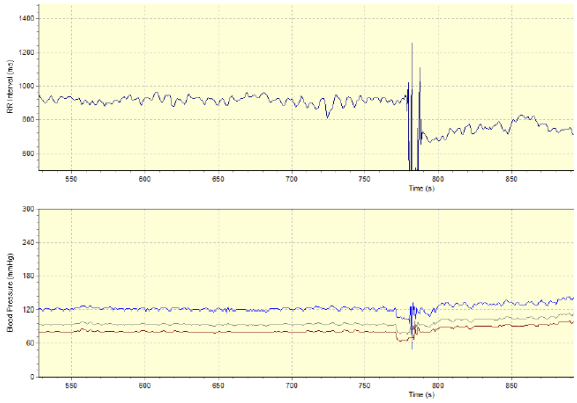
Upon standing, approximately 750 mL of thoracic blood is abruptly translocated downward to the splanchnic region and lower periphery (Mukai and Lipsitz, 2002). This substantial amount of arterial blood moving from the chest to venous circulation below the diaphragm results in a considerable orthostatic stress. More recently standing from a squatting position has been used as a means to induce a greater orthostatic stress than standing from a supine or seated position. The squat manoeuvre has been shown to produce greater local vasodilatation in the legs, combined with a marked pooling of blood in the venous vessels of the legs and abdomen that have been compressed in the squat position (Krediet et al., 2006). Standing methods are effective and do not require specialized equipment, making them ideal for laboratories or clinics with limited resources. However, the practitioner must be aware that active standing invokes the muscle pump, which is thought to mitigate the full effects of orthostatic intolerance, and may thereby increase the risk of a false negative diagnosis (Wieling et al., 2007). Figure 2 illustrates the ECG and blood pressure response to a stand test.

Heat Up Tilt

The HUT manoeuvre has been shown to be a very effective means of assessing blood pressure control (Abi-Samra et al., 1988). Following a supine rest period, the participant is placed upright (at 60-90 degrees from horizontal) and responses are assessed for a minimum of 10 minutes. Although some fundamental differences are observed between the early response to tilt and the early response to standing (especially during

the first few minutes), HUT and standing tests become essentially equivalent following that early response period (Wieling et al., 2007). When assessing individuals with spinal cord injury or other mobility issues, the tilt table method is often preferred.

Figure 2: Haemodynamic responses during active standing for one individual.

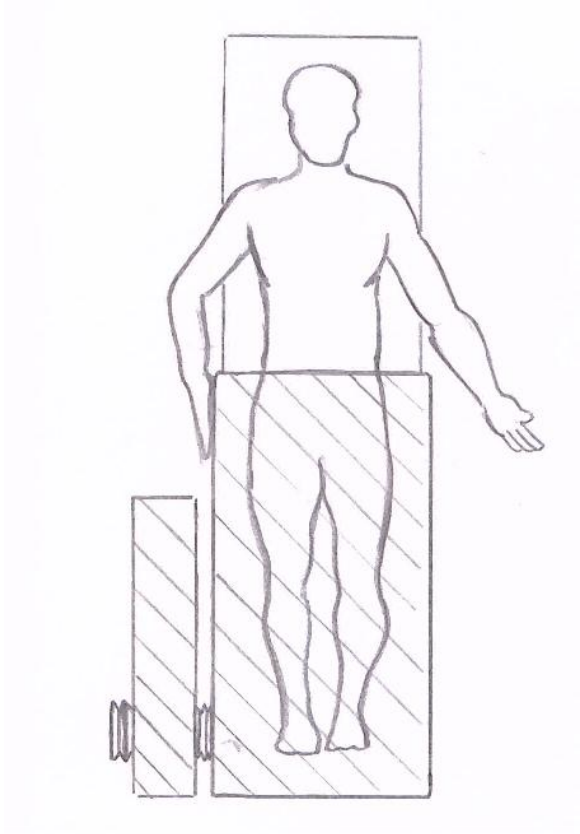


Lower Body Negative Pressure

The LBNP method has been shown to be a useful tool for inducing orthostatic stress and to study cardiovascular response to haemorrhage (Cooke et al., 2004). The LBNP test stimulates orthostasis by using external negative pressure on the legs, buttocks, and lower abdomen using a sealed chamber (Figure 3). Graded LBNP leads to increased sympathetic activity resulting in vasoconstriction and tachycardia as well as reductions in cardiac preload (Goswami et al., 2008). Fluid displacement from central to peripheral regions may be 500-1000 mL after 5 minutes of LBNP at 20-40 mmHg, and in excess of 1000 mL with 60 mmHg LBNP (Cooke et al., 2004).

Some investigations involve LBNP combined with HUT. The combination of these two methods has been shown to safely and reliably induce presyncope in normal subjects (LeLorier et al., 2003).

Figure 3: An illustration of a lower body negative pressure chamber.



Factors Affecting Orthostatic Intolerance

There have been a number of factors proposed to influence orthostatic intolerance. Some of the most studied factors include gender, fitness status, prior exercise, bed rest, and temperature. These factors will be discussed below in further detail.

Gender

It has been well recognized that the incidence of orthostatic intolerance is higher in women than men (Convertino,

1998a; Fu et al., 2004). While women are typically smaller than males, the direct association of orthostatic tolerance to body size has not been found (Franke et al., 2003). A lower stroke volume in women has been implicated in the higher incidence of orthostatic intolerance seen in women versus males (Fu et al., 2005) and is in agreement with the differences found between tolerant and intolerant males (Convertino et al., 2004; Gasiorowska et al., 2005). These researchers also found significantly lower vascular resistance to be a distinguishing factor between tolerance and intolerance to LBNP. However, the relationship between vascular resistance and orthostatic intolerance is not clear. Whether vascular resistance is a causative factor or a consequence of orthostatic intolerance is up for debate.

Vascular resistance is important for the maintenance of blood pressure during orthostasis (Hainsworth, 2004); however, the literature reveals conflicting results. Women have displayed impaired vasoconstriction to LBNP (Lindenberger et al., 2008) and post spaceflight (Waters et al., 2002). By contrast, lower tolerant females were shown to have greater increases in total peripheral resistance than more tolerant males (Convertino, 1998a). Further, Fu and colleagues (Fu et al., 2004) found no gender differences in vascular resistance during a maximal LBNP test and similar muscle sympathetic nerve activity in men and women (Fu et al., 2005). The reasons for these discrepancies remain unclear.

Fitness and Exercise

Endurance-trained individuals have displayed a greater intolerance to orthostatic stress (Levine et al., 1991; Raven, 1993; Raven and Pawelczyk, 1993). Increased ventricular compliance due to endurance training may potentially result in larger reductions in stroke volume for a given cardiac filling pressure when subjected to an orthostatic stress (Levine, 1993). While a more compliant ventricle would benefit an individual during exercise, during orthostatic stress, this physiological adaptation exaggerates the reduction in stroke volume for a given reduction in left ventricular filling pressure (Esch et al., 2007). By contradiction, three months of endurance training has been shown to improve orthostatic tolerance (Winker et al., 2005). It has yet to be determined if this response to training is found in only deconditioned individuals. Short-term training adaptations such as an increase in plasma volume may improve orthostatic tolerance, whereas long-term training adaptations, such as improved ventricular compliance, would likely offset the impact of an increased plasma volume on orthostatic tolerance.

Finally, prior exercise is known to affect orthostatic intolerance. Following an acute bout of moderate intensity, dynamic exercise, the reduced vascular resistance impairs one's ability to regulate blood pressure (Halliwill, 2001). In addition, the cardiac/vasomotor baroreflex is attenuated acutely after exercise (Ogoh et al., 2003). Interestingly, type of exercise was not found to modify the response to LBNP in an investigation comparing an acute bout of moderate intensity continuous exercise versus high intensity interval exercise (Scott et al., 2008), or between a group of highly trained swimmers versus runners (Franke et al., 2003).

Bed rest and prolonged immobility

The incidence of orthostatic intolerance has been shown to increase following spaceflight (Buckey et al., 1996;

Convertino, 1998b) and prolonged immobility (Convertino et al., 1990). Researchers use bedrest studies to replicate the physiological effects of space as gravitational deconditioning occurs with both bedrest and microgravity. Bedrest studies also provide insight into prolonged immobility due to illness, injury or an extreme sedentary behaviour.

Both cardiac function and plasma volume reductions have been implicated in this increased orthostatic intolerance post spaceflight and following bedrest. For instance, Levine and colleagues (Levine et al., 1997) showed ventricular performance was altered after bed rest, as a result of left ventricle atrophy and reduced distensibility, as well as a decrease in plasma volume. Blood volume reductions have also been implicated in the impairments in the baroreflex seen in astronauts after spaceflight (Convertino et al., 1990). However, plasma volume alone does not appear to be responsible for reductions in orthostatic intolerance as induced diuresis was not found to affect stroke volume during orthostasis, unlike 2 weeks of bedrest where the heart became smaller and less distensible (Perhonen et al., 2001). There has also been evidence to suggest that a decrease in sympathetic nerve activity following bedrest may further compound the effects of cardiac atrophy and hypovolemia (Kamiya et al., 2003). Additional factors such as reductions in muscle volume that may occur with time in space or prolonged bed rest, and how this may alter the effectiveness of the skeletal muscle pump must also be considered.

Environmental Temperature

Recent work in heat stressed individuals has demonstrated a contribution of an impaired cutaneous vasoconstrictor responsiveness to the reductions seen in orthostatic intolerance in warm environments (Wilson et al., 2002) and the preservation of cerebral blood flow velocity and orthostatic tolerance with skin cooling (Wilson et al., 2002). Specifically, the effects of temperature have been shown to alter Frank-Starling curves, shifting to the left with heating and a rightward shift with cooling (Wilson et al., 2009). Thus, investigations of orthostatic intolerance must control for environmental temperature.

Conclusions

Acute orthostatic intolerance appears to be a common phenomenon affecting primarily, women, endurance-trained athletes, and those whom have had prolonged periods of immobility. In addition, warm environmental temperatures potentiate the development of orthostatic hypotension. However, the mechanisms responsible for the development of orthostatic intolerance are still highly speculative and this topic remains one of the most intriguing within applied physiology. Future research must control for as many factors as possible to ascertain the main determinants of orthostatic intolerance.

Authors' Qualifications

The author qualifications are as follows: Anita Cote MSc, CSEP CEP, CSEP CPT-CC; Aaron Phillips, MSc, CSEP CEP; Shannon Bredin, MSc, PhD, CSEP CPT-ME; Darren Warburton, MSc, PhD, CSEP CEP, CSEP CPT-ME.

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