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ARTICLE *in* JOURNAL OF ELECTROMYOGRAPHY AND KINESIOLOGY · NOVEMBER 2008

Impact Factor: 1.65 · DOI: 10.1016/j.jelekin.2008.08.007 · Source: PubMed

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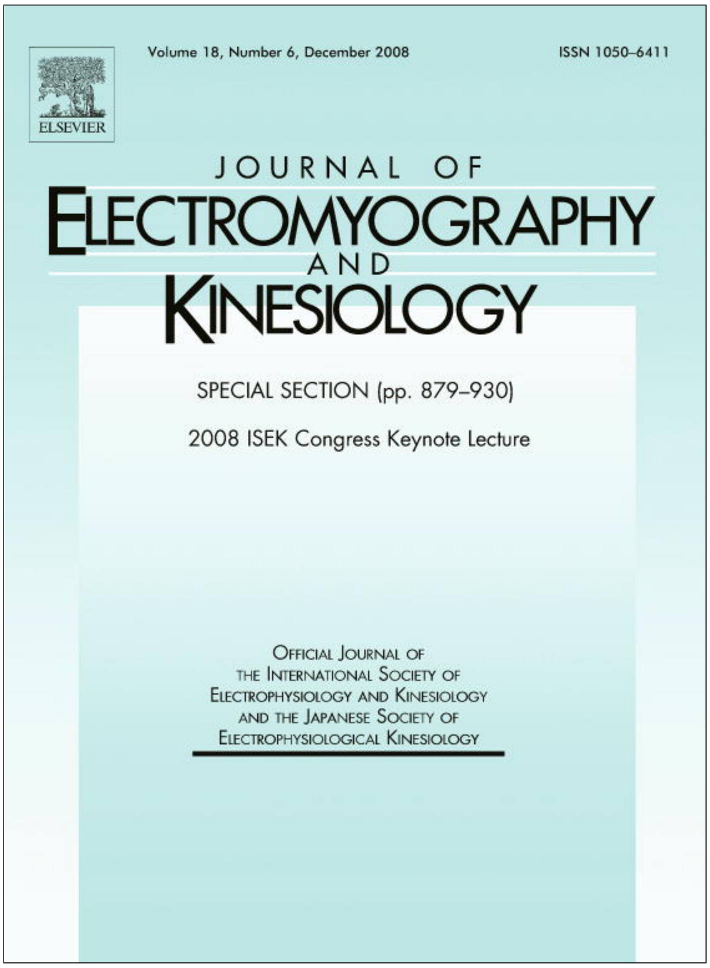
Volume 18, Number 6, December 2008
ISSN 1050-6411
ELSEVIER
JOURNAL OF
ELECTROMYOGRAPHY
AND
KINESIOLOGY
SPECIAL SECTION (pp. 879–930)
2008 ISEK Congress Keynote Lecture
Official Journal of
the International Society of
Electrophysiology and Kinesiology
and the Japanese Society of
Electrophysiological Kinesiology

Available online at www.sciencedirect.com
ScienceDirect
Journal of Electromyography and Kinesiology 18 (2008) 900–907
JOURNAL OF ELECTROMYOGRAPHY AND KINESIOLOGY
www.elsevier.com/locate/jelekin

2008 ISEK Congress Keynote Lecture

Cardiovascular response to functional electrical stimulation and dynamic tilt table therapy to improve orthostatic tolerance ☆

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Received 16 July 2008; received in revised form 18 August 2008; accepted 18 August 2008

Abstract

Orthostatic hypotension is a common condition for individuals with stroke or spinal cord injury. The inability to regulate the central nervous system will result in pooling of blood in the lower extremities leading to orthostatic intolerance. This study compared the use of functional electrical stimulation (FES) and passive leg movements to improve orthostatic tolerance during head-up tilt. Four trial conditions were assessed during head-up tilt: (1) rest, (2) isometric FES of the hamstring, gastrocnemius and quadriceps muscle group, (3) passive mobilization using the Erigo dynamic tilt table; and (4) dynamic FES (combined 2 and 3). Ten healthy male subjects experienced 70° head-up tilt for 15 min under each trial condition. Heart rate, blood pressure and abdominal echograms of the inferior vena cava were recorded for each trial. Passive mobilization and dynamic FES resulted in an increase in intravascular blood volume, while isometric FES only resulted in elevating heart rate. No significant differences in blood pressure were observed under each condition. We conclude that FES combined with passive stepping movements may be an effective modality to increase circulating blood volume and thereby tolerance to postural hypotension in healthy subjects.

Keywords: Head-up tilt; Orthostatic intolerance; Functional electrical stimulation; Passive mobilization

1. Introduction

Orthostatic hypotension (OH) is a clinical condition defined as a sudden drop in blood pressure upon upright postural change (Schatz et al., 1996). In the first 3–5 min following head-up tilt (HUT), up to one litre of blood can pool in the lower extremities, resulting in a decrease in venous return and a subsequent reduction in cardiac output by up to 20% (Rowell, 1993; Smit et al., 1999). This condition is common in cases of traumatic brain injury (Luther et al., 2007) or spinal cord injury (SCI) (Claydon et al., 2006; Smit et al., 1999). These individuals will experience venous pooling resulting from sympathetic nervous system dysfunction. In fact, 74% of individuals with SCI experience episodes of dizziness, lightheadedness (pre-syncope) or loss of consciousness (syncope) upon postural change (Illman et al., 2000). These symptoms may impair the individual during the acute phase of SCI, and in some cases may persist for years (Frisbie and Steele, 1997).

☆ Preliminary data were presented in poster format at the Festival of International Conferences on Caregiving, Disability, Aging and Technology: Advanced in Neurorehabilitation Conference, June 16–19, 2007, Toronto, Ontario, Canada.

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doi:10.1016/j.jelekin.2008.08.007

Furthermore, OH interferes with the patient's rehabilitation, which is necessary to promote neural recovery, prevent muscle atrophy, mitigate osteoporosis, and to maximize clinical outcomes (Dietz and Colombo, 2004). Therefore, OH delays rehabilitation, prolongs bed rest and promotes further cardiovascular deconditioning.

Current OH treatment modalities include the use of elastic compression stockings, abdominal binders, pharmacological measures, and progressive mobilization exercises from supine to vertical posture (Mathias and Kimber, 1998). However, there are many individuals with SCI for whom these treatments are ineffective (Barber et al., 2000). Thus, new therapies are needed to improve orthostatic tolerance. One such approach is the use of functional electrical stimulation (FES) to improve venous return (Laughlin and Schrage, 1999; Smit et al., 1999). We have found that FES can reproduce functional movements, such as walking (Thrasher et al., 2006) and grasping (Popovic et al., 2006). In addition, several recent studies have investigated the use of FES to improve venous return in healthy (Faghri and Yount, 2002; Man et al., 2003; van Beekvelt et al., 2000) and SCI populations (Chao and Cheing, 2005; Faghri et al., 2001; Faghri and Yount, 2002; van Beekvelt et al., 2000). Alternatively, venous return can also be enhanced by exercise, since lengthening and shortening of muscle fibers will contribute to muscle pump activation (Laughlin, 1987). Thus, another approach for improving orthostatic tolerance in individuals with SCI is to create locomotor movements, such as stepping. Based on the rat model, the literature suggests locomotion is more effective for increasing venous return when compared to isometric FES (Laughlin, 1987). To date, one study has examined the effects of passive leg movements on improving orthostatic tolerance in humans (Czell et al., 2004), showing that passive mobilization therapy performed on the Erigo dynamic tilt table was effective in improving OH during tilt. However there is no information comparing the effectiveness of isometric FES to passive mobilization. In addition to isometric FES and passive mobilization, the combination of the two modalities, which consequently produces a dynamic FES modality, is an untested model which may be effective in improving venous return during head up tilt. Thus, the purpose of this study was to investigate the effect of isometric FES, passive mobilization, and dynamic FES on improving orthostatic tolerance in healthy subjects.

2. Materials and methods

2.1. Participants

A convenience sample of ten healthy male subjects who reported no history of cardiovascular, endocrine, or neuromuscular disease participated in this study. Subjects were non-smokers and were not taking any type of medication. Subjects were instructed to avoid alcohol and caffeine for 24 h, fast for 8 h, and drink nothing 2 h prior to the study. All tests were conducted between 1600 and 2200 h, in a quiet room with an ambient temperature between 19 and 21 °C. Approval was acquired from the local university ethics committee and all subjects provided written informed consent.

2.2. Experimental protocol

This study employed a randomized cross-over design, wherein each subject participated in a single session consisting of four 70° head-up tilt conditions. Previous studies have shown that syncope is most likely to occur at angles above 60° (Fitzpatrick et al., 1991):

(A) Control (HUT)
(B) Isometric FES (IFES)
(C) Passive mobilization (STEP)
(D) Dynamic FES (DFES).

Subjects were positioned supine on an Erigo dynamic tilt table (Erigo. Hocoma AG, Switzerland) and secured using torso and shoulder harnesses (Fig. 1). Subjects' thighs were attached to robotic actuators with soft straps and feet were loosely secured to the foot plates via a strap placed over the metatarsal joints so that the heels could separate from the

Fig. 1. The experimental setup. Subjects were secured onto the tilt-stepper with torso and shoulder harnesses. Actuators attached to the thighs perform passive movements. FES was applied to the left and right quadriceps, hamstring and gastrocnemius muscles.

foot plates to allow for non-obstructed venous pooling when upright. An automated blood pressure cuff and pulse monitor (HEM-637. Omron Healthcare, USA) was placed over the left brachial artery, which remained at heart level for the duration of the experiment. The cross-sectional area of the inferior vena cava (IVC_{CSA}) was measured by Doppler ultrasound (Acuson Aspen, Aspen Corporation, USA) imaging (Fig. 2). The probe was positioned 1.5 cm below the diaphragm in the hepatic segment of the IVC (Iida et al., 2007; Ishizaki et al., 2004; Krause et al., 2001; Lyon et al., 2005). Participants were scanned in the supine and upright positions prior to the start of the experiment in order to accommodate for vessel movement resulting from postural change.

To obtain baseline hemodynamic measurements, all subjects rested in the supine position for 20 min prior to the start of the experiment, although 5 min is sufficient based on the literature (Toska and Walloe, 2002). To control respiration, subjects were instructed to breathe in synchrony with a metronome at a rate of 15 breaths per min. Subjects experienced randomized head-up tilt conditions for 15 min periods. Blood pressure, heart rate and IVC_{CSA} measurements were recorded at baseline immediately prior to each tilt and at the onset, 5, 10 and 15 min interval of tilt. Elevation to 70° from the supine position took approximately 25 s. Following each tilt condition, subjects were returned to the supine position for 10 min to re-establish steady-state hemodynamic conditions. Baseline hemodynamic stability was verified in each case.

2.3. Apparatus and setup

Two programmable 4-channel neuromuscular electrical stimulators (Compex Motion, Compex SA, Switzerland) were used to deliver transcutaneous FES to the left and right hamstring, gastrocnemius, and quadriceps muscle group using 9 cm × 5 cm electrodes at the onset of tilt. The stimulators produced a biphasic waveform with 30 Hz frequency, 300 μs pulse duration, at the maximum tolerable stimulation amplitude (amplitude varied from 17 to 40 mA between subjects) for 15 min. For each muscle, the motor threshold was determined by gradually increasing the stimulation amplitude until palpable contraction occurred. The stimulation sequence, consisting of 24 isometric FES cycles per min, contracted the left gastrocnemius and quadriceps simultaneously with the right hamstring for one half of the cycle, and the right gastrocnemius and quadriceps simultaneously with the left hamstring during the second half of the cycle. Palpable muscle contractions and slight movement of the subject's legs were evident for all individuals.

An Erigo dynamic tilt table (Erigo, Hocoma AG, Switzerland) was used to induce passive mobilization through the use of robotic actuators. The tilt-table (Fig. 1) induces a stepping motion by alternating hip and knee flexion and extension as well as a small range of ankle dorsiflexion, in a sequence that imitates gait (Czell et al., 2004). When both Erigo and FES were used in combination FES systems and the tilt-table stepping were synchronized at 24 steps per min, such that left hip and knee extension coincided with left gastrocnemius and quadriceps stimulation.

Intravascular circulatory blood flow was estimated by Doppler ultrasound (Acuson Aspen, Acuson Corporation, USA) imaging of the IVC_{CSA} in sequential B-mode with a 5 MHz probe. The probe was fixed in place with a custom made holder, which prevented rotational and translational movements of the probe head throughout the experiment.

Due to the distensibilty of the IVC and the non-pulsatile conditions which resulted in constant velocity flow profiles, the blood flow returning from the lower limbs has been found to correlated closely with the change IVC_{CSA} (Ishizaki et al., 2004; Krause et al., 2001; Lyon et al., 2005). Therefore, changes in the IVC_{CSA} reflect changes to venous return, and so 1 min recordings of the IVC_{CSA} were imaged for each interval period and frame-by-frame analysis was performed using image processing software (ImageJ. NIH, USA) to calculate the IVC_{CSA}. In accordance with pervious studies, the IVC_{CSA} was calculated as the mean maximal cross-sectional areas for each 1 min recording period (Ishizaki et al., 2004).

2.4. Statistical analysis

All values of heart rate, blood pressure, and IVC_{CSA} were normalized with respect to the values measured at the end of each supine rest period immediately before tilt. A three-way repeated measures ANOVA was used to test the independent effect of FES, passive mobilization and

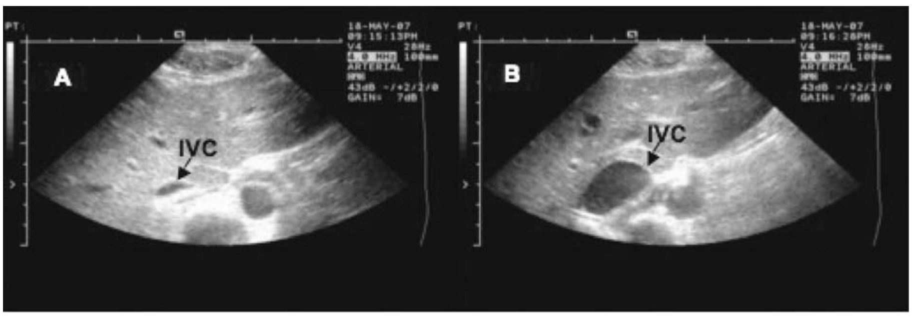

Fig. 2. Representative changes in IVC_{CSA} from same subject. (A) IVC at 15 min of rest condition. (B) IVC at 15 min of dynamic FES condition.

tilting duration on heart rate, blood pressure, and IVC_{CSA}. Alpha was set at 0.05 for all procedures. Where significant within-subject effects were found with the ANOVA, Dunnett's post hoc test was used to compare mean values of each condition to the HUT condition. Statistical significance was assumed when *p*-values were less than 0.05. All data are reported as means ± SE.

3. Results

Anthropometric data from all subjects are presented in Table 1. One subject experienced pre-syncope during the 15 min HUT condition. No subjects experienced any symptoms of pre-syncope or syncope during IFES, STEP or DFES conditions.

Changes in normalized IVC_{CSA} for each condition over 15 min of HUT are shown in Fig. 3. A progressive decline in the IVC_{CSA} from rest was observed for both the HUT (0.80 ± 0.10) and IFES (0.80 ± 0.07) conditions. For the first 10 min of tilt, STEP (1.13 ± 0.15) and DFES (1.08 ± 0.08) conditions were able to increase the IVC_{CSA} from rest. However, STEP (1.02 ± 0.12) was unable to maintain the increased IVC_{CSA} after 15 min of tilt, whereas DFES (1.15 ± 0.07) did manage. By comparing each condition to that of HUT, a 44% ($p = 0.04$) increase in IVC_{CSA} was observed for the DFES condition after the 15 min interval.

Normalized heart rate was elevated for each condition over the 15 min tilt duration (Fig. 4). During HUT, heart rate increased gradually for the first 10 min (1.35 ± 0.05) but reverted to initial tilt values (1.30 ± 0.03) over the last 5 min of tilting. Similarly, DFES produced a gradual increase in heart rate, with a more pronounced peak occurring at 5 min post-tilt (1.36 ± 0.06). IFES produced an abrupt increase in heart rate at tilt onset (1.44 ± 0.07) which was sustained for the duration of tilt (1.45 ± 0.04). STEP elevated and sustained the heart rate through the duration of the tilt. In comparing each condition to HUT, a 12% ($p = 0.02$) increase in heart rate was observed during the IFES condition after 15 min.

There was no significant change in the normalized systolic blood pressure (SBP) and diastolic blood pressure (DBP) values when compared to the HUT condition. SBP increased slightly over the tilting duration under HUT (1.09 ± 0.02), IFES (1.09 ± 0.02), and DFES (1.09 ± 0.01) conditions. For STEP, SBP (Fig. 5) remained consistent (1.04 ± 0.02) after 15 min. DBP increased during the first 5 min of HUT (1.20 ± 0.04), and then remained constant for the remainder of the condition (Fig. 6). DBP decreased during gradually during IFES. Both STEP and DFES produced an initial increase in DBP, which was attenuated after 5 min of tilt.

Table 1
Summary of subject data

Subject	Age (yr)	Height (cm)	Weight (kg)	Body mass index
1	21	182	82	24.8
2	23	177	63	20.1
3	23	182	80	24.2
4	22	188	88	24.9
5	23	175	65	21.2
6	30	183	82	24.5
7	21	186	86	24.9
8	27	178	75	23.7
9	31	169	64	22.4
10	19	193	79	21.2
Mean	24	181.3	76.4	23.2
SD	4.0	6.9	9.3	1.8
SE	1.3	2.2	2.9	0.6

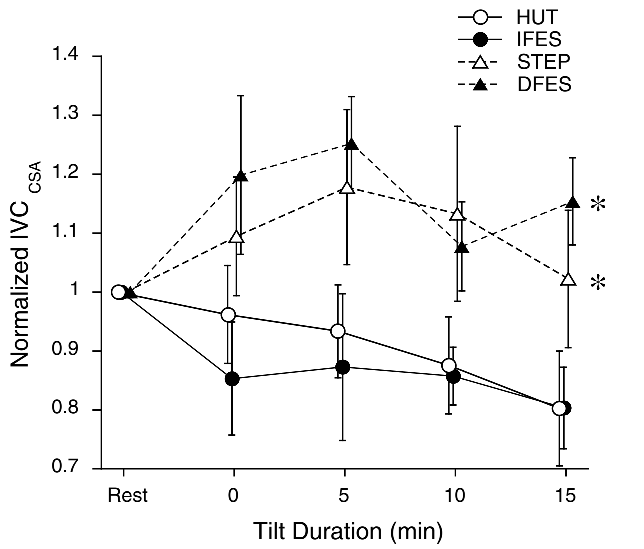

Fig. 3. Inferior vena cava cross-sectional area values normalized to supine baseline measurements for each condition over 15 min of HUT. Passive stepping ($p < 0.001$) and dynamic FES ($p = 0.007$) were found to exert significant effects on IVC_{CSA}. * indicates $P < 0.05$ for the post hoc test.

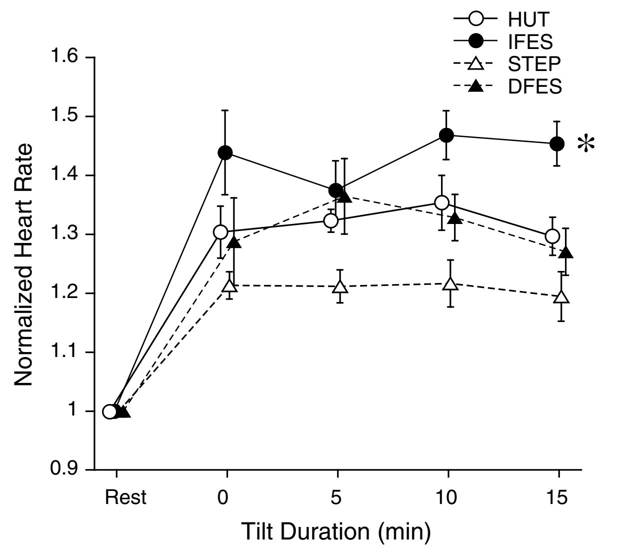

Fig. 4. Heart rate values normalized to supine baseline measurements for each condition over 15 min of HUT. Isometric FES ($p = 0.002$) and passive Stepping ($p = 0.001$) were found to exert significant effects on heart rate. * indicates $P < 0.05$ for the post hoc test.

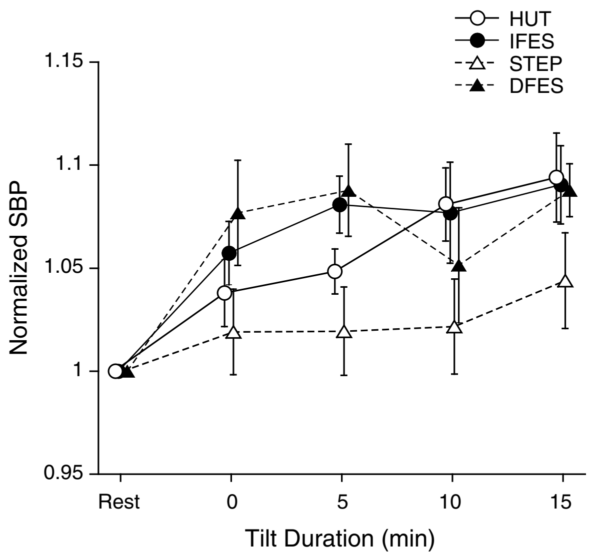

Fig. 5. Systolic blood pressure values normalized to supine baseline measurements for each condition over 15 min of HUT. The ANOVA did not find any significant effects on systolic blood pressure.

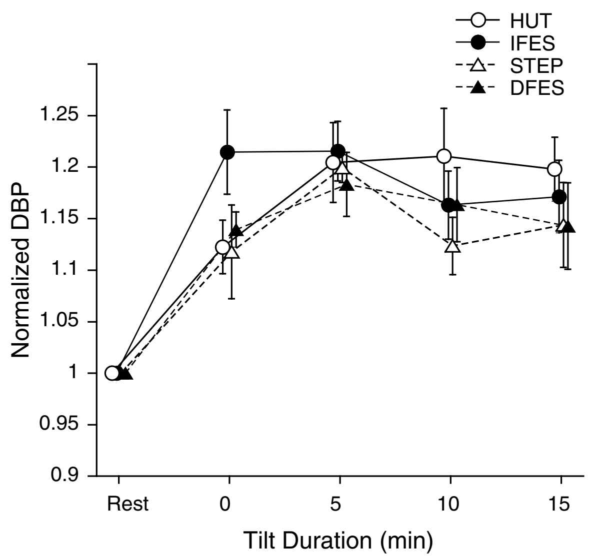

Fig. 6. Diastolic blood pressure values normalized to supine baseline measurements for each condition over 15 min of HUT. The ANOVA did not find any significant effects on diastolic blood pressure.

4. Discussion

This study compared the effects of isometric FES, passive movement and dynamic FES during orthostasis by monitoring the change in blood pressure, heart rate, and blood flow. Our results show that during orthostatic challenges, blood pressure was maintained, while heart rate increased and blood flow decreased. The application of isometric FES was able to increase the heart rate, but did not significantly affect blood flow. Passive mobilization did not produce significant effects. The application of dynamic FES was able to attenuate the decrease in blood flow during the head up tilt protocol. Therefore, dynamic FES has the greatest potential to increase the duration of orthostatic tolerance.

4.1. Blood flow response

During HUT, a 20% reduction in the size of the IVC_{CSA} was observed over 15 min. This is in accordance with healthy subjects' response to orthostatic stress (Smit et al., 1999). It is interesting to note that isometric FES conditions also resulted in a 20% reduction in mean IVC_{CSA}, whereas passive mobilization maintained (2%) and dynamic FES increased mean IVC_{CSA} (15%).

The reduction in mean IVC_{CSA} during isometric FES is in accordance with a study that assessed muscle pump function on venous return in healthy and SCI subjects (Faghri and Yount, 2002). However, contrary to our findings, another study had demonstrated that isometric FES can minimize venous pooling after 30 min of quiet standing in healthy subjects (Man et al., 2003). The disparity between our results when compared to quiet standing suggests individuals may experience differing cardiovascular responses under HUT and quiet standing conditions. This is possible, since brief static contractions in the leg muscles during upright stance will trigger the exercise and baroreceptor reflexes (Borst et al., 1982), thus resulting in an immediate increase in heart rate and thereby affecting blood flow. Furthermore, quiet standing was found to have a greater tendency to induce syncope when compared to HUT (Matsushima et al., 2004), which suggests that autonomic function and cardiovascular response differ between tilt and standing situations. Compared to isometric FES, passive mobilization and dynamic FES were able to either maintain or increase the mean IVC_{CSA}, suggesting that these modalities are more effective for maintaining or improving circulatory hemodynamics under orthostatic conditions.

4.2. Heart rate response

Healthy subjects experiencing orthostatic conditions will compensate by increasing heart rate to maintain cardiac output (Rowell, 1993). This was found to be true in our study, as mean heart rate increased by 30% for HUT. The most significant increase in mean heart rate (45%) occurred during isometric FES. Heart rate also increased for passive mobilization (19%) and dynamic FES (27%) but these occurred at levels less than that of the control condition.

It is possible that the main effect accounting for the dramatic 45% increase in heart rate during isometric FES is a consequence of sympathetic activity rather than cardiovascular function. This would help explain how isometric FES and the control condition both resulted in a 20% reduction in IVC_{CSA}. In this case, the increased heart rate during isometric FES can be attributed to increased sympathetic activity caused by electrical stimulation. The heart rate response for dynamic FES should reflect isometric FES, but does not. This may be caused by parasympathetic activation resulting from a feedback mechanism to equilibrate the increased blood flow and stroke volume thereby counteracting the FES-induced sympathetic activity. This parasympathetic activity can also be used to explain the slight 19% increase in heart rate observed during passive mobilization.

4.3. Blood pressure response

The literature on healthy subjects reports little or no change in SBP, and a gradual increase in DBP when experiencing HUT (Petersen et al., 2000). Our study was able to validate this finding, as SBP increased slightly (7%) and DBP increased gradually (18%) over the duration of tilt. We did not find significant differences in the blood pressures from the control condition for isometric FES, passive mobilization or dynamic FES conditions. This suggests that the regulation of blood pressure in healthy subjects is tightly controlled by the autonomic nervous system, and that any changes, such as increased blood flow or venous pooling will be mitigated by neurohormonal pathways.

4.4. Dynamic FES modality

Our study found that combing FES with passive mobilization significantly increases blood flow when compared to isometric FES or passive mobilization separately. This is important, since many studies in SCI rehabilitation have focused on the use of isometric FES for improving blood flow, but none have assessed the effects of the combination of FES with passive movement therapy during head-up tilt. One study does note that higher blood flow is possible during dynamic exercise, as locomotive movements will cause muscle fiber length changes and thereby produce enhanced skeletal muscle pump activity (Laughlin, 1987). Our finding is further strengthened by two more studies that assessed the differences in skeletal muscle blood flow during isometric and dynamic exercise. In the first study (Laaksonen et al., 2003), dynamic exercise was found to improve blood flow in the quadriceps femoris by 61% when compared to isometric exercise. In the second study (Faghri et al., 1998), hemodynamic functions of healthy subjects was enhanced during isometric FES combined with voluntary tip-toe contractions as compared to each independent modality.

The muscle pump should be most efficient under dynamic FES conditions for two reasons. First, we understand that blood flows freely during the period of muscle relaxation and is obstructed during the period of muscle contraction. Thus, optimal flow should occur during normal gait, where 60% of the stride pattern is spent in the stance phase and 40% during the swing phase (Winter, 2005). Additionally, muscle contractions during isometric FES will involve simultaneous contraction of all the muscle fibers being stimulated, whereas, during dynamic movement, the muscle fibers are activated on unique time frames during the contracting and relaxing phase of the stride pattern. This enhances blood flow as the individual fibers are contracting on a physiologically relevant time scale. Compared to isometric FES and passive mobilization, dynamic FES is the best model to represent this motion as it combines both movement and muscle fiber activation.

4.5. Determinants of blood flow

The major determinants of muscle blood flow during exercise are workload and muscle metabolic rate. It is known that skeletal muscle blood flow during exercise is closely related to power output, regardless of subject's exercise capacity or training status (Saltin et al., 1998). Thus, by simply increasing the workload during exercise, one can increase muscle blood flow. In this study, we were unable to measure power output. However, it should be clear that dynamic FES provides a higher workload than passive mobilization or isometric FES. Additionally, sustained exercise, will release metabolites that will cause local vasodilatation and capillary recruitment, leading to an increase in muscle blood flow (Rowland and Obert, 2002). Consequently the greatest increase in tissue metabolism, which occurs during dynamic FES, will correlate with the highest increase in blood flow.

4.6. Imaging venous return using doppler ultrasound

The present study also demonstrates the possibility of measuring venous flow in the assessment of OH by using Doppler ultrasound. Two dimensional ultrasound imaging of the inferior vena cava diameter has been established for the evaluation of venous return under orthostatic stress (Ishizaki et al., 2004). In our study we chose to image the inferior vena cava cross-sectional area for enhanced resolution. A limitation of the ultrasound imaging method is the possibility of motion artifacts in ultrasound data due to lower limb movement during dynamic exercise. To overcome this, steps were taken to secure subjects to the tilt table and fix the ultrasound probe (described in protocol). Another limitation is occlusion of the femoral and brachial vessels by the tilt table harness, which we attempted to avoid using padded harness straps. Although several subjects commented about feeling occluded, IVC_{CSA} imaging did not show venous flow reduction or obstruction. In future studies, it would be important to develop a harness system which does not occlude lower limb blood flow during HUT maneuvers. Nevertheless, because the same imaging technique and tilt duration were used for all subjects, changes in intra-subject blood flow were consistent.

5. Conclusion

This study demonstrates the potential use of dynamic FES versus isometric FES and passive mobilization therapy in improving orthostatic tolerance in healthy subjects, possibly due to synergistic effects of combining isometric FES with passive mobilization. Future studies are needed to evaluate the benefit of dynamic FES in individuals with SCI as this method could potentially be used in clinical practice as a means of improving orthostatic tolerance during the acute phase of SCI and stroke.

Acknowledgements

This work was financially assisted by the Toronto Rehabilitation Institute, Canadian Paraplegic Association of Ontario, Natural Sciences and Engineering Research Council of Canada (No. 249669), and Ontario Ministry of Health and Long-Term Care.

References

Barber DB, Rogers SJ, Fredrickson MD, Able AC. Midodrine hydrochloride and the treatment of orthostatic hypotension in tetraplegia: two cases and a review of the literature. Spinal Cord 2000;38(2):109–11.

Borst C, Wieling W, van Brederode JF, Hond A, de Rijk LG, Dunning AJ. Mechanisms of initial heart rate response to postural change. Am J Physiol 1982;243(5):H676–81.

Chao CY, Cheing GL. The effects of lower-extremity functional electric stimulation on the orthostatic responses of people with tetraplegia. Arch Phys Med Rehabil 2005;86(7):1427–33.

Claydon VE, Steeves JD, Krassioukov A. Orthostatic hypotension following spinal cord injury: understanding clinical pathophysiology. Spinal Cord 2006;44(6):341–51.

Czell D, Schreier R, Rupp R, Eberhard S, Colombo G, Dietz V. Influence of passive leg movements on blood circulation on the tilt table in healthy adults. J Neuroengin Rehabil 2004;1(1):4.

Dietz V, Colombo G. Recovery from spinal cord injury – underlying mechanisms and efficacy of rehabilitation. Acta Neurochir 2004;89(Suppl.):95–100.

Faghri PD, Yount J. Electrically induced and voluntary activation of physiologic muscle pump: a comparison between spinal cord-injured and able-bodied individuals. Clin Rehabil 2002;16(8):878–85.

Faghri PD, Votto JJ, Hovorka CF. Venous hemodynamics of the lower extremities in response to electrical stimulation. Arch Phys Med Rehabil 1998;79(7):842–8.

Faghri PD, Yount JP, Pesce WJ, Seetharama S, Votto JJ. Circulatory hypokinesis and functional electric stimulation during standing in persons with spinal cord injury. Arch Phys Med Rehabil 2001;82(11):1587–95.

Fitzpatrick AP, Theodorakis G, Vardas P, Sutton R. Methodology of head-up tilt testing in patients with unexplained syncope. J Am Coll Cardiol 1991;17(1):125–30.

Frisbie JH, Steele DJ. Postural hypotension and abnormalities of salt and water metabolism in myelopathy patients. Spinal Cord 1997;35(5):303–7.

Iida H, Kurano M, Takano H, Kubota N, Morita T, Meguro K, et al. Hemodynamic and neurohumoral responses to the restriction of femoral blood flow by KAATSU in healthy subjects. Eur J Appl Physiol 2007;100(3):275–85.

Illman A, Stiller K, Williams M. The prevalence of orthostatic hypotension during physiotherapy treatment in patients with an acute spinal cord injury. Spinal Cord 2000;38(12):741–7.

Ishizaki Y, Fukuoka H, Ishizaki T, Kino M, Higashino H, Ueda N, et al. Measurement of inferior vena cava diameter for evaluation of venous return in subjects on day 10 of a bed-rest experiment. J Appl Physiol 2004;96(6):2179–86.

Krause I, Birk E, Davidovits M, Cleper R, Blieden L, Pinhas L, et al. Inferior vena cava diameter: a useful method for estimation of fluid status in children on haemodialysis. Nephrol Dial Transplant 2001;16(6):1203–6.

Laaksonen MS, Kalliokoski KK, Kyrolainen H, Kemppainen J, Teras M, Sipila H, et al.. Skeletal muscle blood flow and flow heterogeneity during dynamic and isometric exercise in humans. Am J Physiol Heart Circ Physiol ;284(3):H979–86.

Laughlin MH. Skeletal muscle blood flow capacity: role of muscle pump in exercise hyperemia. Am J Physiol 1987;253(5 Pt 2):H993–H1004.

Laughlin MH, Schrage WG. Effects of muscle contraction on skeletal muscle blood flow: when is there a muscle pump?. Med Sci Sports Exerc 1999;31(7):1027–35.

Luther MS, Krewer C, Muller F, Koenig E. Orthostatic circulatory disorders in early neurorehabilitation: a case report and management overview. Brain Inj 2007;21(7):763–7.

Lyon M, Blaivas M, Brannam L. Sonographic measurement of the inferior vena cava as a marker of blood loss. Am J Emerg Med 2005;23(1):45–50.

Man IO, Lepar GS, Morrissey MC, Cywinski JK. Effect of neuromuscular electrical stimulation on foot/ankle volume during standing. Med Sci Sports Exerc 2003;35(4):630–4.

Mathias CJ, Kimber JR. Treatment of postural hypotension. J Neurol Neurosurg Psychiatry 1998;65(3):285–9.

Matsushima R, Tanaka H, Tamai H. Comparison of the active standing test and head-up tilt test for diagnosis of syncope in childhood and adolescence. Clin Auton Res 2004;14(6):376–84.

Petersen ME, Williams TR, Gordon C, Chamberlain-Webber R, Sutton R. The normal response to prolonged passive head up tilt testing. Heart 2000;84(5):509–14.

Popovic MR, Thrasher TA, Adams ME, Takes V, Zivanovic V, Tonack MI. Functional electrical therapy: retraining grasping in spinal cord injury. Spinal Cord 2006;44(3):143–51.

Rowell LB. Human cardiovascular control. New York: Oxford University Press; 1993.

Rowland T, Obert P. Doppler echocardiography for the estimation of cardiac output with exercise. Sports Med 2002;32(15):973–86.

Saltin B, Radegran G, Koskolou MD, Roach RC. Skeletal muscle blood flow in humans and its regulation during exercise. Acta Physiol Scand 1998;162(3):421–36.

Schatz IJ, Bannister R, Freeman RL, Koller WC, Low PA, Mathias CJ, et al.. Consensus statement on the definition of orthostatic hypotension, pure autonomic failure, and multiple system atrophy. The consensus committee of the American autonomic society and the American academy of neurology. Neurology 1996;46(5):1470.

Smit AA, Halliwill JR, Low PA, Wieling W. Pathophysiological basis of orthostatic hypotension in autonomic failure. J Physiol 1999;519:1–10, Pt 1.

Thrasher TA, Flett HM, Popovic MR. Gait training regimen for incomplete spinal cord injury using functional electrical stimulation. Spinal Cord 2006;44(6):357–61.

Toska K, Walloe L. Dynamic time course of hemodynamic responses after passive head-up tilt and tilt back to supine position. J Appl Physiol 2002;92(4):1671–6.

van Beekvelt MC, van Asten WN, Hopman MT. The effect of electrical stimulation on leg muscle pump activity in spinal cord-injured and able-bodied individuals. Eur J Appl Physiol 2000;82(5–6):510–6.

Winter DA. Biomechanics and motor control of human movement. Hoboken, NJ: John Wiley & Sons; 2005, c2005.

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