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Management of initial orthostatic hypotension: Lower body muscle tensing attenuates the transient arterial blood pressure decrease upon standing from squatting

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ABSTRACT

Initial orthostatic hypotension (IOH) comprises symptoms of cerebral hypoperfusion caused by an abnormally large transient mean arterial blood pressure (MAP) decrease 5-15 s after arising from a supine, sitting or squatting position. Few treatment options are available. We set out to test the hypothesis that lower body muscle tensing (LBMT) attenuates IOH after rising from squatting and its symptoms in daily life. Thirteen IOH patients (9 males, 27 years) rose twice from squatting; once with LBMT. In addition seven healthy volunteers (5 males, median age 27 years) were studied in a cross-over study design. They stood up from the squatting position three times, once combined with LBMT. Blood pressure (Finometer) was continuously measured and cardiac output (CO by Modelflow) and total peripheral resistance (TPR) were computed. MAP, CO and TPR were compared with and without LBMT. Using a questionnaire, the perceived effectiveness of LBMT in the patients' daily lives was evaluated. With LBMT the minimal MAP after standing up was higher, in both groups (19 mmHg in patients and 13 mmHg in healthy subjects). In healthy subjects the underlying mechanism was a blunted TPR decrease (to 47% vs. to 60%, $p < 0.05$), whereas in the patients no clear CO or TPR pattern was discernible. In follow up, 8 of 10 patients using LBMT reported fewer IOH symptoms. LBMT is a new intervention to attenuate the transient blood pressure decrease after standing up from squatting. IOH patients should be advised about the use of this manoeuvre.

INTRODUCTION

Transient loss of consciousness (TLOC) is a common medical problem, usually caused by intermittent disturbances in neural blood pressure (BP) control [1]. One of its causes is initial orthostatic hypotension (IOH). IOH is defined as symptoms of cerebral and retinal hypoperfusion (e.g. light-headedness, visual disturbances and/ or syncope) within 15 s after standing up from a supine, sitting or squatting position caused by an abnormally large transient BP decrease (e.g. > 40 mmHg systolic) [2]. Especially standing up from squatting has been recognised as an acute hemodynamic stressor [3; 4] which can provoke these complaints.

As with vasovagal syncope, for which according to current guidelines history taking rather than tilt testing is of diagnostic importance [5-7], the diagnosis of IOH also depends on a typical history. The active standing test as a diagnostic provocation for IOH has probably an even lower “sensitivity” than the tilt test for vasovagal syncope; the latter is estimated to amount to only 50% in patients with a classical history [2; 5; 7].

In a hospital setting IOH is the underlying cause of TLOC in about 3 – 4 % of syncope cases [2]. Syncope and pre-syncope, regardless of their aetiology may markedly decrease quality of life [8; 9]. Therapeutic management of IOH is thus an important issue. However the current therapeutic options are limited to general volume measures (e.g. salt loading [10]) that may have hypertensive side effects. The advice to rise slowly [2] may not always be feasible, especially when rising from squatting.

Tensing of leg, buttock and abdominal skeletal muscles, i.e. “lower body muscle tensing” (LBMT), is effective in increasing BP both in patients with postural hypotension due to autonomic failure [11] and during vasovagal reactions [12-14]. LBMT acutely minimises blood pooling in the veins of the lower body and thereby reinfuses blood into the thoracic circulation, enhancing cardiac output (CO) during hypotensive episodes [13; 15]. IOH is thought to be caused by active large skeletal muscle contractions [2]. So although LBMT has been shown effective in other forms of (episodic) hypotension, it is unclear whether this intervention would have any beneficial effects on IOH.

With this information as background, we set out to test the hypothesis that LBMT blunts the BP response to standing up from squatting. In addition we hypothesised that the beneficial effects of LBMT when applied to attenuate IOH would be caused by an increase in CO. We studied healthy subjects and IOH patients during standing up manoeuvres from squatting and used a combination of non-invasive continuous BP recording and pulse wave analysis to assess hemodynamic changes.

METHODS

We studied 13 patients who were referred to our syncope unit for the evaluation of TLOC (9 males, median height 180 cm (range 152 - 204), median body weight 77 kg (range 55 - 97), median age 27 years (range 15 - 59), with a median of 4.5 episodes of syncopes in their lifetimes (range 0 - 100)).

All patients had a clinical diagnosis of IOH based on a consistent history of (pre-)syncope occurring 5 - 15 s after rising from a supine or squatting position. There was no classic orthostatic hypotension (i.e. Δ SBP >20 mmHg and / or Δ DBP >10 mmHg, 3 minutes after standing up) [16]. The median duration of (pre-)syncopal symptoms was 2 years (range 4 months – 10 years). Two patients had experienced frequent pre-syncope after standing up (i.e. daily to weekly) but this had never resulted in loss of consciousness. Of the patients with syncope 4 also had daily pre-syncopal complaints after standing up; 6 experienced such complaints on a weekly basis and one patient had occasional complaints.

Protocol

BP was measured continuously by finger volume clamp photoplethysmography (Finometer, Finapres Medical Systems, The Netherlands). After ~5 min free standing the patients squatted for ~1 min, rose within 1 s and stood for ~1 min. On repeat squat-stand after another ~1 min of squatting, they performed LBMT for 30 - 60 s immediately after rising. If patients reported light-headedness or other pre-syncopal symptoms these were documented. LBMT consisted of tensing of all skeletal muscles in the abdomen, buttocks and legs at maximal voluntary capacity for 40 s.

The experiments were performed during the evaluation of the patients for IOH. Patients were positioned in front of the monitor and could observe their BP responses. The duration of squatting varied slightly among patients and was of shorter duration compared to the healthy subjects because of the patient evaluation setting. Repeated squatting for long periods is experienced as uncomfortable by some patients.

After completing the protocol, a subset of 5 patients repeated the squatting protocol twice. (This was done to give them further explanation and instruction.) The first of the three “trials” was used for the comparison described below.

To reduce the potential confounding influence of the fixed order of control and intervention in the patient series, we additionally studied 7 healthy volunteers (5 males, median age 27 years (range 25 - 59), height 179 cm (range 164 - 202), body weight 74 kg (range 52 - 85)) who had not experienced significant IOH symptoms over the last year. In a cross-over study design we assessed the effects of LBMT after standing up from squatting. First, all subjects squatted for 2 min, rose within 1 s and stood

for 2 min. Standing up from the squatting position was repeated twice. Four randomly assigned subjects performed LBMT after rising from the second squatting, while the remaining 3 subjects performed LBMT after rising from the third squatting.

These experiments were performed in accordance to the standards set in the Declaration of Helsinki after approval by the Medical Ethics Committee of the Academic Medical Center at the University of Amsterdam and obtaining written informed consent.

Analysis

Off-line, beat-to-beat systolic (SBP) and diastolic (DBP) arterial blood pressure and heart rate (HR) were derived from the arterial pulse wave. Mean arterial pressure (MAP) was the time-integral over the beat-to-beat pressure recording. Corrupted data-points (e.g. artefacts in the continuous BP recording) were identified by visual inspection and omitted (< 2 %). Relative changes in left ventricular stroke volume (SV) were obtained using pulse wave analysis (Modelflow, Finapres Medical Systems, The Netherlands [17]). This method has been validated during active and passive postural stress against thermo-dilution [18], during rapid changes in posture against Doppler ultrasound [19], and during physical counter-manoevres against gas re-breathing [15]. CO was $HR * SV$. Beat-to-beat TPR was $MAP * CO^{-1}$. After pulse wave analysis all beat-to-beat data were re-sampled at 1Hz.

Baseline values were taken from the interval -40 to -10 s before each standing up manoeuvre. MAP nadir (MAP_{min}) induced by each manoeuvre was identified and the synchronous CO and TPR were calculated. All variables are given as median and range. Using Wilcoxon's signed rank test we compared MAP_{min} , CO and TPR respectively, in the patients after standing from squatting without and with LBMT. In the healthy subjects Friedman's repeated measures ANOVA on ranks identified differences between the two squats without and the single squat with LBMT. For all tests a p-value < 0.05 was considered significant.

Follow up

Using a questionnaire, the perceived effectiveness of LBMT in the patients' daily lives was evaluated addressing the use of the LBMT (daily, weekly/monthly, or never), the frequency of (pre-) syncopal spells after learning LBMT as compared to before (less, same, disappeared), and the perceived benefit from the manoeuvre (some benefit, much benefit; no benefit).

Results

After rising from the first squat, the patients' MAP decreased from 110 mmHg (range 88 - 144) to 69 mmHg (range (53 - 91); SBP from 145 mmHg (range 121 - 201) to 90 mmHg (range 70 - 123); DBP from 88 mmHg (range 69 - 105) to 58 mmHg (range 40 - 76); Figure 1). Δ SBP was > 40 mmHg in 12 patients and all experienced pre-syncope symptoms.

At baseline there were no differences between the first and the second squat in MAP (110 vs. 109 mmHg), CO (6.5 vs. 6.4 arbitrary units) and TPR (1.0 vs. 1.0 arbitrary units). When the stand up was repeated with LBMT, MAP_{min} was 19 mmHg higher than without LBMT (88 vs. 69 mmHg, $p < 0.05$). SBP at MAP_{min} was 111 mmHg (range 67 - 163); DBP 69 mmHg (range 43 - 87)) (Figure 1). Δ SBP was > 40 mmHg in 5 patients.

Figure 2 shows the continuous blood pressure recording in a representative patient during consecutive stand up manoeuvres from squatting with and without LBMT.

At group level ($n = 13$) CO and TPR at MAP_{min} did not differ between control and LBMT. In 4 patients the MAP_{min} with LBMT was accompanied by a >10% higher TPR as compared to without LBMT; and in 8 subjects CO was > 10 % higher. Also in a sub-analysis of patients with a difference of MAP_{min} > 10 mmHg between control and LBMT ($n = 5$) there was no single pattern in TPR and / or CO.

Repeated squat-stand manoeuvres in a subset of 5 subjects revealed a trend for a larger Δ MAP after successive squats (Figure 3). However the effect of LBMT seemed to increase over the course of 3 successive trials, suggesting a learning effect (Figure 3).

In the healthy subjects there was also no difference in MAP during the three squats (95 vs. 97 vs. 98 mmHg), CO (5.5 vs. 5.2 vs. 5.2 arbitrary units) or TPR (1.0 vs. 1.1 vs. 1.1 arbitrary units) at baseline. When the subjects used LBMT after standing up, MAP_{min} was higher than after either of the two squat-to stand manoeuvres without intervention (76 mmHg vs. 63 mmHg and 57 mmHg, $p < 0.05$, Figure 4). This was associated with a higher TPR at MAP_{min} (50 % vs. 45 % and 38 % of baseline, $p < 0.05$); CO at this point did not differ among interventions (Figure 4). Over the interval 20 - 30 s after standing up CO was higher during LBMT than without (144 % vs. 100 % of squatted baseline, $p < 0.05$), TPR did not differ.

In clinical follow-up 12 of 13 patients were contacted after 2 months (range 1-26). Two patients had experienced no IOH symptoms since consulting with us and had not used LBMT. The remaining 10 patients reported using LBMT on a daily to weekly basis both after rising from squatting and from

supine. In 8 of them the frequency of their complaints had decreased. Nine patients perceived some or much benefit from the manoeuvre in daily life. General comments included that patients sometimes would rise a first time not using LBMT, forcing them to sit or lay down again; on repeat standing up they would use LBMT and experience no symptoms.

DISCUSSION

The main new finding of this study is that LBMT attenuated the BP decrease after standing from squatting in both IOH patients and healthy subjects. In the patients, CO and TPR at MAP_{min} did not differ consistently for LBMT and control. In healthy subjects the underlying mechanism was a blunting of the transient reduction of TPR related to assumption of the upright position. In clinical follow-up patients perceived beneficial effects of LBMT on IOH complaints in daily life. Rising from squatting is an every day orthostatic stress that may result in IOH complaints in otherwise healthy persons [20] and our results are directly applicable to them. We speculate that LBMT will be similarly effective in combating IOH after standing up from supine.

Testing the initial hemodynamic adaptation standing up from squatting has been used by various groups [21-24]. The manoeuvre's reproducibility has however never been systematically documented. Our findings in both patients (Figure 3) and healthy controls (Figure 4) suggest that the blood pressure decrease after successive standing up manoeuvres from squatting is augmented.

Rossberg & Peñáz documented a $\Delta\text{MAP}_{\text{max}}$ when standing up after 6 min of squatting of ~45 mmHg, [24]. Rickard and Newmann found a ΔDBP of 25 ± 2 mmHg, 10 s after standing up from 4 min of squatting (ΔMAP 24 ± 2 mmHg), but did not document the exact timing of the ΔBP [25]. During the squat-stand manoeuvre in healthy subjects in our study the maximum ΔMAP (-31 mmHg) was somewhat smaller compared to Rossberg & Peñáz's data which may be related to the shorter squatting period. The nadir of the ΔMAP in Rickard & Newmann's study may have been passed before the measurement. We conclude that based on the heterogeneity of the squat-stand protocols available in the literature, that vary in duration of squatting and standing times [21; 22; 24; 26], there is a need for studies that relate the duration of squatting to its initial (seconds) and prolonged (minutes) hemodynamic effects after standing up.

Several factors may play a role in the immediate decrease in blood pressure when standing up from squatting [2; 22; 24]. Most important is the acute fall in TPR [22], which is caused by a combination of the following factors [2; 24; 27]. 1) The acute decompression of arterial vessels in the legs causes an instantaneous mechanical decrease in vascular resistance. 2) There is an increase of the arterio-venous pressure gradient, due to decompression of the venous vessels. 3) The relative ischemia in the leg muscles during squatting augments the fall in arterial resistance by local factors ("the post-tourniquet effect" [22]). 4) The muscle activity during the standing up manoeuvre may promote venous return which can trigger cardiopulmonary pressure receptors and lead to a transient decrease of sympathetic vasoconstrictor outflow [28]. The vastly decreased TPR is not completely offset by the concomitant increase in CO [2; 22; 24].

How LBMT affects the hemodynamic transient in IOH patients after standing up from squatting is not fully explained by the data from this study, in terms of consistent differences in CO and/ or TPR between control and intervention. The findings from the healthy subjects however suggest that, unlike our hypothesis that predicted primarily an effect on CO, an increased TPR at MAP_{min} may also play a role. In general the mechanical effects of tensing of large muscle groups on TPR (e.g. by “kinking” of arteries) are insignificant because they are off-set by fast (reflex) adaptations of the arteriolar conductance [29]. We suggest that LBMT augments TPR after standing up from squatting because arteriolar conductance is very high at MAP_{min} (see above) and unable to further off-set the mechanical effects of LBMT.

After the initial phase, LBMT causes a sustained elevated CO in both patients and healthy subjects. As CO during orthostatic stress is a function of cardiac filling rather than HR [30] this increase of CO is most likely facilitated by an augmented venous return. This finding is also in agreement with previous studies [15; 31] and supports the notion that LBMT acts as a natural antigravity suit that optimizes venous return to the heart and thereby optimizes CO. Previous work showed that central command as a determinant of arterial blood pressure [32], does not play a significant role in the effectiveness of physical counter manoeuvres [14].

A limitation to the study design is that we did not use a validated measure to quantify the effect of LBMT on symptoms while measuring BP. However in the IOH patients we found a difference in MAP_{min} with LBMT (as compared to control) of 19 mmHg which would generally be accepted as of clinical relevance [33].

Another concern may be that the order in which control and LBMT were performed in the patients was not alternated or randomised. However the results from the series of healthy subjects show that the effect of the LBMT is consistent irrespective of order of control and intervention experiment.

Additional support for the efficacy of LBMT is found in results from the 5 patients who alternated LBMT and control during successive stand up manoeuvres (Figure 3). The results of the follow up (albeit limited) indicate that LBMT may also be effective in daily life.

In conclusion, this study shows that the transient blood pressure decrease after standing up from the squatting position can be attenuated by LBMT. This manoeuvre is an essentially costless, easy to perform intervention without side effects. Future studies may compare LBMT with traditional therapeutic advice for IOH after rising (e.g. rising slowly) and test its efficacy in daily life. Based on this laboratory study and its limited follow-up data, LBMT seems a worthwhile addition to existing management options.

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Figure Legends

Figure 1

Hemodynamic changes from baseline, at mean arterial pressure nadir (MAP_{min}) in individual IOH patients ($n=13$) in two squat-stand manoeuvres; first without, second with LBMT. Black dots represent median, error bars are 25th and 75th percentile. n.s.: statistically non-significant differences between interventions.

Figure 2

Continuous blood pressure recording in a 17 year old male IOH patient during consecutive standing up manoeuvres from squatting. Standing up manoeuvres B, D and F are combined with LBMT. Black bars indicate standing up.

Figure 3

Continuous systolic and diastolic blood pressures in 5 IOH patients who performed a standing up from squatting 6 times, alternating no intervention (grey) with the LBMT (black). In patient A only during the third trial LBMT seems effective, suggesting a learning effect.

Figure 4

Hemodynamic changes from baselines, at mean arterial pressure nadir (MAP_{min}) in individual healthy subjects ($n = 7$) in three squatting conditions: two controls (Squat 1, Squat 2), one with LBMT. Black dots represent median, error bars indicate 25th and 75th percentile. * $p<0.05$, n.s.: statistically non-significant differences.

Fig 1

Fig 2

Fig 3

Fig 4