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

IOH (initial orthostatic hypotension) comprises symptoms of cerebral hypoperfusion caused by an abnormally large transient MAP (mean arterial pressure) decrease 5–15 s after arising from a supine, sitting or squatting position. Few treatment options are available. In the present study, we set out to test the hypothesis that LBMT (lower body muscle tensing) attenuates IOH after rising from squatting and its symptoms in daily life. A total of 13 IOH patients (nine men; median age, 27 years) rose from squatting twice, once with LBMT and once without. In addition, seven healthy volunteers (five men; 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 measured continuously, and CO (cardiac output) by Modelflow and TPR (total peripheral resistance) were computed. MAP, CO and TPR were compared without and with 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% compared with 60%; $P < 0.05$), whereas in the patients no clear CO or TPR pattern was discernible. During follow-up, eight out of ten patients using LBMT reported fewer IOH symptoms. In conclusion, LBMT is a new intervention to attenuate the transient blood pressure decrease after standing up from squatting, and IOH patients should be advised about the use of this manoeuvre.

INTRODUCTION

TLOC (transient loss of consciousness) is a common medical problem, usually caused by intermittent disturbances in neural BP (blood pressure) control [1]. One of its causes is IOH (initial orthostatic hypotension). 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

Key words: blood pressure, haemodynamics, initial orthostatic hypotension (IOH), lower body muscle tensing, posture, pre-syncope, syncope.

Abbreviations: BP, blood pressure; CO, cardiac output; DBP, diastolic BP; HR, heart rate; IOH, initial orthostatic hypotension; LBMT, lower body muscle tensing; MAP, mean arterial pressure; MAPmin, MAP nadir; SBP, systolic BP; SV, stroke volume; TLOC, transient loss of consciousness; TPR, total peripheral resistance.

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abnormally large transient BP decrease [e.g. > 40 mmHg SBP (systolic BP)] [2]. In particular, standing up from squatting has been recognized as an acute haemodynamic 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 stimulus 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 approx. 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. LBMT (lower body muscle tensing), is effective in increasing BP both in patients with postural hypotension due to autonomic failure [11] and during vasovagal reactions [12–14]. LBMT acutely minimizes blood pooling in the veins of the lower body and thereby re-infuses blood into the thoracic circulation, enhancing CO (cardiac output) during hypotensive episodes [13,15]. IOH is thought to be caused by active large skeletal muscle contractions [2]. Thus, although LBMT has been shown to be 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 hypothesized 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 haemodynamic changes.

**MATERIALS AND METHODS**

We studied 13 patients who were referred to our syncope unit for the evaluation of TLOC [nine men; height, 180 (152–204) cm; body weight, 77 (55–97) kg; age, 27 (15–59) years, with 4.5 (0–100) episodes of syncope in their lifetimes; values are medians (range)].

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. ∆SBP > 20 mmHg and/or ∆DBP (diastolic BP) > 10 mmHg at 3 min after standing up; where ∆ refers to a change in the parameter] [16]. The median duration of (pre-)syncope symptoms was 2 years (range, 4 months to 10 years). Two patients 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, four also had daily pre-syncope complaints after standing up, six 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). After approx. 5 min of free standing, the patients squatted for approx. 1 min, rose within 1 s and stood for approx. 1 min. On repeating squatting-to-standing after another approx. 1 min of squatting, they performed LBMT for 30–60 s immediately after rising. If patients reported light-headedness or other pre-syncope symptoms these were documented. LBMT consisted of tensing of all the 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 with 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 five 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 seven healthy volunteers [five men; age, 27 (25–59) years; height, 179 (164–202) cm; body weight, 74 (52–85) kg], who had not experienced significant IOH symptoms over the last year. In a crossover 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 subjects assigned randomly performed LBMT after rising from the second squatting, whereas the remaining three subjects performed LBMT after rising from the third squatting.

These experiments were performed in accordance with 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 after obtaining written informed consent from the subjects.
Analysis
Off-line beat-to-beat SBP and DBP and HR (heart rate) were derived from the arterial pulse wave. MAP (mean arterial pressure) 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 SV (stroke volume) were obtained using pulse wave analysis (Modelflow; Finapres Medical Systems) [17]. This method has been validated during active and passive postural stress against thermodilution [18], during rapid changes in posture against Doppler ultrasound [19] and during physical counter-manoeuvres against gas re-breathing [15]. CO was calculated as HR × SV. Beat-to-beat TPR was calculated as MAP × CO⁻¹. After pulse wave analysis, all beat-to-beat data were re-sampled at 1 Hz.

Baseline values were taken from the interval −40 to −10 s before each standing-up manoeuvre. MAPmin (MAP nadir) induced by each manoeuvre was identified and the synchronous CO and TPR were calculated. All variables are given as medians (range). Using Wilcoxon’s signed-rank test, we compared MAPmin, 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 compared with before (less, same or disappeared), and the perceived benefit of the manoeuvre (some benefit, much benefit or no benefit).

RESULTS
After rising from the first squat, the patients’ MAP decreased from 110 (88–144) mmHg to 69 (53–91) mmHg, SBP from 145 (121–201) mmHg to 90 (70–123) mmHg and DBP from 88 (69–105) mmHg to 58 (40–76) mmHg. ΔSBP was > 40 mmHg in 12 patients and all experienced pre-syncopal symptoms.

At baseline, there were no differences between the first and the second squat in MAP (110 compared with 109 mmHg), CO (6.5 compared with 6.4 arbitrary units) and TPR (1.0 compared with 1.0 arbitrary units). When the stand up was repeated with LBMT, MAPmin was 19 mmHg higher than without LBMT (88 compared with 69 mmHg; P < 0.05; Figure 1). SBP at MAPmin was 111 (67–163) mmHg and DBP was 69 (43–87) mmHg. ΔSBP was > 40 mmHg in five patients.

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

At the group level (n = 13), CO and TPR at MAPmin did not differ between control and LBMT (Figure 1). In four patients, MAPmin with LBMT was accompanied by a > 10% higher TPR compared with without LBMT; and in eight subjects CO was > 10% higher. Also in a subanalysis of patients with a difference of MAPmin > 10 mmHg between control and LBMT (n = 5), there was no single pattern in TPR and/or CO.

Repeated squat-to-stand manoeuvres in a subset of five subjects revealed a trend for a larger difference in MAP after successive squats (Figure 3); however, the effect of LBMT appeared to increase over the course of three successive trials, suggesting a learning effect (Figure 3).

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

**Figure 2** Continuous BP 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. Filled squares indicate standing up.

**Figure 3** Continuous SBP and DBP in five IOH patients who performed a standing up from squatting manoeuvre six times, alternating no intervention with LBMT.

Grey-shaded line, no intervention; black line, LMBT. Filled squares indicate standing up. In patient A, only during the third trial did LBMT appear effective, suggesting a learning effect.
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**DISCUSSION**

The main new finding of the present 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\textsubscript{min} did not differ consistently for LBMT and control. In healthy subjects, the underlying mechanism was a blunting of the transient reduction in TPR related to resumption of the upright position. During clinical follow-up, patients perceived beneficial effects of LBMT on IOH complaints in daily life. Rising from squatting is an everyday orthostatic stress that may result in IOH complaints in otherwise healthy subjects [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 haemodynamic adaptation to standing up from squatting has been used by various groups [21–24]. The reproducibility of the manoeuvre has, however, never been systematically documented. Our findings in both patients (Figure 3) and healthy controls (Figure 4) suggest that the BP decrease after successive standing up manoeuvres from squatting is augmented.

Rossberg and Peňáz [24] reported a ΔMAP\textsubscript{max} (maximum ΔMAP) when standing up after 6 min of squatting of approx. 45 mmHg, and Rickards and Newman [25] observed 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. During the squat-to-stand manoeuvre in healthy subjects in our present study, the maximum ΔMAP (~31 mmHg) was somewhat smaller compared with the findings of Rossberg & Peňáz [24], which may be related to the shorter squatting period. The ΔMAP\textsubscript{min} in the study by Rickards and Newman [25] may have been passed before the measurement. We conclude that, on the basis of the heterogeneity of the squat-to-stand protocols available in the literature, which 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 (s) and prolonged (min) haemodynamic effects after standing up.

Several factors may play a role in the immediate decrease in BP 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]: (i) the acute decompression of arterial vessels in the legs causing an instantaneous mechanical decrease in vascular resistance; (ii) an increase of the arteriovenous pressure gradient, due to decompression of the venous vessels; (iii) relative ischaemia in the leg muscles during squatting augmenting the fall in arterial resistance by local factors (‘the post-tourniquet effect’ [22]); and (iv) the muscle activity during the standing up manoeuvre promoting 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 haemodynamic transient in IOH patients after standing up from squatting is not fully explained by the results from the present study in terms of consistent differences in CO and/or TPR between the

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**Figure 4** Haemodynamic changes from baseline and at MAP\textsubscript{min} in individual healthy subjects (n = 7) in three squatting conditions

The squatting conditions were: two controls (Squat 1 and Squat 2) and one with LBMT. Filled circles represent medians, and error bars indicate 25th and 75th percentiles. *P < 0.05; n.s., no statistically significant differences.

without (144 compared with 100 % of squatted baseline; *P < 0.05), but TPR did not differ.

During clinical follow-up, 12 out of 13 patients were contacted after 2 (1–26) months. Two patients experienced no IOH symptoms since consulting with us and had not used LBMT. The remaining ten patients reported using LBMT on a daily-to-weekly basis both after rising from squatting and from supine. In eight 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 without using LBMT, forcing them to sit or lay down again; on repeat standing up, they would use LBMT and experience no symptoms.
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 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 off-set further 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 in CO is most probably 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 antigavity suit that optimizes venous return to the heart and thereby optimizes CO. Previous work has shown that central command as a determinant of arterial BP [32] does not play a significant role in the effectiveness of physical counter-manoeuvres [14].

A limitation to the present 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 (compared with 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 patients was not alternated or randomized. However, the results from the series of healthy subjects show that the effect of the LBMT is consistent irrespective of the order of the control and intervention experiment.

Additional support for the efficacy of LBMT is found in results from the five 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, the present study shows that the transient BP decrease after standing up from the squatting position can be attenuated by LBMT. This manoeuvre is an essentially costless and easy to perform intervention without side effects. Future studies should compare LBMT with traditional therapeutic advice for IOH after rising (e.g. rising slowly) and test its efficacy in daily life. On the basis of this laboratory study and its limited follow-up findings, LBMT seems a worthwhile addition to existing management options.

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