Effects of leg muscle pumping and tensing on orthostatic arterial pressure: a study in normal subjects and patients with autonomic failure

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1. The effects of leg muscle pumping (tiptoeing) and tensing (leg-crossing) on orthostatic blood pressure were investigated in six healthy adult subjects (aged 28–34 years) and in seven patients with severe hypoadrenergic orthostatic hypotension (aged 20–65 years).

2. Finger arterial pressure was monitored. Relative changes in left ventricular stroke volume were computed by a pulse contour method.

3. Tiptoeing increased mean arterial pressure (7±5 mmHg) in the healthy subjects, but not in the patients, whereas cardiac output increased in both groups, although by more in the healthy adults than in the patients (35±10% versus 20±11%, P <0.05). Systemic vascular resistance decreased substantially in both groups while tiptoeing. Leg-crossing did not affect arterial pressure in the healthy subjects, although stroke volume had increased. In contrast, in the patients an increase in cardiac output (16±12%) and mean blood pressure (13±13 mmHg) was observed.

4. Tiptoeing and leg-crossing have different effects on orthostatic blood pressure in healthy adult subjects and in patients with autonomic failure. In normal humans, tiptoeing increases arterial pressure, whereas leg-crossing has little effect. In the patients, in contrast, tiptoeing has little effect, whereas leg-crossing increases arterial pressure considerably. Patients with autonomic failure should be instructed to apply leg-crossing to combat orthostatic dizziness.

INTRODUCTION

In normal subjects [1, 2] and in patients with autonomic failure [3, 4] it has been reported that mechanical factors play an important role in promoting venous return and, thereby, in the maintenance of cardiac filling pressure and stroke volume (SV) in the upright posture. Beneficial effects of leg muscle pumping [5–7] and leg tensing [3, 4, 8, 9] have been described.

The magnitude of the circulatory responses induced by these manoeuvres in normal subjects, their effectiveness in combating orthostatic dizziness in patients with autonomic failure and the underlying mechanisms are, however, not well understood. We investigated the circulatory effects of leg muscle pumping (tiptoeing) and tensing (leg-crossing) on orthostatic blood pressure in young adult subjects and in patients with severe orthostatic hypotension due to autonomic failure.

METHODS

Subjects

Six normotensive male subjects and two female and five male patients with hypoadrenergic orthostatic hypotension were studied. The mean age of the normal subjects was 30 years (range 28–34 years). All had normal physical fitness without special sports training, were non-smokers, used no medication and had normal dietary habits.

The patients had a mean age of 45 years (range 20–65 years). All patients had abnormally low plasma levels of noradrenaline when supine (mean 120 ng/l; range 40–210 ng/l) and an abnormally low rise in noradrenaline upon standing (mean increase +45 ng/l; range 0–130 ng/l). Four patients suffered from pure autonomic failure (PAF), while orthostatic hypotension in the three other patients (non-PAF) was related to Hodgkin’s disease [10], to multiple sympathectomies [10] and to damage of the vasomotor centres in the medulla oblongata due to bleeding in a vascular malformation. The patients with PAF had impaired parasympathetic heart rate (HR) control with attenuated HR variations. HR control was unaffected in the other patients [10].

At the time of the study four patients were being managed with a combination of sleeping in the head-up tilt position and 0.1–0.2 mg of fludrocortisone [11], one patient was managed with sleeping in the head-up position only, one patient with fludrocortisone only and one patient was subject to neither intervention. All patients were in a stable

Key words: autonomic failure, cardiac output, central blood volume, heart rate, orthostatic hypotension, stroke volume, systemic vascular resistance, venous pooling.

Abbreviations: BP, blood pressure; CO, cardiac output; HR, heart rate; PAF, pure autonomic function; PSA, pulsatile systolic area; SV, stroke volume; SVR, systemic vascular resistance.

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condition and had relatively mild orthostatic complaints, but a considerable degree of orthostatic hypotension at the time of the study. The experimental protocol started at 09.00 hours in a room with an ambient temperature of 22°C. All subjects abstained from coffee and tea and had only a light breakfast more than 2 h before the investigations.

Measurements

Continuous blood pressure (BP) was measured non-invasively in the finger by a TNO model 5 Finapres, which is now commercially available as the Ohmeda 2300E Finapres NIBP monitor. The Finapres measurement is based on the volume clamp technique of Peñáz and the physical criteria of Wesseling [12], and accurately reflects systolic, mean and diastolic BP changes during orthostatic stress [13] as well as during hypotensive periods [14, 15]. To avoid hydrostatic level differences the cuffed finger was held at right atrial level in the mid-axillary line. Respiratory phase was derived from a Nihon Kohden nose thermistor. All signals were recorded simultaneously on a Sanborn thermopaper writer for direct inspection and on a four-channel FM instrumentation tape recorder for off-line evaluation.

Protocol

The protocol was started after pilot experiments which had shown that tiptoeing and leg-crossing yielded reproducible results both in the healthy subjects and in the patients with autonomic failure. Typical examples of the BP responses and the pulse contour computations (see below) in a normal subject and in a patient with PAF are given in Fig. 1.

After a supine resting period of 5 min the subjects were requested to stand up. The standing period lasted for 2 min, after which the circulatory effects of either tiptoeing or leg-crossing were investigated in random order. The manoeuvre was performed during 1 min and was followed by 1 min of quiet standing. Tiptoeing was done with a frequency of 15–20 min. During tiptoeing, subjects inspired during each muscle contraction and exhaled during each relaxation phase. Crossing the legs was performed by crossing one leg in direct contact with the other while actively standing on both legs.

Analysis

For off-line analysis all signals were analog-to-digital converted by computer at a sampling rate of 100 Hz. Beat-to-beat systolic, mean and diastolic BP values were derived. Mean BP was obtained as the integral of pressure over one beat divided by the corresponding beat interval. Instantaneous HR in beats/min was computed as the inverse of the R–R interval. Beat-to-beat data were interpolated [16] and transformed to equidistant values at 2 Hz. Group mean values were then calculated.

Stroke volume computation. The finger arterial pulse wave was analysed by a pulse contour method, which computed changes in left ventricular SV from the pulsatile systolic area (PSA). We used
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The improved method of Wesseling and co-workers [17, 18]. In this method PSA is considered proportional to SV. Mean arterial pressure is used to correct for pressure-dependent properties of the arterial input impedance and HR is used to compensate for early reflections from the periphery. The corrections depend on the age of the subject. To obtain absolute SV values, calibration with a standard method, such as thermodilution, is needed [17–19], but without such calibration one can use the relative changes in SV [17, 19].

Cardiac output (CO) was computed as the product of SV and HR and systemic vascular resistance (SVR) as mean BP divided by CO. A 5 s moving average was used in the computation of SVR to account for the delays between changes in instantaneous CO at the aortic root and their transformation to changes in tissue perfusion flow due to the Windkessel buffering effect of the arterial system [19].

Aortic pressure is the preferred waveform for the computation of PSA. This pressure can be replaced by brachial, radial or finger pressure if the changes in PSA in these waveforms are similar, even if the absolute values differ. We have shown that changes in PSA during phenylephrine-induced vasoconstriction are similar for finger and intrabrachial pressures [20] and also during the rapid circulatory changes of the standing-up manoeuvre in young adult male subjects [21]. Comparisons of the corrected pulse contour method, applied to intra-radial pressure with thermodilution [17, 18] and applied to finger arterial pressure with the acetylene-rebreathing technique [22], show that it accurately estimates changes in CO.

Circulatory adjustment to standing up. Supine control values for all circulatory parameters (BP, HR, SV, CO and SVR) were obtained by averaging a 10 s period before the standing up manoeuvre. BP (mmHg) and HR (beats/min) were expressed as absolute values, and SV, CO and SVR were expressed as relative changes (%) from this supine control period. Orthostatic circulatory responses to standing were quantified by averaging a 10 s period around 1 min (55–65 s) of standing.

Circulatory effects of tiptoeing and leg-crossing. The circulatory effects of tiptoeing and leg-crossing were expressed as changes from the upright control condition here defined as the averaged values over the last 10 s of the 2 min standing period (110–120 s) before the two manoeuvres. The initial circulatory effects were defined as the largest changes in the first 10 s after onset (0–10 s) of the two manoeuvres. Sustained circulatory effects were defined as the averaged values during the last 10 s of the 1 min (50–60 s) tiptoeing and leg-crossing.

Statistical analysis

The effect of standing and of tiptoeing and leg-crossing on circulatory variables were tested by paired t-tests [23]. Unpaired t-tests were used to detect a difference between the normal subjects and the patients. A P value of less than 0.05 was considered to indicate a statistically significant difference.

RESULTS

Standing up

In normal subjects, after 1 min of standing, CO had decreased by 16% on average, but mean BP had increased by 10 mmHg, since SVR was higher (Fig. 2, Table 1). In the patient group systolic BP decreased from $137 \pm 32$ mmHg to $86 \pm 27$ mmHg,
mean BP from 98±26 mmHg to 64±19 mmHg and diastolic BP from 75±20 mmHg to 54±15 mmHg. The decrease in CO in the patients was larger than in the normal subjects, and the SVR values after 1 min standing were not different from supine levels (Fig. 2). Little further change in circulatory parameters was observed from 1 to 2 min of standing in both normal subjects and patients with autonomic failure (Fig. 2). The rise in HR in the patients (on average 21 beats/min) was due to a marked increase in HR in the three non-PAF patients (+39±9 versus +7±4 beats/min in the four PAF patients). Non-PAF patients showed a larger decrease in SV than the PAF patients (−61±10% versus −32±10%; \( P < 0.001 \)). The decrease in CO, however, did not differ in the non-PAF and PAF patients (−37±4% versus −26±11% in the PAF patients).

**Tiptoeing**

This manoeuvre did not result in a clear distinction between initial and sustained effects and between PAF and non-PAF patients. Therefore, only the sustained effects will be discussed. In normal subjects after 1 min of tiptoeing BP had risen. The manoeuvre increased SV and CO, whereas SVR decreased (Fig. 3, Table 2). In the patient group tiptoeing led also to a rise in SV and CO, but these increases were less pronounced than in the

**Leg-crossing**

Crossing the legs induced an initial increase in BP, SV and CO (Fig. 4) both in the normal subjects and in the patients with PAF and non-PAF. The initial effect of leg-crossing on CO and BP were more pronounced in the normal subjects than in the patients (49±13% for CO and 13±2 mmHg for
mean BP versus $38 \pm 15\%$ and $9 \pm 7\text{mmHg}; P < 0.05$ and $P < 0.05$). The sustained effects on BP were also different in the two groups. In normal subjects, after the pronounced initial increase, BP decreased during sustained leg-crossing; after 1 min BP was not different from control. In the patients BP increased steadily during the manoeuvre (Fig. 4). After release of both tiptoeing and leg-crossing, BP gradually returned to normal standing levels, as seen before onset of the manoeuvres (Figs. 3 and 4).

DISCUSSION

Tiptoeing and leg-crossing increased SV in normal adult subjects and patients with autonomic failure, but these manoeuvres had different sustained effects on orthostatic BP in the two groups. In normal subjects, tiptoeing increased BP, whereas leg-crossing had little effect. In the patients, in contrast, tiptoeing had little effect, whereas leg-crossing of the lower limbs increased BP considerably.

The aim of the present study was to compare the effects of the two manoeuvres in healthy young adults with those in patients with autonomic failure. We did not study age-matched controls. However, little change in circulatory responses are to be expected between 30- and 45-year-old healthy adults. More importantly the effects of autonomic failure on circulatory control are far greater than the age effects over this small age range.

Standing versus supine

The fall in SV ($36\%$) and CO ($16\%$) upon rising in the young adults is comparable with data from literature [1]. The severe orthostatic hypotension in the patients is explained by the combination of a slightly larger decrease in SV and a lack of reflex increase of SVR (Fig. 2, Table 1). Two factors should be considered to explain the former. First, an excessive fall in venous return impairs the ability of the heart to limit the fall in CO by increasing HR. Thus the tachycardia is inevitably associated with decreased SV [1, 24]. Secondly, impairment of myocardial contractility and slower ventricular filling rate due to defective sympathetic cardiac innervation with diminished cardiac performance have been reported [25–27].

Tiptoeing

In normal subjects tiptoeing increased SV and CO output considerably (Fig. 3). These increases can be explained straightforwardly by the activation of the skeletal muscle pumps [1]. Rhythmic contractions of the muscles of the lower limbs, in the presence of competent venous valves, pump blood back to the right side of the heart and enhance cardiac filling pressure, thereby increasing SV [5–7]. These mechanical factors can be considered as a ‘second heart’ [1]. The decrease in SVR that we observed is typical for rhythmic exercise with large muscle groups and is due to dilatation of resistance vessels in the working muscles. During rhythmic exercise the systolic BP usually increases, whereas diastolic BP remains constant [1].

In our patients, no change in BP was observed during rhythmic exercise. This contrasts with previous reports [28, 29], where patients with autonomic failure decreased their BP during supine dynamic whole body exercise (cycling). This fall was attributed to vasodilatation in active muscles with no compensatory constriction of resistance vessels in other vascular areas [28, 29]. The key difference between these studies is that our patients exercised upright, and started the manoeuvre with a low SV and BP. Therefore, an increase in SV, due to the pumping action of the muscles, can compensate for the observed decrease in SVR (Fig. 3, Table 2). The rise in SV was smaller in the patient group. We attribute this difference, as discussed above, to the impairment of myocardial contractility and slower ventricular filling [26, 27].

Leg-crossing

Leg-crossing involves tensing and compression of the muscles in the upper legs, which can be expected to raise their intramuscular pressure [8, 30]. Such a rise has been reported to affect cardiovascular responses in two ways. First, mechanical compression of the venous vascular beds in the legs into which blood pools during standing, translocates blood to the chest. This results in an increase in cardiac filling pressure, SV and CO and, thereby, in a rise in systemic arterial pressure [8]. Secondly, the rise in intramuscular pressure is thought to activate group III and IV mechanosensitive receptors, which in turn could elicit a reflex rise in arterial pressure by increases in SVR [8, 30]. The first factor appears the most important in our study. The sudden increase in SV and CO at the onset of leg-crossing in our normal subjects is more likely to be explained by a mechanical increase in venous return than by neural reflex effects. This is supported by the finding that leg-crossing induced an instantaneous increase in CO also in the patients in whom neural reflex control is largely lacking. In the normal subjects the initial increase in BP was followed by a reflex decrease in HR and SVR (Fig. 4). Apparently, the arterial baroreflex adjusted arterial pressure to the normal standing levels. Due to impaired cardiovascular reflex control in the patients, a sudden increase in BP is not followed by an arterial baroreflex-mediated decrease in HR and SVR; this explains the progressive increase in arterial pressure during sustained leg-crossing.
Clinical relevance of manoeuvres that improve orthostatic tolerance

The effect of leg-crossing on upright blood pressure was relatively small, with an increase in mean arterial pressure of only 13 mmHg (Fig. 4, Table 2). Similar increases were found previously when patients with hypoadrenergic orthostatic hypotension applied these manoeuvres [3, 4]. It is important to note that treatment with fludrocortisone, erythropoietin and midodrine results in similar small BP increases [11, 31]. Despite the small effects of these different treatment modalities on the level of upright BP, orthostatic tolerance is improved markedly by all three [3, 4, 31, 32]. This discrepancy can be explained by the fact that upright BP is shifted from just below, to just above, the critical level for perfusion of the brain [3, 4, 24]. The great advantage of leg-crossing is that the beneficial effect is additive to those induced by volume expansion induced by fludrocortisone and head-up sleeping [3, 4] (this study) and, presumably, to other treatment modalities as well. Moreover, this manoeuvre can be applied without much effort and without bringing attention to the patient’s problem at the moment that BP is low. In our experience, after proper instruction, patients start to apply leg crossing automatically in daily life.

REFERENCES