

Orthostatic hypotension (OH) is the most disabling and serious manifestation of adrenergic failure, occurring in the autonomic neuropathies, pure autonomic failure (PAF) and multiple system atrophy (MSA). No specific treatment is currently available for most etiologies of OH. A reduction in venous capacity, secondary to some physical counter maneuvers (e.g., squatting or leg crossing), or the use of compressive garments, can ameliorate OH. However, there is little information on the differential efficacy, or the mechanisms of improvement, engendered by compression of specific capacitance beds. We therefore evaluated the efficacy of compression of specific compartments (calves, thighs, low abdomen, calves and thighs, and all compartments combined), using a modified antigravity suit, on the end-points of orthostatic blood pressure, and symptoms of orthostatic intolerance. Fourteen patients (PAF, $n = 9$; MSA, $n = 3$; diabetic autonomic neuropathy, $n = 2$; five males and nine females) with clinical OH were studied. The mean age was 62 years (range 31–78). The mean \pm SEM orthostatic systolic blood pressure when all compartments were compressed was 115.9 ± 7.4 mmHg, significantly improved ($p < 0.001$) over the head-up tilt value without compression of 89.6 ± 7.0 mmHg. The abdomen was the only single compartment whose compression significantly reduced OH ($p < 0.005$). There was a significant increase of peripheral resistance index (PRI) with compression of abdomen ($p < 0.001$) or all compartments ($p < 0.001$); end-diastolic index and cardiac index did not change. We conclude that denervation increases vascular capacity, and that venous compression improves OH by reducing this capacity and increasing PRI. Compression of all compartments is the most efficacious, followed by abdominal compression, whereas leg compression alone was less effective, presumably reflecting the large capacity of the abdomen relative to the legs.

Keywords: orthostatic hypotension; antigravity suit; pure autonomic failure; multiple system atrophy; blood pressure

Introduction

Orthostatic hypotension (OH) is the most serious manifestation of adrenergic failure, occurring in the progressive autonomic disorders such as the autonomic neuropathies, pure autonomic failure (PAF) and multiple system atrophy (MSA). OH is also a common problem in old age.¹

No specific treatment is currently available for most of the underlying etiologies of OH.² The therapeutic approaches primarily consist of the use of vasoconstrictor drugs, increasing blood volume, and the use of compression garments. Vasoconstrictor drugs, while of value, are not universally successful, and cause supine hypertension.³ Volume expansion, acutely by infusions of saline, or chronically by fludrocortisone and a high-salt diet, causes sustained supine hypertension.

Crile introduced lower body positive pressure with the antigravity suit (G suit) or medical anti-shock trousers in 1903. The principle of the G suit has been applied to the treatment of OH. The development of new materials and advances in garment design have now allowed the fabrication of an elastic suit that can apply effective even pressure without being inordinately restrictive.⁴ However, there is little systematic

Efficacy of compression of different capacitance beds in the amelioration of orthostatic hypotension

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information about the effects of compression of the various venous capacitance beds.

We used a modified G suit to evaluate the effectiveness of compression of different capacitance beds. The aim of this study was to evaluate, in patients with chronic symptomatic OH, the differential efficacy of compression of the limbs versus the abdomen versus combined compression.

Materials and methods

Patients

Studies were carried out on 14 patients who had been confirmed to have neurogenic OH. OH was defined as being present when there was a sustained (over 3 min) orthostatic decrement in blood pressure (BP) of: systolic BP (SBP) ≥ 30 mmHg or mean BP (MBP) ≥ 20 mmHg. The age range was 31–78 years (62 ± 12 years, mean \pm SD); nine were females and five males. All had symptoms of OH; duration of symptoms ranged from 2 to 10 years.

Inclusion criteria

Patients were required to be adult males or females, age 18 years or older, with clinically definite MSA, PAF or

autonomic neuropathy with OH. MSA and PAF were defined using the Consensus criteria for MSA and PAF⁵ which requires early and prominent autonomic failure in addition to extrapyramidal and/or cerebellar involvement, and PAF is defined as OH without involvement of the central nervous system, in the absence of a somatic peripheral neuropathy. Autonomic neuropathy was defined as a peripheral neuropathy where the autonomic fibers are disproportionately affected, resulting in generalized autonomic failure, including OH. The cause of autonomic neuropathy in this study was diabetic autonomic neuropathy (Table 1).

Cardiovascular recordings and compressive maneuvers

Patients were fasted from midnight. Caffeine and tobacco were forbidden on the day of the study. Patients emptied their urinary bladder, and their body weight and height were recorded. Each patient donned a G suit which had five separate compartments: one lower abdominal, two thigh and two calf bladders. The suit was filled with air, and a regulator connected to the bladders made it possible to control pressure continuously. We inflated the different site(s): (1) bilateral calves (Calves); (2) bilateral thighs (Thighs); (3) combination of 1 and 2 (C + T); (4) low abdomen (Abdo); (5) all sites combined (All); (6) baseline tilt without compression (Non-comp). In randomized order, we inflated the different bladder(s) with a pressure of 40 mmHg. The time taken to inflate or deflate the G suit was less than 40 s. Non-comp values were derived as the mean values of two head-up tilt procedures done without compression. The first was done before any compressions were undertaken and the second at the end of the study.

Beat-to-beat BP was monitored using a Finapres monitor (Ohmeda, Englewood, CO, USA) and input into a computer console which displayed SBP, diastolic BP (DBP) and MBP continuously.⁶ BP was also recorded using a sphygmomanometer cuff and mercury manometer over the brachial artery. Also displayed were beat-to-beat thoracic electrical bioimpedance recordings (NCCOM3-R7, BOMED Medical Manufacturing Ltd, Irvine CA, USA) of end-diastolic index (EDI), cardiac index (CI), and peripheral resistance index (PRI). These measurements were continuously recorded beat-to-beat during supine rest, head-up tilt, and compression of the vascular beds.

Evaluation

The protocol was approved by the Institutional Review Board. Informed consent was obtained after the subjects had been fully briefed as to the purpose and nature of the study. All patients underwent the following evaluations: (1) an autonomic reflex screen, which evaluated the distribution and severity of sudomotor, cardiovascular, and adrenergic failure;⁷ (2) composite autonomic scoring scale (CASS) was derived from an analysis of the autonomic reflex screen, that corrected for the con-

Table 1. Age, gender, diagnosis and severity of autonomic failure (composite autonomic scoring scale, CASS)

Patient no.	Sex	Age	Diagnosis	CASS score
1	F	51	MSA	10
2	F	31	PAF	5
3	F	63	PAF	10
4	M	78	PAF	5
5	M	67	MSA	6
6	F	52	PAF	5
7	M	59	PAF	6
8	M	60	PAF	9
9	F	67	PAF	8
10	F	73	PAF	9
11	F	54	DAN	10
12	M	69	PAF	8
13	F	76	MSA	5
14	F	65	DAN	8

MSA, Multiple system atrophy; PAF, pure autonomic failure; DAN, diabetic autonomic neuropathy.

founding effects of age and gender.⁸ Sudomotor and cardiovascular deficits were scored from 0 (absent) to 3 (maximum), and adrenergic from 0 to 4, yielding a CASS of 0 to 10. Scores of < 3 comprise mild, 4–6 moderate, and 7–10 severe autonomic failure. The CASS values ranged from 5 to 10 (Table 1).

Tilt study

Following a 15-min rest period, 5 min of data were recorded with the patient supine, loosely strapped to the tilt-table and breathing spontaneously. The patient was then tilted to an angle of 80 degrees for 5 min, then tilted back for 5 min. All recordings occurred with the G suit deflated. For each physiological perturbation, a period of at least 20 min was provided for a return of the cardiovascular parameters to baseline. The study was then repeated with the selected compartments inflated.

Endpoints

Two sets of endpoints were used: cardiovascular measurements and parameters.

Cardiovascular measurements: With the compression of each capacitance bed and following head-up tilt, the patient recorded independently a verbal scale of change in symptoms. We used a balance scale. The patient responded to the question: "As a result of the compressive maneuver, are you able to stay on your feet longer or have less symptoms on your feet?"

- 3 = much worse
- 2 = moderately worse
- 1 = mildly worse
- 0 = no change
- + 1 = mildly improved
- + 2 = moderately improved
- + 3 = much improved

Visual analog scales of symptoms were also scored after each session. This scale graded the severity of

orthostatic symptoms occurring during 5 min of head-up tilt to 80 degrees of the standing position. The patient marked on a visual analog scale, with only 0 (no symptoms) and 10 (syncope/presyncope) indicated at two extremes, the severity of symptoms. The descriptive terms that approximated severity for 2, 4, 6, 8, 10 are respectively: tiredness/momentary light-headedness, mental sluggishness/difficulty concentrating, dizziness/unsteadiness, blurred vision/fainting and presyncope/syncope.

Cardiovascular parameters: We measured the cardiovascular efficacy endpoints of the change in BP (SBP, MBP, DBP). We also measured the preload (EDI, stroke index) and afterload (PRI) indices to evaluate the mechanism of improvement.

Data acquisition and analysis

All data were averaged in 1-min segments during all stages. To evaluate the efficacy of the different maneuvers, we compared the test maneuvers against Non-comp using analysis of variance (ANOVA) and *post hoc* analysis was performed using the Durmest test. Data were expressed as mean \pm SD when emphasis was on distribution and SEM when the focus was on comparison of means. The null hypothesis was rejected when $p < 0.05$.

Results

Head-up tilt resulted in a significant reduction in the BP, CI, stroke index and total peripheral index (Table 2).

Symptomatic improvement

Verbal scale: Table 3 summarizes the change in orthostatic symptoms following compression of specific capacitance beds. The rank order of efficacy in reducing orthostatic symptoms, in descending order from best to worst (with number of patients in brackets) were: All (13) > Abdo (5) > C+T = Calves (2) > Thighs (1). Another index of efficacy was evaluated by

identifying the maneuvers that resulted in either worsening, or no change in orthostatic symptoms. The rank order from best to poorest (least number of inadequate responses) were: All (1) < Abdo (5) < C+T (4) < Calves (9) = Thighs (9).

Visual analog scale: Individuals varied in their responses to compression. Ten of 14 patients chose All as the most efficacious maneuver in reducing their symptoms. Two of 14 chose Abdo as the preferred compression (better than All). One patient preferred Calves alone. One patient did not feel there was any significant improvement with any of the compressions.

Cardiovascular parameters: Two sets of parameters, BP (SBP, DBP, MBP) and PRI, were significantly ($p < 0.005$) improved by compression of capacitance beds (ANOVA). For all the BPs, the maximal improvement in orthostatic BP occurred with All, followed by Abdo (Figure 1). The mean and SEM of SBP with All was 115.9 ± 7.4 mmHg, compared to the Non-comp value of 89.6 ± 7.0 mmHg ($p < 0.005$). Abdominal compression (SBP, 102.0 ± 6.7 mmHg) was the only single compartment to significantly reduce OH ($p < 0.01$). There was a significant increase of PRI with low abdominal compression and the compression of all compartments ($p < 0.01$; Figure 2). The values (mean \pm SEM) for EDI and CI for Calves, Thighs, C + T, Abdo and All were not significantly different from Non-comp for either index. CI (l/min per m²): Non-comp, 3.5 ± 0.27 ; Calves, 3.2 ± 0.29 ; Thighs, 3.3 ± 0.29 ; C + T, 3.1 ± 0.21 ; Abdo, 3.2 ± 0.27 ; and All, 3.0 ± 0.21 . EDI (ml/m²): Non-comp, 73.6 ± 6.60 ; Calves, 69.4 ± 4.33 ; Thighs, 71.9 ± 5.51 ; C + T, 69.6 ± 4.65 ; Abdo, 74.1 ± 5.45 ; and All, 72.2 ± 4.94 .

There was some individual variability in the response to regional compression. Figures 3 and 4 show two patterns of responses in two representative patients. In Figure 3, baseline recordings (no compression) show a large orthostatic fall in BP, with insignifi-

Table 2. Cardiovascular parameters during supine and head-up tilt positions for the non-compression study

	SBP	DBP	HR	EDI	CI	PRI
Supine	156 \pm 24.7	77.4 \pm 13.1	73.2 \pm 14.6	81.8 \pm 29.5	3.70 \pm 1.29	2489 \pm 876
Head-up tilt	89.6 \pm 26.0	53.5 \pm 12.3	88.6 \pm 18.2	73.6 \pm 24.9	3.45 \pm 1.04	1617 \pm 585

SBP, Systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate; EDI, end-diastolic volume index; CI, cardiac output index; PRI, peripheral resistance index. Values expressed as mean \pm SD.

Table 3. Verbal scale of improvement in orthostatic symptoms following compression of different vascular beds: comparison with baseline study

Region	Mod worse	Mildly worse	No change	Mildly improved	Mod improved	Much improved
Calves (C)	2	2	5	3	2	0
Thighs (T)	1	2	6	4	1	0
C + T	0	0	4	8	2	0
Abdomen	0	1	4	4	3	2
All	0	0	1	0	7	6

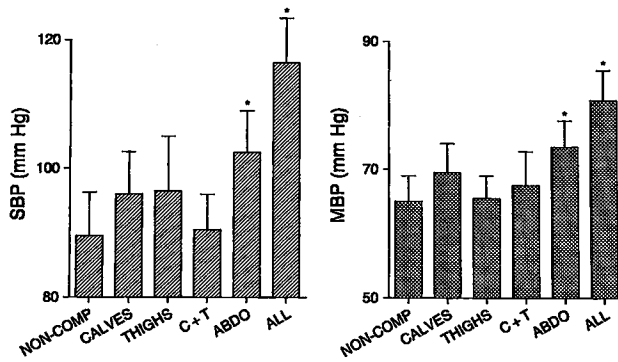


Figure 1. Effect of compression of specific vascular beds on orthostatic blood pressure. Relative to non-compressed orthostatic blood pressure (Non-comp), patients who received compression of all compartments (All) or low abdominal (Abdo) compression had a significant increase in systolic (SBP; left panel) and mean (MBP; right panel) blood pressure. * $p < 0.01$.

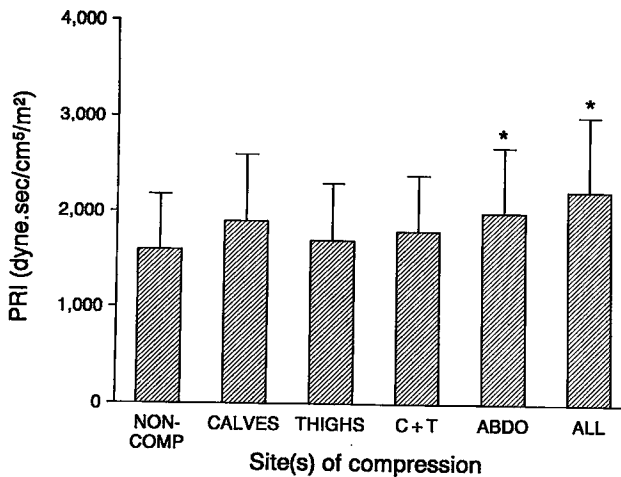


Figure 2. Effect of compression of vascular beds on peripheral resistance index (PRI). Relative to non-compressed orthostatic blood pressure (Non-comp), patients who received compression of all compartments (All) or low abdominal (Abdo) compression had a significant increase in PRI. * $p < 0.01$.

cant improvement with compression of either the calves or thighs. However, compression of both the calves and thighs (C + T), Abdo or All resulted in major amelioration of the orthostatic fall in BP. In Figure 4, a more graded response of compression is evident. Compression of Calves or Thighs was not beneficial. Some initial improvement was seen with C + T and Abdo. However, Abdo resulted in a progressive amelioration of orthostatic BP, whereas the improvement with C + T was not sustained. All resulted in a near total prevention of the orthostatic fall in BP.

Discussion

The main findings of our study were that compression of capacitance beds will reduce the deficit in standing BP if both the legs and the abdomen (13/14; 93%) are compressed or if the abdomen alone is compressed (9/14; 64%). The improvement is due primarily to an increase in total peripheral resistance. The improve-

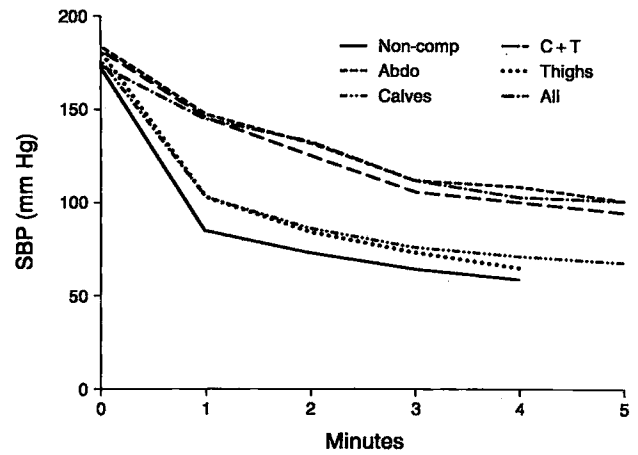


Figure 3. Effect of compression of vascular beds on systolic blood pressure (SBP) in a patient with orthostatic hypotension. Compression of the abdomen (Abdo), calves plus thighs (C + T) and all sites (All) improved orthostatic blood pressure, while compression of the calves alone (Calves) or thighs (Thighs) was ineffective.

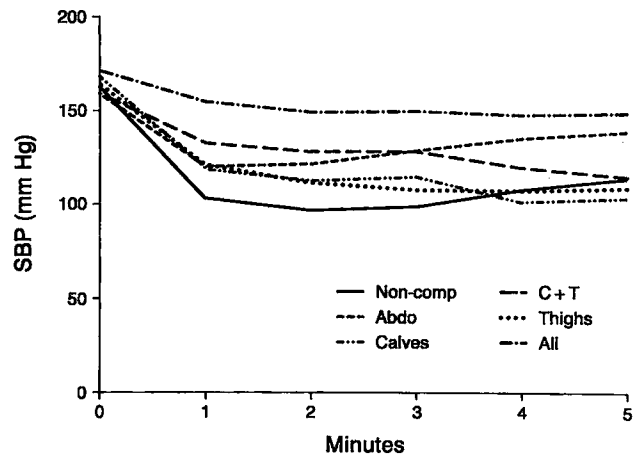


Figure 4. Effect of compression of vascular beds on systolic blood pressure (SBP) in a patient with orthostatic hypotension. Compression of all sites (All) prevented orthostatic hypotension. Compression of the abdomen (Abdo) resulted in a gradual improvement in orthostatic blood pressure: compression of calves plus thighs (C + T) was partially effective, while compression of the calves alone (Calves) or thighs (Thighs) was ineffective.

ment in BP is accompanied by an improvement in orthostatic symptoms. Compression of the legs alone is much less beneficial.

The degree of improvement correlates relatively well with the amount of blood in the regional vascular beds involved. On standing up there is an orthostatic shift of approximately 500 ml of blood to the limbs.⁹ The splanchnic mesenteric bed is two- to three-fold larger, comprising 20–30% of total blood volume.¹⁰ In the postprandial state, there is a further increase of two- to three-fold.¹¹ Denervation results in an increase in vascular capacitance, resulting in a state of relative hypovolemia. On standing up there is a failure to vasoconstrict and PRI fails to increase.

Insights into the relative quantitative importance of these vascular beds can be obtained from the effects of denervation. Bilateral lumbar sympathectomy results in denervation to both lower extremities, but OH