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Acute Effects of Graduated Elastic Compression Stockings in Patients with Symptomatic Varicose Veins: A Randomised Double Blind Placebo Controlled Trial☆

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WHAT THIS PAPER ADDS

There is currently lack of high quality trial evidence that graduated elastic compression stockings (GECS) improve symptoms in patients with varicose veins. In this randomised double blind placebo controlled trial in patients presenting with primary varicose veins causing calf pain or aching, GECS were more effective than placebo stockings in reducing the patient score for pain or aching in the most affected leg, providing trial evidence for the first time.

Objectives: To investigate the effectiveness of graduated elastic compression stockings (GECS) below the knee in improving symptoms in patients with varicose veins in the absence of high quality evidence.

Methods: This was a randomised double blind placebo controlled trial. Thirty patients with no experience of elastic stockings, presenting with primary varicose veins causing calf pain or aching were randomised to a GECS (18-21 mmHg at the ankle level, $n=15$) or a placebo stocking (0 mmHg, $n=15$). Pain or aching of the index leg after 1 week was the primary outcome measure. In patients with bilateral varicose veins the leg with the most severe pain/aching was considered. Other defined symptoms were secondary outcome measures. All symptoms were scored on a visual analogue scale (VAS).

Results: The two study groups were well balanced at baseline. At the completion of the study after 1 week, GECS were more effective than placebo stockings in reducing pain or aching (VAS score 1.7±3.0 vs. 4.5±2.8 for placebo, $p=.02$), while non-significant trends were observed for some of the remaining symptoms of the index leg, including feeling of swelling (VAS score 0.9±1.9 vs. 3.3±3.5 for placebo), paraesthesiae (VAS score 0.2±0.6 vs. 2.1±3.1 for placebo), and the number of symptoms other than pain or aching (1.3±1.1 vs. 2.8±1.7 for placebo). Number needed to treat (95% CI) for a 50% or complete improvement of pain or aching in the index leg was 2 (95% CI 1.2–5.5) and 2 (95% CI 1.2–5.3), respectively. Mean daily use of the placebo stockings and GECS was 8.0 hours and 10.2 hours, respectively ($p=.13$).

Conclusions: Among patients with varicose veins, GECS seem effective in ameliorating symptoms, particularly pain or aching, compared with placebo stockings after 1 week of use. Long-term studies are justified.

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INTRODUCTION

Treatment of venous diseases of the lower limbs using compression has been performed effectively for centuries. However, there is little published evidence (and what exists is of low quality) to demonstrate the efficacy of compression,[1,2] including its use as a standalone modality,[3–5] after venous surgery,[6] or to prevent post-thrombotic syndrome.[7] More specifically, there are no clinical trials demonstrating any possible benefit of graduated elastic compression stockings (GECS) in patients with varicose veins of the lower extremities, including a particular type and compression profile across the CEAP clinical class spectrum.[1,2,4] The only randomised trials that compared GECS with placebo stockings investigated low compression profile stockings in the active arm.[8,9] In contrast, the effectiveness of therapeutic GECS (around 20 mmHg or more at the ankle level) has been tested in non-randomised studies comparing two GECS types worn sequentially, or more often patient symptoms before use were compared

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with those reported with the stockings in place, facts that introduce a certain degree of bias.[4]

The aim of the present study was to compare the acute effects of wearing below knee active (18-21 mmHg) or placebo GECS (0 mmHg) on pain or aching and also on a number of secondary symptoms and signs, using a modified version of the revised Venous Clinical Severity Score (rVCSS) obtained at baseline and after 1 week in patients with primary varicose veins.

PATIENTS AND METHODS

Patients with primary varicose veins of the lower extremities were recruited through the vascular outpatient clinics of the University Hospital and the vascular outpatient clinic of a primary care provider, all in Patras, Greece between December 2015 and August 2016. Inclusion criteria included primary varicose veins causing pain/aching located only at calf level in patients of both genders, aged 18-90 years. Exclusion criteria included venous ulceration, venous eczema, itching, superficial vein thrombosis, peripheral arterial disease (intermittent claudication, critical limb ischaemia, or a vascular intervention), symptoms not of venous origin, and previous use of elastic stockings. The following baseline information was recorded: age, gender, body mass index (BMI), comorbidities, the presence of family history of varicose veins, prolonged standing, number of pregnancies (for women), patient age when varicose veins occurred, laterality of varicose veins, varicose vein complications, history of treatment for varicose veins, and CEAP clinical class. Duplex scanning was performed in a standard fashion to exclude deep vein pathology and investigate superficial vein pathology by identifying reflux distribution.

Outcome measures

The primary outcome measure of the trial was dull pain or aching graded by the patient using a visual analogue scale (VAS, 1-10 at baseline) of the leg with the varicose veins.[10] For bilateral varicose veins, the leg with the highest VAS score was considered to be the index leg. Secondary outcomes included leg symptoms of heaviness, swelling sensation, varicose vein throbbing, burning sensation, paraesthesiae, night cramps and restless legs, and insomnia, considered to be a secondary symptom caused by the leg symptoms,[10,11] all graded with VAS (0-10), a modification of previously described methodology.[12–15] The same outcome measures of the index leg were assessed for the contralateral leg, all graded similarly with VAS (0-10), only if there were varicose veins. These were also considered to be secondary outcomes. Other secondary outcome measures included a modified version of the revised Venous Clinical Severity Score (rVCSS-S),[16,17] which did not account for the attribute of compression, and ankle circumference (in cm) measured just above the malleolus, at the smallest point, both for the index and contralateral (if applicable) leg. All outcome measure scores and readings were recorded at baseline and after 1 week of GECS or placebo stocking use, with the aim of investigating the acute effects of the former. Compliance was monitored by log sheets on which patients entered the hours they had used their stockings each day. Complaints of complications of the two types of stockings were noted in addition of any pruritus (graded on a 0-10 VAS).

Description of active and placebo GECS

Active Comparator: Graduated elastic stockings VARISAN TOP, off the shelf knee length Class 1 (18-21 mmHg, RAL certified, at the ankle level) (Cizeta Medicali S. p. A., Cuggiono, MI, Italy).

The placebo comparator was a similar looking knee length VARISAN diabetic (0 mmHg at the ankle level; Cizeta Medicali).

Randomisation and blinding

On patient agreement to participate in the trial (signed informed consent), randomisation was performed using sequentially numbered, sealed, opaque envelopes that contained a paper slip showing the randomisation group. This parallel group trial had a 1:1 allocation ratio. A member of the group who was unaware of the clinical characteristics of the patients handled all randomisation envelopes and notified the manufacturer's local distributor by sending the randomisation group, leg measurements required to fit the stockings, and patient's address. A pair of active or placebo GECS was sent by courier to the patient the same or next day. The randomisation group was not communicated to the patient or outcome assessors. To guarantee blinding of patients and outcome assessors for performance bias and detection bias, respectively, all stocking labels were removed by the manufacturer's local distributor before shipping, so that the two stocking types looked similar. Additionally, all patients were instructed to remove their stocking and conceal them from the outcome assessors at the time of their follow-up visit. The ethics committee of the University Hospital of Patras approved the study protocol (approval No 35/18.02.2015).

Statistical analysis

A priori power calculations were based on a previous study in which a mean VAS of 4.5/10 before use of a Class 1 (20 mmHg) GECS was reduced to 1.5/10 afterwards.[18] Assuming a reduction of mean VAS of 4.5/10 to 3.5/10 using a placebo stocking, and also a standard deviation of 1.5 for the two groups, a total of 24 patients (12 in each group) would be required to demonstrate statistical significance (α=0.05) at a power of 90%. To compensate for possible losses to follow-up or patient withdrawal from the study, it was decided to include a total of 30 patients (15 in each group). Pre-planned interim statistical analysis after 15 patients were randomised and followed up revealed a non-significant trend for the primary outcome measure, so that the study was continued and finished as planned.

All data were entered into a Microsoft Office Access database (Microsoft Inc., Redmond, WA, USA) and analysed with IBM SPSS Statistics 24 (IBM Corp., Armonk, NY, USA).

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