REVIEW

Compression Therapy for Occupational Leg Symptoms and Chronic Venous Disorders — a Meta-analysis of Randomised Controlled Trials

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Objective. Leg discomfort and oedema are commonly attributed to a venous disorder (CVD) or chronic venous insufficiency (CVI) and treated with compression hosiery. The pressure needed to achieve clinical benefit is a matter of debate.

Design. We performed a meta-analysis of randomised controlled trials (RCT) that compared stockings exerting an ankle pressure of 10–20 mmHg with placebo or no treatment and with stockings exerting a pressure of more than 20 mmHg.

Methods. RCT were retrieved and analysed with the tools of the Cochrane Collaboration. Each study was reviewed independently. Subjective dichotomous and continuous factors and objective findings were pooled for statistical treatment.

Results. Eleven RCT fulfilled the predefined criteria. They included 1453 randomised subjects, 794 healthy people exposed to various forms of stress, 552 patients with a chronic venous disorder or chronic venous insufficiency and 141 patients after varicose vein surgery. Over all, compression with 10–20 mmHg had a clear effect on oedema and symptoms compared with <10 mmHg pressure, placebo stockings, or no treatment (p < .0001). No study showed a difference between 10–20 and >20 mmHg stockings.

Conclusions. Despite important methodological heterogeneity and sometimes sub-standard reporting the meta-analysis suggests that leg compression with 10–15 mmHg is an effective treatment for CVD. Less pressure is ineffective and higher pressure may be of no additional benefit.

Keywords: Chronic venous disorder; Chronic venous insufficiency; Occupational disorders; Compression therapy; Medical compression stockings; Randomised controlled trial; Meta-analysis.

Introduction

Symptoms of chronic venous disorders (CVD) and chronic venous insufficiency (CVI) include heaviness, swelling, bursting, and diffuse leg aching, which is difficult to characterise. A key finding is oedema with preponderance in the evening and in a warm environment. Either or both of these phenomena are highly prevalent in the general population and may be present without objective disorders such as varicose veins or skin induration, hyperpigmentation, and trophic lesions. The correlation between symptoms and oedema on one hand and objective venous pathology on the other is notoriously poor. In the absence of objective disease, symptoms and mild oedema are usually said to be features of incipient or “functional” venous insufficiency. Regardless of these uncertainties, treatment follows an experience-based strategy: measures of hygiene and leg compression.

Few randomised controlled trials have investigated the effects of medical compression stockings (MCS) in healthy people suffering evening and/or occupational leg symptoms and in patients with mild to moderate CVD. Selection of study subjects and trial protocols have been highly heterogeneous. Most studies were performed on a small number of selected subjects and patients and a few were supplemented with tests of venous function. Most trials found an improvement of quality-of-life and well-being. The amount of pressure needed to prevent or alleviate the symptoms was astonishingly low in some studies.

We performed a meta-analysis of the accessible literature of randomised controlled trials (RCT) using the methodology recommended by the Cochrane Collaboration. The hypothesis was that MCS exerting an
ankle pressure of 10–20 mmHg would eliminate or improve oedema and symptoms of CVD.

Methods

Most studies of compression therapy for mild CVI were published in journals not listed in Medline and Current Contents. Therefore, we started with a review of the publications cited in the reports of two consensus conferences on compression therapy.13,14 The reference lists of all publications were screened for further studies. EUROCOM, the scientific platform of companies producing medical compression stockings in Europe provided information on studies sponsored by their members. An additional Medline search using the MeSH-terms bandages, leg, randomized controlled trial venous insufficiency, pain, and oedema revealed no further articles. Studies published in English, French or German were included but no unpublished or ongoing studies.

A systematic review was performed of all studies that assessed the role of medical compression stockings (MCS) exerting a pressure of 10–20 mmHg at the ankle. Studies were considered for the meta-analysis if they included a control group with either no compression or a placebo stocking and/or a MCS delivering an ankle pressure of more than 20 mmHg. Studies had to be performed on healthy people exposed to conditions associated with symptoms and oedema of CVD or on patients with objectively diagnosed mild to moderate CVI (CEAP-classes C1–C3). A randomised trial design was mandatory. Outcome measures had to include the evaluation of pain, discomfort, quality-of-life and/or quantification of oedema. Studies performed with pregnant women were not included.

Subjective outcome information was quantified by dichotomous or continuous variables. Dichotomous data were used to discriminate between two types of compression stockings. Continuous variables were employed to assess the individual ratings of pain, swelling, discomfort. Data of single visual analogue scales (VAS) or scores summarizing several questions were analysed. Oedema quantification used various techniques (Table 1). These data were processed as continuous variables using both absolute values and measurements of difference before and after treatment. Means were calculated if more than one outcome measure fitted the inclusion criteria. Sums were built if more than one type of stocking fitted the group criteria.

The results of trials with a similar design were pooled using a fixed effects method which weights each study by the inverse of its variance. Results of the dichotomous variables are presented as odds ratio (OR) with 95% confidence intervals (CI). Results of continuous variables are shown as the standardized mean difference (SMD) with the 95% CI. A negative SMD favours the low compression group; a positive SMD favours the placebo or the high compression group.

The analysis was executed with the Review Manager 4.2 of the Cochrane Collaboration.

Results

Eleven trials fulfilling the pre-defined criteria were identified (Table 1). The number of randomly allocated subjects ranged from 11 to 341. The studies included a total of 1453 subjects, 508 men and 945 women. Their overall mean age was 44.1 years with a range per study between 23.0 and 48.7 years. Data were collected from 790 healthy subjects (142 volunteers exposed to everyday stress or provocation tests and 648 flight attendants) and 663 patients (522 patients with CVD or CVI (CEAP C1–C3) and 141 patients after varicose vein surgery). We did not identify studies in patients treated with stockings after sclerotherapy providing the required endpoint assessment. Calf length stockings were used exclusively.

Effects on subjective factors of low compression as compared with no or placebo compression

Eight studies investigated this question. Three assessed the symptoms as dichotomous, three as continuous variables and two used both types of measurements for outcome evaluation (Figs. 1 and 2).

Healthy volunteers subject to various forms of provocation were monitored in 3 trials for symptoms of swelling and leg discomfort using a crossover design. One study with 12 volunteers showed that MCS (15 mmHg) but not a placebo stocking reduced the adverse effects of standing for a period of 8 hours.15 Another study in 118 volunteers assessed the symptoms of heaviness, swelling, restlessness and pain after a full day of regular work. The left and the right leg were fitted with either a low compression (14 or 18 mmHg) or a placebo stocking (6 mmHg). A significant benefit was found with either stocking but there was no significant difference between them.16 Another study in 12 healthy factory employees investigated occupational leg symptoms. Low compression but not placebo stockings reduced the adverse feelings after a regular working day.17

Flight attendants served as test subjects in 2 trials exploring occupation-associated leg symptoms. One
Table 1. Studies included in the meta-analysis

<table>
<thead>
<tr>
<th>Trial</th>
<th>Participants</th>
<th>Design</th>
<th>Interventions</th>
<th>Duration</th>
<th>Subj. outcome</th>
<th>Oedema</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kraemer 2000</td>
<td>12 volunteers (females, mean age 23.0)</td>
<td>Crossover design - experimental prolonged standing</td>
<td>15 mmHg vs placebo</td>
<td>twice 7 days</td>
<td>Discomfort rating in standing protocol</td>
<td>Ankle &amp; calf circumference (measuring tape)</td>
</tr>
<tr>
<td>Jonker 2001</td>
<td>118 volunteers (60 males, 58 females, mean age 39.3)</td>
<td>Paired comparison left vs right leg</td>
<td>14 and 18 mmHg vs 6 mmHg</td>
<td>3 times 5 days</td>
<td>Score of mean number of complaints in 4 dimensions</td>
<td>Optical leg volume meter significant difference not entered into meta-analysis*</td>
</tr>
<tr>
<td>Partsch 2004</td>
<td>12 volunteers (4 males, 8 females, mean age 41.2)</td>
<td>Crossover design comparing legs with and without compression</td>
<td>6 mmHg vs 11–18 mmHg vs 22 mmHg</td>
<td>4 times 1 day</td>
<td>Feeling of compressed leg compared with leg not compressed</td>
<td>Water plethysmography significant reduction not entered into meta-analysis**</td>
</tr>
<tr>
<td>Belcaro 2002</td>
<td>358 (part 1) (199 males, 159 females, mean age 48.7)</td>
<td>Two group design</td>
<td>14–17 mmHg vs no stocking</td>
<td>8 hour and 11 hour flight</td>
<td>VAS subjective swelling and discomfort</td>
<td>Oedema tester, ankle circumference, water plethysmography significant difference not entered into meta-analysis*</td>
</tr>
<tr>
<td>Weiss 1999</td>
<td>19 flight attendants (females, no age)</td>
<td>Two time points - paired comparison</td>
<td>8–15 mmHg vs no stocking</td>
<td>4 weeks</td>
<td>VAS discomfort</td>
<td>-</td>
</tr>
<tr>
<td>Benigni 2000</td>
<td>120 pts (females, no age) C1–3 SEPAS1 C5</td>
<td>Crossover study – paired comparison</td>
<td>10–15 mmHg vs placebo</td>
<td>2 weeks</td>
<td>VAS pain</td>
<td>Leg volumetry (method not described) difference not significant - not entered into meta-analysis*</td>
</tr>
<tr>
<td>Chauveau 1997</td>
<td>30 pts (females, mean age 28.2) CVD</td>
<td>Crossover study – paired comparison</td>
<td>12–17 mmHg vs placebo</td>
<td>6 times 1 day</td>
<td>Number of complaints and VAS symptoms</td>
<td>-</td>
</tr>
<tr>
<td>Vassyairat 2000</td>
<td>341 patients*** (females, mean age 41.5) C1–3 SEPAS1 C5</td>
<td>Two group design</td>
<td>10–15 mmHg vs 6 mmHg</td>
<td>1 month</td>
<td>VAS discomfort</td>
<td>Water plethysmography</td>
</tr>
<tr>
<td>Jungbeck 1997</td>
<td>31 (9 males, 22 females, no age) (59 legs) CVI II (Widmer)</td>
<td>2 groups measurement before and after treatment</td>
<td>20 mmHg vs 30 mmHg</td>
<td>8 weeks</td>
<td>Subjective symptoms (pain, ankle swelling, tired legs, restless legs and night cramps)</td>
<td>Water plethysmography significant difference not entered into meta-analysis*</td>
</tr>
<tr>
<td>Shouler 1989</td>
<td>99 patients (57 males, 42 females, mean age 41.7) after varicose vein surgery</td>
<td>Two group design</td>
<td>15 mmHg vs 40 mmHg</td>
<td>6 weeks</td>
<td>Discomfort rating</td>
<td>-</td>
</tr>
<tr>
<td>Bond 1999</td>
<td>42 pts (31 females, 11 males, median age 40) after varicose vein surgery</td>
<td>3 groups each leg treated with a different stocking</td>
<td>10–12 mmHg vs 30–40 mmHg</td>
<td>1 week</td>
<td>Comparison of pain and discomfort between two legs</td>
<td>-</td>
</tr>
</tbody>
</table>

* data not presented adequately.
** numerical data not shown.
*** 254 pts included for subj. outcome and 231 pts for oedema.
of them, including 643 participants, revealed a significant reduction of discomfort by stockings providing a pressure of 14–17 mmHg. The other study, with 19 participants, found a reduction of discomfort and oedema with the use of MCS providing an ankle pressure of 8–15 mmHg.

Patients with documented CVD or CVI (C1–C3) were examined in three trials. A cross-over study included 120 female patients and found a significant decrease of VAS scores of painful discomfort by the wearing of 10–15 mmHg MCS. Another study using a similar design with 30 patients reported a significant benefit of wearing MCS providing 12–17 mmHg. No significant difference in the discomfort ratings but a significant improvement of the global quality-of-life score was found when placebo stockings were compared with 10–15 mmHg stockings in a study with 341 patients.

Overall, in 8 of 10 studies, compression with an ankle pressure of >10 mmHg was significantly better than placebo compression or no treatment. Analysis of dichotomous data revealed a mean weighted odds ratio of 0.38 (95% CI 0.25–0.57; Z = 4.64; p < .00001). The chance to obtain a benefit was 62% with stockings when compared with no compression therapy. Analysis of the continuous data showed a difference of 1.45 SMD (95% CI −1.60–1.29; Z = 18.87; p < .00001). The term signifies that the mean difference between treatment and no treatment is 1.45 standard deviations.

Effect on objective factors of low compression as compared with no or placebo compression

Six studies investigated leg oedema under various conditions. All studies used quantitative techniques and monitored continuous variables (Fig. 3).

Healthy subjects were investigated in three studies involving 142 subjects. Stockings significantly reduced ankle and calf circumference in a test of oedema

<table>
<thead>
<tr>
<th>Study (N)</th>
<th>SMD (95% CI)</th>
<th>Weight (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kraemer 2000 (12 vs 12)</td>
<td>1.8</td>
<td>1.8</td>
</tr>
<tr>
<td>Chauveau 1997 (30 vs 30)</td>
<td>6.1</td>
<td>6.1</td>
</tr>
<tr>
<td>Benigni 2000 (115 vs 113)</td>
<td>23.8</td>
<td>23.8</td>
</tr>
<tr>
<td>Vayssairat 2000 (125 vs 129)</td>
<td>28.0</td>
<td>28.0</td>
</tr>
<tr>
<td>Belcaro 2002 (321 vs 322)</td>
<td>40.3</td>
<td>40.3</td>
</tr>
<tr>
<td>Pooled (603 vs 606)</td>
<td>100.0</td>
<td>100.0</td>
</tr>
</tbody>
</table>

Fig. 2. Subjective continuous factors comparing low compression (10–20 mmHg) with placebo (≤6 mmHg) or no compression.

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provocation by prolonged standing. Two further studies evaluated the effect of compression on evening oedema. The amount of evening oedema was significantly reduced by stockings exerting an ankle pressure of 15–20 mmHg after even one day of use and similarly after five days of use. Unfortunately, these data could not be standardised to allow inclusion into the meta-analysis.

Flight attendants also took part in a placebo-controlled trial. Stockings reduced the amount of leg swelling after a long-haul flight and decreased the incidence of deep-vein and superficial vein thrombosis.

Patients with CVI (CEAP C1–3, E1, A1–5, PS) were included in 2 trials but data analysis was possible from only one. Foot volumetry showed no significant difference when 10–15 mmHg stockings were compared with 6 mmHg stockings. The other study also mentioned a lack of influence but provided no useable numeric information.

Overall, in the 3 studies that allowed data processing, a significant benefit of stockings was observed (SMD –1.01, 95% CI –0.83––1.2; Z = 18.42; p < .00001).

Effect on subjective factors of low compression as compared with high compression

Four studies explored this topic (Fig. 4).

Occupational oedema was assessed in a study with 12 healthy factory workers. No difference of symptoms was found after one day of use when stockings providing 11–18 mmHg were compared with stockings exerting 22 mmHg.

An effect on oedema and symptoms following varicose vein surgery was monitored in two trials comparing 10–15 mmHg with 30–40 mmHg stockings, worn for 6 weeks. The studies included 99 and 42 patients respectively. No significant differences were found for discomfort, pain, bruising, and thrombophlebitis.

Patients with CVI were treated over a period of 8 weeks with stockings providing either 20 or 30 mm Hg. An equally important improvement of subjective symptoms was documented in both groups.

Overall, no difference of effect on symptoms was observed when low and high compression stockings were compared (OR 0.99; 95% CI 0.56–1.74; Z = 0.04; p = .97).

Discussion

Leg compression is a treatment modality with a history of two thousand years or more. Its indications, however, have only recently become an object of clinical investigation. The use of stockings and bandages for the treatment of severe chronic venous insufficiency and lymphoedema is based on experience and tradition. The use of stockings for the initial treatment of deep venous thrombosis and the prevention of its sequels is evidence based.

This meta-analysis deals with reports on occupational symptoms and oedema, the condition nowadays termed chronic venous disorder. It reveals that MCS exerting an ankle pressure of 10–20 mmHg provide an important benefit for people suffering evening and occupational leg symptoms and oedema. In 12 of 16 direct comparisons, moderate-strength compression was better than placebo or no compression. One study found 6 mmHg also effective (though less so) and one study found subjective but not objective improvement. One study could not document a benefit in patients with CVI. Stockings providing less pressure had no comparable effect and stockings exerting higher pressure showed no advantage over those exerting moderate pressure.
The meta-analysis was confronted with several difficulties: Most studies were not published in indexed journals and so required unusual steps for their retrieval. Reporting standards were often poor. Most studies were performed on selected groups of healthy people at risk of occupational leg symptoms and oedema and some included predominantly or exclusively women. Other studies compared clinical parameters with data of venous function but included only a few subjects. Most trials covered only a short period of stocking use. However, all such studies had a randomised design and compared stockings with placebo or no treatment with stronger compression. In 8 of 11 studies the participants and/or investigators were blinded with regard to the strength of compression. All studies documented the symptoms objectively and quantitatively but much heterogeneity was observed in the assessment techniques. These difficulties clearly affect the quality of the information provided by this meta-analysis.

The amount of pressure applied to the leg was given by the manufacturer of the stockings. In only a few studies it was measured directly beneath the stockings using various techniques. We accepted the pressure data as presented in the articles and have no suspicion that they were wrong. The manufacture of the stockings, i.e. the type of yarn and knitting, was not stated in most papers. Its potential influence on effectiveness and acceptance was not an issue in any of the studies.

The CEAP C3-stage is a very heterogenous group in which very slight pitting oedema or massive leg oedema can be present. A differentiation has not been made in most of the studies covered in this analysis. Therefore, we do not know whether only patients with mild oedema benefited from the treatment or those with severe leg swelling as well.

The various symptoms of this “functional” venous insufficiency have been separately addressed in only a few studies. The improvement brought about by wearing stockings was consistent for all symptoms with the exception of restless legs. The feelings of restlessness and the urge to move the legs were not improved by compression. Restless leg symptoms may represent a different pathology as a poor correlation with venous disease was found in a detailed analysis of epidemiological data. Other causes of restless legs, including metabolic, neurological and psychological, have been reported.

Summary

Subjects with symptoms of mild venous insufficiency (in the broadest sense of the term) benefit from wearing MCS providing an ankle pressure of 10–20 mmHg.

Lower pressure is ineffective and higher pressure adds nothing.

The published information has many shortcomings and many issues have not been addressed. More and better studies are needed to optimise the use of compression therapy to benefit the extremely large number of people experiencing symptoms of CVD as well as mild CVI and to provide the information necessary to those who bear the costs of such treatment.

Conflict of interest statement

This study was ordered by Ganzoni Management SA, Winterthur, Switzerland. F.A. is the owner of amsler

![Figure 4. Subjective dichotomous factors comparing low compression (10–20 mmHg) with high compression (20–40 mmHg).](image-url)
consulting, W.B. a consultant for Ganzoni. Ganzoni SA had no influence on the design of the study and the interpretation of the results. The authors declare no conflict of interest relevant to this publication.

References