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Control of lower extremity edema in patients with diabetes: double blind randomized controlled trial assessing the efficacy of mild compression diabetic socks

The aim of this study was to assess the efficacy of a diabetic sock exerting mild pressure (18-25 mmHg) in improving lower leg oedema in patients with diabetes and lower extremity oedema, compared to no compression. The study indicates that a mild compression, knee-high, diabetic sock may be effective, and safe, in patients with diabetes.

Effects of compression stockings on elevation of leg lymph pumping pressure and improvement of quality of life in healthy female volunteers: A randomized controlled trial

The trial was designed to compare the efficacy of two different compression stockings in increasing low leg pumping lymph pressure in healthy female volunteers with reduced leg pumping lymph pressure. Treatment with either Stocking A or Stocking B resulted in significant increases in leg pumping lymph pressure with a significantly greater increase with the stocking A that exerted 18-29 mmHg at the ankle and 15-23 mmHg at the calf.

Compression use in the era of endovenous interventions and wound care centres

As new techniques for treating chronic venous disease develop, this article provides a review of the use of compression therapy alongside emerging endovenous treatments. The authors concluded that compression therapy should be the treatment initiated in the majority of patients presenting with CVD, compression failure identified promptly and surgical intervention may be preferable to prolonged compression treatment in many CVD patients.

Acceptance, compliance and effects of compression stockings on venous functional symptoms and quality of life of Italian pregnant women

The goal of the study was to report the rate of pregnant women with venous functional symptoms who agreed to wear therapeutic compression stockings and to identify particular characteristics of those agreeing to stocking use. Further the authors assess the impact of stocking use on functional symptoms and quality-of-life (QoL) according to compliance. Women that accepted to wear stockings every day had a higher CEAP classification and benefited more from the compression treatment, e.g. less leg pain, better quality of life, than women that were wearing the stockings every second day or not at all.

Twice a year, the Compression Bulletin presents a selection of the latest scientific publications in the fields of phlebology, lymphology and compression therapy. All Compression Bulletins can be downloaded from the Medical Online Hub Platform (MOH). The MOH Platform replaces the well known, but unfortunately outdated Stemmer Library. The Stemmer Library was originally created by Dr. Robert Stemmer who was recognized as one of the most respected phlebologists of his time. The Medical Online Hub Platform is regularly updated with the latest scientific materials produced by SIGVARIS GROUP to support medical professionals in the field of phlebology and lymphology.

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Wu SC, Crews RT, Skratsky M, Overstreet J, Yalla SV, Winder M, Ortiz J, Andersen CA

Control of lower extremity edema in patients with diabetes: double blind randomized controlled trial assessing the efficacy of mild compression diabetic socks

Veins and Lymphatics 2017;6(6637):35-36

Aim

The aim of this study was to assess the efficacy of a diabetic sock exerting mild pressure (18-25 mmHg) in improving lower leg oedema in patients with diabetes and lower extremity oedema, compared to no compression. Investigators simultaneously monitored any effect on macro and microcirculation.

Methods

This was a multi-centre, double-blind, randomized controlled trial over 5 weeks. Patients with diabetes and lower extremity oedema were randomized to receive either mild or non-compression, knee-high diabetic socks, and instructed to wear them during waking hours.

Assessment of oedema was quantified through midfoot, ankle, and calf circumferences and cutaneous fluid measurements. Vascular status was recorded via ankle brachial index (ABI), toe brachial index (TBI), and skin perfusion pressure (SPP).

Measurements were taken at baseline and at weekly follow-up visits for 4 consecutive weeks.

Results

Of 80 patients enrolled, 77 completed the study (38 receiving mild compression and 39 controls). Baseline demographics were similar between the two groups. Significant decreases in calf and ankle circumference were recorded at week 5 compared with baseline for the patients using the mild compression socks. At the same time, lower extremity circulation remained unaffected, with no significant changes in ABI, TBI or SPP in either the mild compression or control group.

Conclusions

Due to concerns regarding the risk of peripheral arterial disease in diabetes patients, foot elevation, as opposed to compression, is the usual recommendation for diabetic patients with lower extremity oedema. The authors conclude that this study indicates that a mild compression, knee-high, diabetic sock may be effective, and safe, in these patients.

Comments of the Editors

This is a practically very important study showing a reduction of the frequently occurring leg oedema by mild compression pressures in diabetics. Different studies in the last few years showed that also mild compression, as it was used in this study, is very effective to reduce oedema.

Older textbooks and guidelines still are warning against any form of compression in a diabetic patient and rather recommend bed rest and leg-elevation. At that time, every form of compression was still considered to be harmful due to a reduction of arterial blood flow, which is certainly not correct. As this was already shown by Bollinger

and Fagrell 1990 using capillaroscopy, the presence of oedema has a negative influence on tissue nutrition since it increases the distance between the capillaries and the cells, thereby blocking the pathway of nutrients. These authors could demonstrate that after compression the micro oedema is diminished and the nutrition in that area is improved. (Bollinger A).

Of course, skin breaks due to friction of the material can happen, especially since diabetics frequently suffer from sensory disturbance due to diabetic neuropathy and would not feel any skin damage. Therefore, it is recommended to carefully inspect the skin by frequent changes of the stockings.

Literature:

Bollinger A, Fagrell B. Clinical capillaroscopy. Hofgrete and Huber, Toronto, 1990

Sugisawa R, Unno N, Saito T, Yamamoto N, Inuzuka K, Tanaka H, Sano M, Katahashi K, Uranaka H, Marumo T, Konno H

Effects of compression stockings on elevation of leg lymph pumping pressure and improvement of quality of life in healthy female volunteers: A randomized controlled trial

Lymphatic Research and Biology 2016; 14:95-103

Aim

The trial was designed to compare the efficacy of 15-29 mmHg and 8-16 mmHg compression stockings in increasing low leg pumping lymph pressure (Plp) in healthy female volunteers with reduced Plp.

Methods

This prospective, double-blind, randomized controlled trial used a novel method for measuring Plp (indocyanine green (ICG) fluorescence lymphography and transparent sphygmomanometer cuff) developed by the authors. Participants were volunteers, females > 30 years of age with no history of leg injury or venous disease, or current pregnancy. A blood test confirmed subjects were healthy.

Following measurement of Plp, those with a value < 20mmHg in one or both legs were randomized to receive either Stocking A or B: stocking A exerted 18-29 mmHg at the ankle and 15-23 mmHg at the

calf; stocking B exerted 8-13 mmHg at the ankle and 10-16 mmHg at the calf. Stockings were to be worn on both legs from morning to night for the 16-week study period. Assessments were made at baseline, 8 and 16 weeks, and stockings were not worn to appointments to ensure blinding by the evaluators. The primary outcome was an increase in leg Plp. Secondary outcomes were measured at baseline and 16-weeks and included prevalence of leg oedema and muscle cramp, and quality-of-life (QoL) assessed by the Short-Form 36 (SF-36).

Results

Between November 2012 and May 2014, 219 female volunteers (mean age 45yrs) were recruited to the study. Of these, 80 had uni- or bilateral measurements of Plp < 20 mmHg and were randomized to receive either Stocking A or Stocking B. Baseline demographics were similar for the two groups.

Primary outcome

Treatment with either Stocking A or Stocking B resulted in significant increases in Plp at both 8 and 16 weeks in legs with Plp < 20 mmHg at baseline. However, the increase was significantly greater with Stocking A vs. Stocking B ($p < 0.05$ at 8 and 16 weeks).

In legs without low Plp at baseline (Plp \geq 20 mmHg), use of stockings did not have any significant effect.

Secondary outcomes

Prevalence of leg cramp was significantly reduced in both treatment groups at week 16 vs. baseline, while leg oedema was only significantly reduced in the group with Stocking A. However, the authors noted that leg cramp were assessed during a medical interview, and oedema was reported subjectively by the participant.

At 16-weeks, body pain and vitality were significantly improved vs. baseline in subjects using Stocking A, with no changes in the remaining categories. No significant changes in any of the SF-36 categories were found with Stocking B.

Compliance

Compliance was good for both stockings. Three participants in each group discontinued use due to the inconvenience of wearing the stocking, a drop-out rate of 7.5%. The researchers had designed the exerting pressures of the study stockings with a view to achieving a high level of compliance.

Conclusions

While recognising the limitations of their study (sample size, female only, no control group), the authors conclude that knee-high compression stocking use with a pressure of 18-29 mmHg at the ankle and 15-23 mmHg at the calf elevates leg Plp, and may be used to alleviate oedema and improve QoL in otherwise healthy women.

Comments of the Editors

In a previous study the authors of this paper have developed a novel method to measure the intralymphatic pressure exerted by the spontaneous contractions of lymph collectors in humans. Using indocyanine green (ICG) fluorescence lymphography and a transparent sphygmomanometer cuff they measured the pressure with a mercury sphygmomanometer, the transparent cuff being wrapped around the participant's lower leg just below the popliteal fossa, and being gradually deflated. Plp is defined as the value of the cuff pressure when the ICG fluorescence signal exceeds the upper border of the cuff. In the title "elevation of leg lymph pumping pressure", the term "elevation", relates to the pressure and not to the leg.

Only young and healthy women were investigated, and individuals were selected who had a Plp of < 20mmHg as an indicator of poor Plp among the general population, who frequently present with more occupational oedema (Saito T)

It should be noted that the randomisation was between two stockings and that the inclusion of (contralateral) legs with a Plp of > 20 mmHg who showed no significant change of the intralymphatic pressure after treatment with compression stockings might be confusing.

However, the surprising finding of the study was, that compression stockings corresponding to a RAL class II model, worn for several weeks obviously caused an increase of the intralymphatic pumping pressure in individuals with a low intralymphatic pressure, measured in the sitting position without leg exercise and after removal of the stockings. The explanations are speculative: It is discussed that wearing compression stockings may raise the wall shear stress in lymphatic vessels, thereby promoting NO production and modulating contractions via the cGMP-PKG pathway. Another explanation could be that compression reduces capillary filtration. By continuous wearing of compression stockings owing to the subsequent decreased filtration, the pumping function in the lymph vessels might recover.

Literature:

Saito T, Unno N, Yamamoto N, et al. Low lymphatic pumping pressure in the legs is associated with leg oedema and lower quality of life in healthy volunteers. *Lymphat Res Biol* 2015; 13:154–159

Raju S, Lurie F, O'Donnell Jr TF

Compression use in the era of endovenous interventions and wound care centres

J Vasc Surg: Venous and Lym Dis 2016;4:346-354

Aim

As new techniques for treating chronic venous disease develop, this article provides a review of the use of compression therapy alongside emerging endovenous treatments.

Methods

The authors reviewed a selection of relevant key publications, including randomized controlled trials and more recent case series articles reflecting a change in clinical practice. Details of the mechanism of action, efficacy and cost of both compression and endovenous techniques are covered.

Results

Compression

The exact mechanism of action behind their impact of compressive leggings on venous disease remains controversial. Recently there has been a change in thought regarding the direction of compression gradient, with new evidence supporting the use of higher pressure being exerted at the calf than the ankle to increase flow.

When discussing the method of compression delivery, the authors found evidence that there is considerable variation in the maintenance of pressure over time between

makes of stocking; and that the use of bandages suffers from variations in the technique and skill of the person applying the bandage. The difficulties in maintaining compression consistency are even evident in clinical trials, with a systematic review concluding that: "identifying the most efficient compression system for wound healing based on existing literature is practically impossible."

Compression is most supported in its use to treat venous leg ulcers (VLU), with data available on time to healing, the percentage of wounds healing and recurrence. However, there is evidence that > 50% of ulcers recur with compression alone, possibly as a result of patient non-compliance with stocking use over time. Indeed, the authors state that: "compliance is the Achilles heel of compression treatment."

With regard to failure of compression to heal an ulcer, studies show that this can be identified by monitoring wound healing metrics as early as 4 weeks, and definitively at 6 weeks; at which point alternative treatments should be introduced. The authors are concerned that this early detection is not common practice, but rather that compres-

sion therapy is continued for long periods. They go on to mention an initiative in Sweden which resulted in a halving of leg ulcer prevalence by using (amongst other measures) early detection of compression failure and appropriate intervention.

Scenarios, where the use of compression is not as clear, include long-term application for the reduction of deep reflux and prevention of post-thrombotic syndrome, where uncertainty was raised with the publication of the SOX trial.

Endovenous treatment

Surgical options for treatment of CVD include endovenous ablation (EVA) of the saphenous vein and iliac vein stenting. EVA of the saphenous vein has been shown to be effective in treating superficial disease but is limited by contraindications such as concomitant deep venous reflux, saphenous vein size or calf pump disease. It has been shown, however, to be comparable to ligation and stripping of varicose veins in terms of recanalization, recurrence, reintervention, and quality of life measures.

The authors also discuss the ESCHAR study of saphenous surgery with compression vs. compression alone in ulcer healing. While no

significant difference in healing at 1 year was found between groups, at 4 years significantly fewer patients receiving surgery had experienced recurrence. The authors highlight that the healing rate with compression alone in this study (89%) was particularly high, so the addition of surgery gave limited extra benefit (93%). Other studies with lower rates of ulcer healing with compression therapy have reported significant improvements with the concomitant use of surgery.

When saphenous ablation is not indicated or has failed, iliac vein stenting can be considered. A review of the evidence reported “low morbidity, high medium and long-term stent patency, and excellent symptom resolution.”

Compression after surgery
Several studies have looked at the use of compression after ablation or stenting and found no significant differences in healing with or without compression stockings following surgery. However, the authors cite the lack of head-to-head randomized controlled trials between compression and ablation.

Cost
Management of CVD comprises a large portion of healthcare costs, and as such, the most cost-effective treatments need to be identified. A comparison of 4-layer bandage (4LB) and EVA for treatment of VLU concluded that while EVA was more expensive in the first year, projected costs based on recurrence rates were lower for EVA vs 4LB at the end of 3 years.

The National Institute for Health and Care Excellence (NICE) recommends EVA for varicose vein treatment instead of compression stockings as they found EVA to be more cost-effective with better quality-adjusted life years (QALYs).

Conclusions

Compression therapy should be the treatment initiated in the majority of patients presenting with CVD, and compression failure identified promptly. Delay in intervention leads to increased costs and chance of recurrence. The authors conclude that, given issues regarding long-term compliance and recurrence rates with compression only therapy, surgical intervention may be preferable to prolonged compression treatment in many CVD patients.

Comments of the Editors

The authors summarize the current discussion on indications for compression and interventions in CVD patients. They conclude that in a part of the patients, interventions like thermal ablation of varicose veins or stenting of iliac vein obstructions may be preferable to long-term compression. In recent guidelines for venous leg ulcer treatment (O'Donnell TF Jr), the ablation of incompetent superficial veins is recommended as part of the ulcer management. However, concomitant compression treatment will continue until the ulcer is healed and has not to be discontinued after varicose vein ablation. Even after ulcer healing, continued compression is recommended to prevent ulcer recurrence. A recent study has demonstrated similar efficacy in recurrence prevention, if 15-20 mmHg and 20-30 mmHg compression stocking were compared, whereas a very high recurrence rate was reported in patients that were non-compliant to compression treatment (Clarke-Moloney M). Concerning compression in active ulcers a recent study could demonstrate an equal effectivity for 2-layer ulcer compression systems compared to compression bandaging (Ashby RL). As compliance with compression treatment is a major issue, the switch from ban-

dages to ulcer compression systems and to moderate pressure may help to improve the situation in recurrence prevention. In addition, awareness of health care providers and reimbursement of compression stockings do also influencing long-term compliance. As an example, compliance with compression after deep venous thrombosis may differ considerably, depending on the country where studies have been performed. In the SOX study, compliance was about 50%, whereas in the IDEAL study, it ranged above 80% (Kahn SR, Mol GC). In summary it can be concluded that endovenous interventions are a very important part of CVD management, but they can't replace the compression treatment.

Literature:

O'Donnell TF Jr et al.
J Vasc Surg. 2014 Aug;60(2 Suppl):3S-59S.

Clarke-Moloney M et al.
Int Wound J 2014;11: 404-408.

Ashby RL et al.
Lancet 2014; 383: 871-879.

Kahn SR et al.
Lancet. 2014 Mar 8;383(9920):880-8.

Mol GC et al.
BMJ. 2016 May 31;353:i2691.

Allegra C, Antignani PL, Will K, Allaert F

Acceptance, compliance and effects of compression stockings on venous functional symptoms and quality of life of Italian pregnant women

International Angiology 2014;33:357-64

Aim

This study aimed to:

- Report the rate of pregnant women with venous functional symptoms who agreed to wear therapeutic compression stockings
- Identify particular characteristics of those agreeing to stocking use
- Assess the impact of stocking use on functional symptoms and quality-of-life (QoL) according to compliance

Methods

Allegra et al. reports on a single-centre, observational study performed at the San Giovanni Hospital in Rome, Italy. The authors recruited women between 4 and 28 weeks pregnant, presenting with symptomatic C0 to C3 CEAP classified venous disease. Women with history of venous thromboembolism were excluded.

Two assessment appointments were performed. At recruitment a medical history was taken and CEAP classification and functional symptoms recorded. Women were then asked if they agreed or refused to wear the thigh length, 15-20 mmHg compression stocking, evaluated their venous pain and discomfort on a visual analog scale (VAS) and completed the venous disease-specific QoL questionnaire, CIVIQ. Follow-up was then performed when the pregnancy was at term.

Results

100 women were recruited for the study, of which 98 had complete data for analysis. Of these, 68 (69.4%) accepted prescription of the stockings, while 30 (30.6%) refused. There were significant differences between the groups; with the women accepting stocking use having higher CEAP classification (42.7% of those accepting had C3S vs. 20% of those refusing), greater leg pain and a greater impact on their QoL, measured as both global score and in all 4 dimensions of the CIVIQ questionnaire.

Compliance

Among the 69.4% of participants who accepted to wear the stockings, the majority of women wore their stockings every day (58.8%) while the remaining 10.6% wore theirs at least once every 2 days. Compliance was significantly and positively associated with all measures of baseline severity of venous disease, including pain and all dimensions of the CIVIQ questionnaire.

Leg pain

Baseline pain was greater in women who had 100% compliance, and this group experienced the greatest benefit, with a reduction in VAS pain score of 17, vs. 10.3 for those wearing every 2 days and 4.2 in women refusing compression use ($P < 0.0001$).

Quality of life

The global impact of venous disease on QoL decreased (and thus QoL improved) for compliant women (-13.5) and those wearing stockings at least every 2 days (-10.7), while in the women who did not accept treatment the impact increased (a

worsening of QoL) by 3.3. The same pattern was recorded for the psychological, social and pain impact of their venous disease as assessed by CIVIQ, while the physical impact improved for women receiving compression therapy, but remained stable in those without.

No issues regarding donning or removing of the stocking were reported, with only 2 women describing itching.

Conclusions

The authors highlight that the benefits seen in their study were achieved with a relatively light level of compression, which may improve compliance in a group who would find high compression stockings difficult to don. This study supports the use of compression stockings in pregnant women presenting with venous disease or predisposing conditions.

Comments of the Editors

This observational study shows clearly that pregnant women with leg symptoms like feeling of swelling, heaviness or pain benefit from wearing low pressure compression stockings compared to those who are non-compliant. The pure venous origin of leg symptoms in COs patients may be questionable but the study also shows that the benefit increases with higher C-classes. Similar results have been demonstrated in a small study by Thaler et al (Thaler). Although in this prospective comparative study-wearing compression stockings did not prevent from developing varicose veins, there was a significant benefit for preventing venous symptoms. In addition, Mendoza et al showed a beneficial effect of compression stockings on nausea and vomiting in early pregnancy (Mendoza). In summary these results demonstrate the benefit of

compression in pregnancy not only in the presence of varicose veins or CVD.

Literature:

Thaler et al: Swiss Med Wkly. 2001 Dec 1;131(45-46):659-62

Mendoza et al: Int J Womens Health. 2017 Feb 22;9:89-99

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SIGVARIS Management AG

CH-8400 Winterthur

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