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Compression therapy and post-thrombotic syndrome.

Compression médicale et syndrome post-thrombotique.

Partsch H.

Summary

Compression is able to reduce pain and swelling in the acute stage of deep vein thrombosis.

It is the aim of ongoing compression to maintain this effect also during the following months in order to prevent the development of a post-thrombotic syndrome.

The analgesic and anti-edematous effect involves more the inflammatory process of the vein-wall than the clot.

A recently published multicenter trial questions any positive effect of wearing compression stockings for the prevention of the post-thrombotic syndrome, as this had been demonstrated in previous studies and meta-analyses.

Some arguments are discussed debating the validity of this trial.

More favorable results than wearing no compression may be expected by a tailored regime terminating compression stockings after 6 months, in those patients who do not show signs and symptoms of a post-thrombotic syndrome at that time point.

In patients with severe stages of a post-thrombotic syndrome proper long-term compression is still the cornerstone of conservative management.

Keywords: *compression therapy, post-thrombotic syndrome, deep vein thrombosis, long-term compression.*

Résumé

La compression médicale permet de réduire la douleur et l'œdème à la phase aiguë de la thrombose veineuse profonde.

Le but du maintien au long cours de la compression médicale est de poursuivre cet effet pendant les mois suivants, afin d'éviter le développement d'un syndrome post-thrombotique.

L'effet analgésique et anti-œdémateux de la compression médicale est plus lié à son action sur le processus inflammatoire de la paroi de la veine, que sur le processus thrombotique.

La récente publication d'un essai multicentrique remet en question l'effet positif du port précoce et au long cours des bas de compression pour la prévention du syndrome post-thrombotique, alors que cet effet avait été démontré par les études et les méta-analyses antérieures.

Certains arguments de cet essai négatif sont discutés et sa validité est remise en question par l'auteur.

Des résultats plus favorables à l'absence du port de la compression au long cours pourraient être attendus d'un autre protocole adapté, indiquant l'arrêt du port de bas de contention au 6e mois chez les patients qui ne présentent pas de signes et de symptômes d'un syndrome post-thrombotique, à cette échéance.

Chez les patients atteints d'un syndrome post-thrombotique à un stade évolué et sévère, le port d'une compression médicale appropriée précoce et au long cours reste toujours la pierre angulaire du traitement conservateur du SPT.

Mots-clés : traitement de compression, syndrome post-thrombotique, thrombose veineuse profonde, compression au long cours.

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Introduction

The post-thrombotic syndrome (PTS) is an inflammatory disorder starting in the acute phase of deep vein thrombosis (DVT).

Optimal management in this acute phase has therefore deciding importance for recurrence and late outcome.

This has clearly been shown for adequate anticoagulation [1], but also for anti-stasis measures like compression and immediate mobilisation [2].

Compression and walking exercises reduce pain and swelling immediately, so that these symptoms disappear already after one week [3]. The aim of continuing wearing compression hosiery is to maintain this situation.

Mechanisms of action of compression

The most obvious objective proof for the efficacy of compression is the reduction of oedema, both in acute DVT [4] and late stages of PTS [5]. The reduction of swelling is explained by a shift of Starlings equilibrium reducing the transmural pressure gradient by external pressure, which results in a decrease of fluid-filtration into the tissue. At the same time lymphatic transport will be enhanced depending on the exerted compression pressure. This is also true for the deep, subfascial lymph transport which is typically reduced in patients with DVT and PTS [6, 7].

In patients with chronic venous oedema it could be shown that there is a correlation between the compression pressures exerted by compression stockings in the range between 20 and 40 mmHg and the amount of oedema reduction, while pressures over 60 mmHg exerted by bandages may be counterproductive [8].

In the acute stage of proximal DVT the oedema reducing effect of thigh-long compression stockings (20-30 mmHg) is comparable with that of firm, inelastic compression bandages [4].

A striking effect of compression is the pain-reduction, documented by visual analogue scale and by a modified Lowenberg-test, demonstrated in acute DVT [4] and in PTS [3]. Since pain sensations appear mainly during walking and far less during rest the Lowenberg test was used as an instrument to obtain a more objective assessment: both calves are compressed using a blood pressure cuff by stepwise increasing pressures and the level of intolerable feeling is marked.

The difference between the healthy and the thrombosed leg is taken as a parameter allowing a more objective assessment of pain. It may be hypothesized that analgesic mediators released from the endothelial cells under the influence of external compression may explain this analgesic effect of compression [9].

Anti-inflammatory mechanisms of compression as described in patients with leg-ulcers [10] involving the vein-wall seem to play an important and still underestimated role.

Only during the last year's inflammation of the vein wall in acute DVT and remodelling with development of fibrosis has been recognized as an important process for the development of PTS [11].

Partial thrombus-recanalization, destruction of vein valves and fibrosed vein walls are the anatomical substrate of a PTS leading to functional impairment of the venous drainage.

Several experimental studies have demonstrated that compression is able to reduce reflux and ambulatory venous hypertension and to improve venous pumping function and that inelastic compression material applied with high pressure is more effective than compression stockings [12, 13].

Clinical studies

Several studies and meta-analyses were able to demonstrate that compression stockings applied for two years after DVT are able to reduce the incidence of PTS to about one half [14, 15, 16, 17].

An effect of compression to reduce recurrent DVT could not be demonstrated [18].

These results were recently questioned by a large randomized controlled multi-centre study which did not find a significant difference between a group of patients wearing so-called placebo stockings (pressure < 10 mmHg) and knee high, 30-40 mmHg stockings for up to two years after a first episode of a proximal DVT [19].

The conclusions of this trial show several major flaws in the design/execution of this trial, including timing of ECS application, how patients were fitted and assessed concerning stocking application, and definition/ evaluation of compliance.

Patients were characterized by the Villalta scale only, CEAP classification or any objective measurements are missing.

A major problem in this study is the poor compliance of the recruited patients to wear their compression stockings, reported as 55% after 2 years [20].

By definition of the authors this group of patients wearing the stockings more than three times per week were termed "frequent users".

It is questionable therefore if missing effects of compression can be generalized if only half of the patients applied this treatment modality.

The poor compliance of the recruited patients is also underlined by the fact that about half of the patients were unable to say if they had a strong or a weak stocking.

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Who ever had to put on a 30-40-mmHg stocking, sent by mail without assistance will certainly declare that this is a very strong stocking.

This underlines the suspicion that several patients had never put on the stocking. Unfortunately in this study the actual pressures exerted by the stockings were not measured which should have been done at least in a subgroup of patients.

In a study comparing the effects of different pressure ranges on the reduction of occupational evening oedema we could show that the so-called placebo stockings (< 10 mmHg) achieved also a significant volume reduction, which means that the concept of taking "placebo-stockings" for comparative trials is a misconception, at least when oedema reduction is a postulated outcome parameter [21].

In contrast to European experience several leg ulcers are reported in the study by Kahn et al., some of them already occurring one year after a first event of a DVT.

It may be speculated that the late start with compression stockings which are sent by mail to the patients only some weeks after the acute event could be one reason for this odd outcome.

As shown by large trials early compression already in the acute stage of DVT have become European tradition [22, 23] while this was obviously not the case in Canada [24].

In most follow up studies many patients show satisfactory results without clinical signs and symptoms of a PTS (Villalta score < 5) already six months after acute DVT [17]. It is questionable therefore if all patients after DVT need to wear compression stockings following the usual standard of two years.

The question of an individually tailored duration of elastic compression therapy in relation to the incidence of the postthrombotic syndrome [25] will be answered by an ongoing randomized controlled trial in the Netherlands (NCT 01429714 and NTR 2597).

Up to now there is only one study comparing the effects of 6 month *versus* 2 years of compression [26].

This study showed that prolonged compression was able to significantly reduce symptoms and that there was also a reduction of skin changes, which however was not significant.

Some specific recommendations

In principle prevention and therapy of PTS should be differentiated.

Prevention of PTS

For preventing a PTS after DVT compression stockings were employed in the published literature. Brandjes et al. used knee length sized to fit stockings in a pressure range around 40 mmHg at the ankle [14].

Prandoni et al. compared flat-knitted, thigh- length *versus* below-knee 30-40 mmHg stockings coming in 3 sizes and did not find a significant difference concerning PTS after 3 years, but fewer side effects with knee length stockings [27].

Taking into account thigh swelling after proximal DVT we used thigh-long 30-40 mmHg stockings after proximal DVT in our own study [3].

Therapy of established PTS

The selection of adequate compression materials is more based on experience than on evidence coming from studies.

In general the choice of compression material will depend on the clinical severity of PTS. Strong compression stockings or double stockings may be used in patients with skin changes or with small leg-ulcers.

In these cases superimposed stockings ("ulcer kits") may be used, where the basic stocking stays overnight, holding the ulcer dressing in place while the second stocking is applied during day time.

In patients with severely indurated oedema, lipodermatosclerosis or large, long-standing leg ulcers we prefer at least for the initial therapy phase stiff bandages applied with strong pressure in order to improve venous hemodynamics and to reduce ambulatory venous hypertension [28].

Velcro band devices like CircAid® may be an alternative with the advantage that such devices can be applied and readjusted by the patients themselves.

An improvement in such severe forms of PTS may also be seen when superficial reflux is abolished by endovenous procedures so that lighter forms of compression may subsequently be sufficient.

Intermittent pneumatic compression may be an additional effective treatment modality in patients with PTS [29], especially in those who are not fully mobile.

Compression works best when combined with exercises. Walking and swimming together with weight control are therefore basic advices for an adequate life style.

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