

Intermittent claudication – reduction of the ischaemic deficit



**PADMA –
For the benefit
of our health.**

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S. Sallon et. al., *Journal of Vascular Investigation*
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Objective criteria for therapeutic success with PADMA 28

Summary

PADMA 28, a multicomponent herbal preparation, has already been used successfully in several clinical studies, in which improvement of the maximum pain-free walking distance in patients with intermittent claudication could be demonstrated [2], [3], [4].

In the following study by Sallon et al., an objective, non-invasive method was used as a reproducible measure for vascular function: the «ischaemic window». The efficacy of PADMA 28 was evaluated vs. placebo for 6 months in patients with mild to moderate peripheral arterial occlusive disease (PAOD).

With PADMA 28 it was possible to achieve a significant systemic improvement of the peripheral arterial vascular function and a shortening of the duration of the ischaemia when walking. The general well-being of the patients was increased significantly.

Context

Background information to the epidemiology of PAOD

Peripheral arterial occlusive disease affects about 12-19% of the elderly above the age of 55 years. If the blood flow can no longer meet the metabolic need of the activated muscles, a painful restriction of the patient's ability to walk results, known as intermittent claudication. Approximately 6% of the population of the Western civilisation older than 55 years are affected by intermittent claudication [5]. As has been demonstrated in epidemiological studies, this pathological condition develops into serious ischaemia that can ultimately require amputation in just 2-5% of all the cases. In view of the well-known local and systemic risks of vascular surgery, the use of non-invasive therapies such as kinesitherapy or the use of drugs that stimulate the blood flow, is of great value [6].

Systemic view of the peripheral arterial blood pressure: ankle/brachial index (ABI)

In healthy subjects the ratio between the resting blood pressure in the ankle and the arm is greater than or equal to 1 (ABI ≥ 1).

In patients with arterial occlusions due to arteriosclerosis this ratio is already decreased while resting ($ABI \leq 0.85$: mild to moderate PAOD, pain on walking, intermittent claudication. $ABI \leq 0.3 - 0.2$: severe PAOD, pain at rest, critical ischaemia, possible gangrene, ulceration). In PAOD patients with mild claudication and correspondingly an ABI value of just under 1.0, it is often problematical to assess the severity of the disease and the efficacy of the treatment [7], [8].

Dynamic blood - pressure ratios before and after exercise: drop in blood pressure and pressure recovery time

Drop in blood pressure (%PD)

Here, the change in the blood-pressure parameters, before and after exercise (walking), provides the possibility for *objective* measurement. In healthy subjects, the arterial blood pressure in the legs only falls for a short time after extreme exercise. In PAOD patients, on the other hand, the situation is different: during exercise, due to stenosis there is a lowering of the blood supply, which is expressed by a measurable fall in the systolic ankle pressure, which is measured before and immediately after exercise. From this, the percentage drop in blood pressure, or %PD, is calculated.

Pressure recovery time (PRT)

A further indicator for the haemodynamic response is the pressure recovery time, PRT, the time needed for the ankle pressure to return to baseline levels after exercise.

The ischaemic window - an indicator of ischaemic stress

These two parameters, pressure recovery time (PRT) and drop in blood pressure (%PD), allow the construction of a triangle, the area of which represents the ischaemic window (Fig. 1). The more severe the PAOD, the greater the drop in blood pressure after exercise, its recovery time and thus also the calculated window. Feinberg et al. observed that the degree of the reduction of this stress indicator appears to correlate with the degree of subjective improvement in the maximum and pain-free walking distance. The haemo-dynamic vascular state of the diseased limb is expressed objectively and quantitatively by the ischaemic window. It represents the severity of the blood flow debt. It is a useful, reproducible method for quantifying the subjective improvement of the walking ability [6].

Design:

Randomised, placebo-controlled, double-blind study.

Patients:

Out of 83 patients, 72 met the inclusion criteria and were randomised (37 PADMA 28, 35 placebo).

Completed the study: 59 patients (31 PADMA 28, 28 placebo). Drop outs: 13 (18%; 6 PADMA 28, 7 placebo).

Inclusion criteria:

Intermittent claudication/PAOD with at least one of the following criteria: abnormal wave-form in the Doppler ultrasound of the lower limbs, $ABI \leq 0.85$, $\%PD \geq 15$, $PRT \geq 3$ min.

Exclusion criteria:

Leg pain at rest pain, ulceration, previous vascular surgery or previous need for same, warfarin therapy, frequent cardiac symptoms or cardiac infarction within the last 6 months, life-threatening disease or mental illness. The use of pentoxifylline (vasodilator) had to be discontinued for the duration of the study.

Treatment:

2 x 2 capsules containing 403 mg of PADMA 28 (active drug) or potato starch (placebo) per day for 6 months. Recommendation for daily exercise, instructions regarding other atherogenic risk factors, such as smoking, obesity and hypertension.

Parameters measured:

Objective: Brachial and tibial (anterior or posterior) systolic arterial blood pressure before and after standardised exercise (max. 3 minutes treadmill, 2 km/h at 10° incline), at 1 minute intervals up to max. 10 min., with simultaneous determination of the pressure recovery time (PRT). Classification of the change in the drop in the blood pressure before and after the treatment: decrease by $\geq 15\%$ = improvement; increase by $\geq 15\%$ = deterioration; change $< 15\%$ = no change. Routine laboratory blood analysis.

Subjective: Pain-free walking distance, everyday activities, general condition, concentration capacity.

Results

- ▶ The calculation of the «ischaemic window» showed a **significant reduction of 52%** following treatment with PADMA 28, compared with 19% in controls (Fig.1).
- ▶ PADMA 28 patients displayed a significant mean improvement of 12.5% in the drop in exercise-induced ankle pressure (%PD) and 0.8 minutes in pressure recovery time (PRT) compared to pre-treatment values. An improvement (= reduction) in the drop in blood pressure at the ankle of more than 15%, compared with a deterioration or no change, was observed in 48% of the PADMA 28 patients, compared with 22% of the patients receiving placebo (close to statistical significance: $p = 0.056$, Fisher's exact test, one-tailed).
- ▶ Self-assessment by the patients showed that the subjective pain-free walking distance in the PADMA 28 group (58%) correlated significantly with the objective decrease in exercise-induced drop in ankle pressure.
- ▶ **A significant improvement of the subjective general well-being was observed in the patients treated with PADMA 28** (40%), compared with placebo (15%) (more vitality, better mood and concentration).
- ▶ The tolerability of PADMA 28 was found to be good, with minimal unwanted side effects (predominantly gastrointestinal disorders such as abdominal discomfort, constipation and bloating).
- ▶ The routine laboratory tests showed no differences between the two groups. Particularly to be emphasised are the liver and kidney values, which remained unchanged.
- ▶ The resting blood pressure values showed no significant changes after the 6 months' treatment, in either group.
- ▶ No significant differences in the patient characteristics (age, everyday activities, concomitant medication) were found between the two groups.

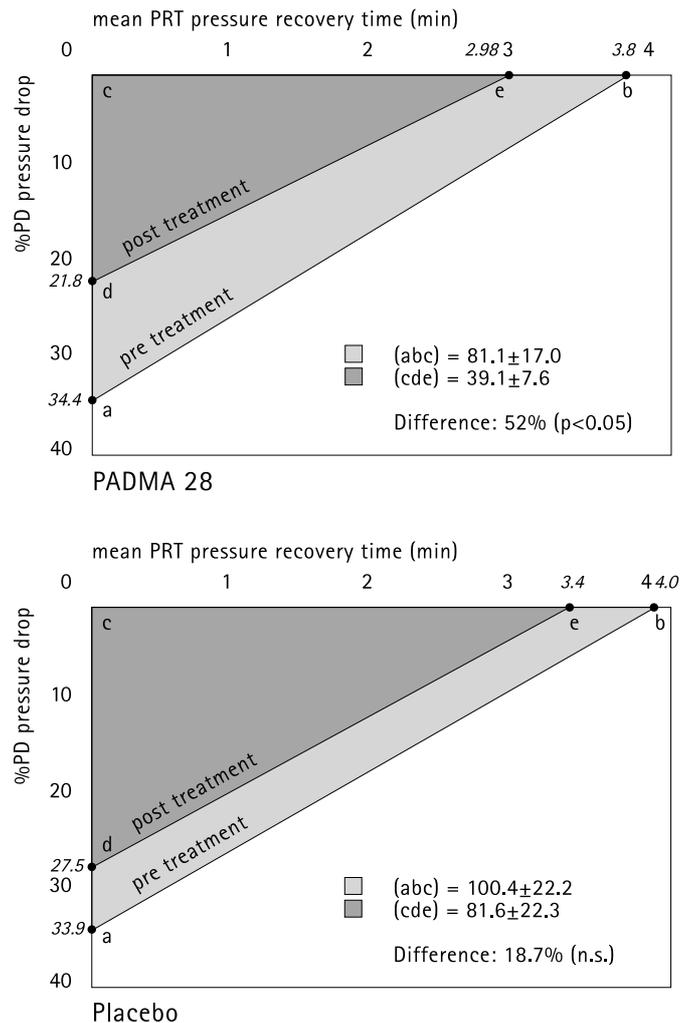


Fig.1: The «ischaemic window», a quantitative expression of the ischaemic deficit during and after exercise, showed a significant reduction of 52% after the treatment with PADMA 28, compared with 19% in controls (size of areas abc respectively cde \pm standard deviation). The slight improvement observed under placebo could be due to the suggested regular walking exercise. Significance according to Wilcoxon Mann Whitney U-test (nonparametric method).

Investigator's conclusions [1]

«This pilot study demonstrates that following stress of exercise, changes in ankle systolic pressure and its recovery time are positively affected by PADMA 28. While the precise mode of action requires further clarification, these results already show that PADMA 28 may be an effective treatment for intermittent claudication».

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- [3] Smulski HS, Wojcicki J: Plazebokontrollierte Doppelblindstudie zur Wirkung des tibetischen Kräuterpräparates PADMA 28 auf die Claudicatio intermittens. *Forsch Komplementärmedizin* 1994;1:11-19, see also *Altern Ther Med* 1995;1:44-49.
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PADMA 28

Composition: Aegle sepiar fructus 20 mg, Amomi fructus 25 mg, Aquilegiae vulgaris herba 15 mg, Calcii sulfas pulv. 20 mg, Calendulae flos 5 mg, Cardamomi fructus 30 mg, Caryophylli flos 12 mg, Costi amari radix 40 mg, Dextrocamphora 4 mg, Hedychii rhizoma 10 mg, Lactucae sativae folium 6 mg, Lichen islandicus 40 mg, Liquiritiae radix 15 mg, Meliae tousem fructus 35 mg, Myrobalani fructus 30 mg, Plantaginis herba 15 mg, Polygoni herba 15 mg, Potentillae aureae herba 15 mg, Santali rubri lignum 30 mg, Sidae cordifoliae herba 10 mg, Aconiti tuber 1 mg, Valerianae radix 10 mg, Excip. pro compr.

Indications: Tingling sensation, formication, heaviness und tenseness in arms and legs, numbness of hands and feet, cramps in the calf (systemma).

Administration/Dosage: Initially, ingest 3 x 2 tablets 1/2 – 1 hours before meals. Depending on the patient's condition, the dosage may subsequently be reduced to 1 – 2 tablets daily.

Side effects: Occasionally gastrointestinal symptoms may occur. Gastric discomfort can be remedied by ingesting plenty of fluid (1 – 2 glasses of fluid) or by taking the tablets during the meals. In a few isolated cases, palpitations and slight restlessness have been observed in predisposed individuals.

Information: Comprehensive information regarding this product can be found in the «Arzneimittelkompendium der Schweiz – Publikumsausgabe».

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