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Repetitive low-energy shock wave application without local anesthesia is more efficient than repetitive low-energy shock wave application with local anesthesia in the treatment of chronic plantar fasciitis

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Abstract

Background: It remains unclear whether application of local anesthesia (LA) interferes with clinical efficacy of extracorporeal shock wave therapy (ESWT) for chronic plantar fasciitis.

Aims: To evaluate the effect of local anesthesia on the clinical outcome after repetitive low-energy ESWT for chronic plantar fasciitis.

Methods: Eighty-six patients with chronic plantar fasciitis were randomly assigned to receive either low-energy ESWT without LA, given weekly for three weeks (Group I, $n = 45$; 3×2000 pulses, total energy flux density per shock 0.09 mJ/mm^2) or identical ESWT with LA (Group II, $n = 41$). Primary outcome measure was: Reduction of pain from baseline to month 3 post-treatment in a pain numeric rating scale [0–10 points] during first steps in the morning, evaluated by an independent blinded observer. Calculations were based on intention-to-treat.

Results: No difference was found between the groups at baseline. At 3 months, the average pain score was 2.2 ± 2.0 points for patients of Group I, and 4.1 ± 1.5 points for patients of Group II. The mean between-group difference was 1.9 points (95% CI: [1.1–2.7 points]; $P < .001$). Significantly more patients of Group I achieved $\geqslant 50\%$ reduction of pain compared to Group II (67% vs 29%, $P < .001$).

Conclusion: ESWT as applied should be done without LA in patients suffering from chronic heel pain. LA applied prior treatment reduced the efficiency of low-energy ESWT.

Keywords: Plantar fasciitis; Shock wave treatment; ESWT; Local anesthesia

Introduction

Plantar heel pain, commonly referred to as insertional plantar fasciitis, is a common condition among athletes as well as the general population. The characteristic complaints are knife-like pain at the calcaneal insertion of the medial part of the plantar fascia, typically

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worse on first arising in the morning, and often lasting months to years. Many treatment regimens exist but effectiveness is variable [8,52,55,63]. Multiple publications focused on the evaluation of a clinically relevant effect of shock wave application on plantar heel pain, either of high-energy extracorporeal shock wave treatment (ESWT), applied in a single session with local or regional anesthesia [3,6,9,28,35,36,38,59] or of low-energy ESWT, applied repetitively without local anesthesia [1,4,7,11,20–23,27,44–46,48,51].

A shock wave is defined as an acoustic wave at the front of which pressure rises from the ambient value to its maximum within a few nanoseconds. Typical characteristics are a high peak-pressure amplitude with a rise time of nanosecond duration, a short lifecycle of microsecond duration, and a frequency spectrum ranging from the audible to the far ultrasonic level. A recently published multicenter trial [16] failed to show effectiveness of repetitive low-energy ESWT compared to placebo ESWT in patients with a recalcitrant plantar fasciitis. In this trial a local anesthesia was used to secure blinding of the patients. However, other authors pointed at flaws in the study design such as use of simultaneous local anesthesia [4,12,34,47]. In an Austrian pilot study [4], 6 weeks after repetitive low-energy ESWT without local anesthesia 60% of cases achieved $\geqslant$50% reduction of pain compared to 29% when identical ESWT was applied under local anesthesia.

This preliminary report provided new important aspects in the use of local anesthesia which needed to be confirmed in a prospective randomized controlled trial.

Patients and methods

The objective of the study was to evaluate the influence of local anesthesia (LA) on the efficiency of repetitive low-energy ESWT for patients with a chronic plantar fasciitis. The study was designed as a randomized, single-center, parallel treatment study with a blinded independent observer. The trial was approved by the hospital's review board.

Patients

Potential participants to the study became aware of the trial by orthopaedic practitioners or hospitals. A total of 112 consecutive patients were referred for inclusion in the study from 2002 to 2003, after indication for ESWT had been checked. For the current study, chronic plantar fasciitis was defined as moderate to severe heel pain in the involved foot at the origin of the proximal plantar fascia on the medial calcaneal tuberosity. All patients reported pain in the morning or after sitting a long time, local pain where the fascia attached to the heel, and increasing pain after extended walking or standing. In order to be eligible to participate in the study, a patient had to meet inclusion criteria and exclusion criteria given in Table 1. All patients were offered active ESWT free of costs. All patients were informed about the study procedure. 19 patients did not fulfill inclusion criteria; 7 patients refused to participate. 86 patients agreed to participate and were treated according to the study protocol (Fig. 1). Patients were assigned, with use of concealed randomization, to receive ESWT without local anesthesia (Group I) or identical ESWT with local anesthesia (Group II). Randomization was performed according to a computer-generated random-numbers list to draw up an allocation schedule. The assignment of patients to either group took place after the final selection by the investigator and after baseline assessment.

Group I

45 patients were allocated to ESWT treatment without local anesthesia, 24 women and 21 men, with a mean age of 50 years (range, 30–67 years). In 19 cases the left foot was affected, in 26 cases the right foot. Mean duration of symptoms was 15 months (range, 6–40 months) (Table 2).

Table 1
Inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
• History of plantar fasciitis for at least 6 months • Unsatisfying subjective result (Numeric Rating Scale (NRS) score persistingly $\geqslant$4 points for pain during the first few steps of walking in the morning) after at least 6 months after $\geqslant$3 of the following 5 conventional therapy programs: $\geqslant$4 weeks of physical therapy and/or heel-cord stretching; heel cushions/orthotic devices; casting/night splints; $\geqslant$4 week course of non-steroidal anti-inflammatory medications; minimum of 2 local (steroid) injections • Localized pain on palpation of the proximal plantar fascia • Be willing to abstain from any other treatments or medications during the treatment and follow up period • Treatment-free interval of 6 weeks before ESWT	• <18 years of age • Receiving local injections within 6 weeks prior to the randomization visit • Receiving physical therapy within 6 weeks prior to the randomization visit • Receiving NSAIDs for any chronic conditions whether or not related to plantar fasciitis within 6 weeks prior to the randomization visit • Receiving systemic therapeutic anticoagulants • Bilateral plantar fasciitis • History and/or physical findings of lower extremity dysfunction, local arthritis, generalized poly-arthritis, rheumatoid arthritis, ankylosing spondylitis, local arthrosis • Neurologic abnormality (changes of deep tendon reflexes, motor or sensory deficit) • Arthrosis of the foot or ankle, as confirmed by X-ray diagnosis (AP, lateral views) • Previous surgery of the foot • Participation in a Workman's Compensation Program or plans to apply for the Program • Thrombopathy, infection, tumor, diabetes mellitus, systemic lupus, severe cardiac disease or other severe systemic diseases • Pregnancy • Allergic against mepivacain

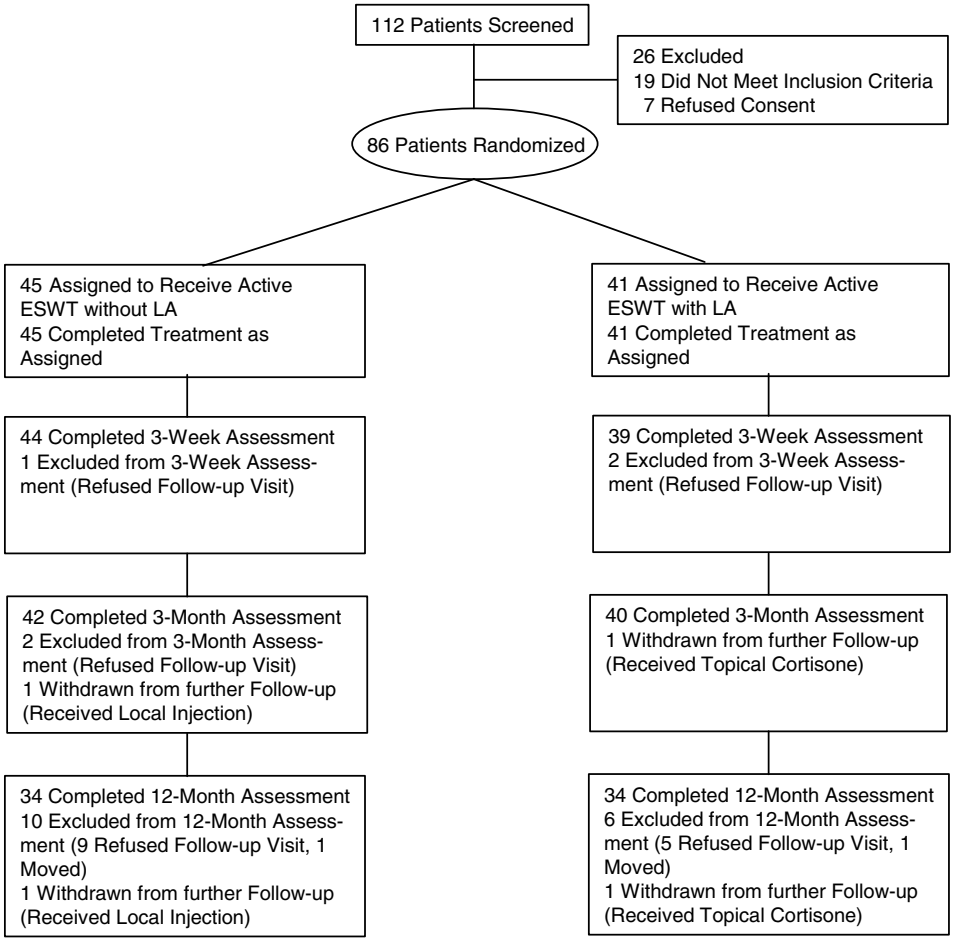

Fig. 1. Flow of participants through the trial.

Group II

Fourty-one patients were allocated to identical ESWT treatment with local anesthesia, 27 women and 14 men, with a mean age of 48 years (range, 22–68 years). In 19 cases the left foot was affected, in 22 cases the right foot. Mean duration of symptoms was 17 months (range, 6–36 months) (Table 2).

Method of treatment

ESWT was applied by a mobile therapy unit designed for orthopaedic use (Sonocur, Siemens AG, Erlangen, Germany), with the shock wave head suspended by an articulating arm for flexible movement of the head in three planes. The shock wave head was equipped with an electromagnetic shock wave emitter. Shock wave focus guidance was established by in-line integration of an ultrasound probe—a 7.5 MHz sector scanner—in the shock head. The region of interest in the ultrasound image was the area of the insertion of the plantar fascia to the calcaneus. The total energy flux density output at energy level "2" was 0.09 mJ/mm^2, based on measurements with glass–fiber hydrophones in accordance with IEC (International Electrotechnical Commission) 61846 procedures [61]. Low-energy ESWT with 2000 pulses was given once a week for 3 weeks using an energy flux density of 0.09 mJ/mm^2 per shock. Repetition frequency of shock wave pulses was 4 Hz. The total dose applied was 540 mJ/mm^2.

Treatment of Group I

Patients were treated in prone position. The pain spot near or over the medial calcaneus was identified by palpation (biofeedback technique) and marked with a pen. Prior to the treatment, a coupling gel was applied to the treatment area. Initially 100 shock waves were delivered at the lowest energy level (level 1) to precisely identify the exact pain spot. In order to achieve this goal the shock head or heel were moved in small increments until the patient reported maximal reproduction of discomfort (clinical focusing). Fine adjustment of shock wave penetration depth was accomplished under in-line ultrasound control by adjusting the amount of fluid in the bellows again with patient feedback to identify maximum trigger point stimulation. Then, the energy level was increased to level "2" (0.09 mJ/mm^2) after 100 pulses, and a total of 2000 shocks of level "2" were delivered to the affected site. Repetition frequency was 4 Hz. The shock head position was re-adjusted after every 200–400 shocks to precisely treat the area of most pronounced tenderness. This was necessary because of small positional movements that occurred during treatment. A complete therapy for heel pain consisted of three treatment sessions in weekly intervals.

Treatment of Group II

Prior to the treatment in prone position, 4 ml mepivacain 1% were injected into the most tender area at the origin of the proximal plantar fascia on the medial calcaneal tuberosity. This led to local numbness and prevented focusing via biofeedback. As creation of a numbing effect of the whole plantar side of the foot including the medial calcaneal branch was not aimed at, the injection was not done proximal to the plantar fascia in the area of the posterior tibial nerve just proximal to its bifurcation.

After 5 minutes coupling gel was applied to the skin. By in-line ultrasound the insertion of the plantar fascia at the medial aspect was identified. Fine adjustment of shock wave penetration depth was accomplished by adjusting the amount of fluid in the bellows. From

Table 2
Demographic and clinical characteristics, and baseline outcome measurements of trial participants

Characteristic	Group I Active ESWT without LA ($n = 45$)	Group II Active ESWT with LA ($n = 41$)
Age, mean (SD), y	50.0 (9.9)	47.9 (10.1)
Women, No. (%)	24 (53)	27 (66)
Duration of symptoms, mean (SD), mo	14.9 (8.7)	16.6 (7.8)
Affected foot, No. (%)		
Left	19 (34)	19 (46)
Right	26 (66)	22 (52)
Previous treatment, No. (%)		
NSAIDs	45 (100)	41 (100)
Physical therapy	45 (100)	41 (100)
Orthotics	45 (100)	41 (100)
Stretching exercises	45 (100)	41 (100)
Casting/Night splints	29 (64)	30 (73)
Cortisone injections	45 (100)	41 (100)
$\geqslant$3Cortisone injections	43 (96)	36 (88)
Radiotherapy	12 (27)	12 (29)
Surgery	0 (0)	0 (0)
Pain during first steps [0–10], mean (SD)	6.9 (1.2)	6.7 (1.1)
Ankle–Hindfoot-Scale [0–100], mean (SD)		
Total	52.3 (8.9)	51.1 (9.6)
Pain [0–40]	5.4 (8.9)	5.9 (9.2)
Activity level [0-10]	4.2 (0.8)	2.9 (1.8)
Walking distance [0-5]	2.3 (0.6)	2.1 (0.9)
Surfaces [0–5]	4.9 (0.6)	4.9 (0.4)
Gait abnormality [0–8]	3.8 (1.2)	3.7 (1.3)
Sagittal motion [0–8]	7.9 (0.6)	7.9 (0.6)
Hindfoot motion [0–6]	5.9 (0.4)	5.9 (0.5)
Ankle stability [0–8]	8.0 (0.0)	8.0 (0.0)
Alignment [0–10]	9.9 (0.7)	9.8 (1.1)
Subjective rating scale [1–4], mean (SD)	3.9 (0.3)	4.0 (0.2)

According to treatment group, LA: local anesthesia.

the beginning energy level "2" was applied. A total of 2000 shocks of level "2" were delivered to the affected site. The shock head position was only re-adjusted if the patient had moved. Exact positioning of the focus was controlled by in-line ultrasound during the whole procedure. A complete therapy for plantar fasciitis consisted of three treatment sessions in weekly intervals.

Care was taken to ensure that study participants did not meet. Individual study participants were asked to wait in separate waiting areas. Patients were informed that it was common to have some soreness after treatment and that the pain could become worse for a few days after ESWT. In addition it was emphasized, that healing might take several weeks to occur and that the patient should not expect maximum improvement until 3–6 months after the last treatment. Participants were able to continue to wear an already used shoe insert.

All co-interventions during the 3-month period were discouraged, but prescription of pain rescue medication if necessary was allowed. Apart from this no other therapies (including physiotherapy; chiropractic; laser; splint; acupuncture; locally injected anesthetic; oral, topical or locally injected corticosteroids) were allowed until 3-month follow-up was completed. Application of these procedures would otherwise lead to exclusion from the trial. Following the 3-month follow-up, concomitant therapies were allowed. Details of each treatment session and of any adverse effect were recorded. Pain was scored immediately after local infiltration, and after ESWT.

Method of evaluation

Patients were assessed prior to treatment, and at 3 weeks, 3 months and 12 months after the last application of low-energy ESWT by an independent treatment-blinded observer. The actual study procedure was exclusively done at the hospital of the principal investigator. The treating physician was aware of the treatment, but did not play any role in assessing the patients before and after treatment.

Primary outcome measure

The primary efficacy endpoint was prospectively defined as reduction of pain from baseline to month 3 post-treatment in a verbally administered validated pain numeric rating scale (NRS; range 0–10 points) [58] during first steps in the morning. The 3-month interval was selected because it was expected that the healing process would likely be complete at this point of time, and because most RCTs in this field used the 3-month follow-up to assess efficacy criteria.

Mean improvement from baseline to week 3, and to month 12 post-treatment in the pain NRS during first steps in the morning was regarded as secondary endpoints.

Secondary outcome measures

A secondary efficacy endpoint was defined as number of patients achieving $\geqslant$50% improvement in the pain NRS during first steps in the morning from baseline to week 3, to month 3, and to month 12 post-treatment.

A secondary efficacy endpoint was defined as the number of patients achieving $\geqslant$80 points at week 3, at month 3, and at month 12 post-treatment in the patient's function assessed using the validated 100-point AOFAS (American Orthopaedic Foot and Ankle Society) Ankle–Hindfoot-Score [26] (Table 3).

A secondary efficacy endpoint was defined as number of patients reaching $\geqslant$50% improvement on a subjective 4-step rating scale at 3 weeks, at 3 months, and at 12 months post-treatment. On the scale [43], one point was defined as excellent, with the patient having no pain, full movement, and full activity. Two points were defined as good, with occasional discomfort, full movement, and full activity. Three points were considered fair, with some discomfort after prolonged activity, and need for further treatment. Four points indicated a poor status, with pain limiting activities, and need for further treatment.

Statistics

Primary aim of this study was to compare the clinical outcome after repetitive low-energy extracorporeal shock wave therapy without local anesthesia with the clinical outcome after repetitive low-energy extracorporeal shock wave therapy with local anesthesia. The primary efficacy endpoint was prospectively defined as reduction of pain from baseline to month 3 post-treatment in a verbally administered pain numeric rating scale (NRS; range 0–10 points) during first steps in the morning. Prior to the start of the trial the number of subjects to treat was calculated to 40 patients for each group. This sample size accounted for a 10% loss to follow up, a type I error rate of 0.05 and a power of 0.8. The assumptions of a delta of 1.3 points in the NRS and a standard deviation of 2.0 were conservatively based on the data of an Austrian study [4].

Summarizations were performed separately for each treatment group. Descriptive statistics were used. Continuous variables were summarized within treatment groups using N, mean, standard deviation, median, minimum, and maximum. Categorical variables were summarized within treatment groups using N and percent. For the primary efficacy endpoint, comparison of mean improvement of NRS assessed at 3 months post-treatment, calculations used the t-test Welsh-corrected (Graphstat, Graphpad Inc., San Diego, CA). Missing responses (3 of 45 in Group I, 1 of 41 in Group II) were imputed as baseline observation carried forward. Baseline observation was defined as the last observed value before the initial treatment. For comparison of the number of patients who reached at least 50% improvement in pain, the Fisher's exact test was performed. Calculation was based on intention-to-treat. Treatment effects for the treatment group I compared to the treatment group II as mean improvement of NRS assessed at 3 weeks, and 12 months post-treatment were calculated using the

Table 3
American Orthopaedic Foot and Ankle Society (AOFAS) Ankle–Hindfoot-Scale

Pain (40 points)	
None	40
Mild	30
Moderate	20
Severe	10
Activity limitation (10 points)	
No limitation	10
Limitation of recreational activity	7
Limited daily and recreational activity	4
Severe limitation, crutches	0
Max. walking distance (5 points)	
>6 blocks	5
4–6 blocks	4
1–3 blocks	2
<1 block	0
Walking surfaces (5 points)	
No difficulty	5
Some difficulty	3
Severe difficulty	0
Gait abnormality (8 points)	
None, slight	8
Obvious	4
Marked	0
Sagittal motion (flexion plus extension) (8 points)	
30° or more	8
15–29°	4
<15°	0
Hindfoot motion (inversion plus eversion) (6 points)	
75–100% normal	6
25–74% normal	3
<25% normal	0
Ankle–Hindfoot Stability (anteroposterior, varus–valgus) (8 points)	
Stable	8
Definitely unstable	0
Alignment (10 points)	
Good, well aligned	10
Fair, some degree of malalignment	5
Poor, non-plantigrade foot, severe malalignment	0

t-test Welsh-corrected. Missing responses were imputed as baseline observation carried forward. Baseline observation was defined as the last observed value before the initial treatment. For comparison of the number of patients who reached at least a 50% improvement on the subjective rating scale, and who reached at least 80 points in the Ankle–Hindfoot-Score, the Fisher's exact test was performed.

Results

Primary outcome measure

The primary efficacy endpoint was defined as reduction of pain from baseline to month 3 post-treatment in the pain numeric rating scale (NRS) during first steps in the morning. The average pain score for patients who received ESWT without local anesthesia (Group I) was 6.9 ± 1.2 points at baseline, and 2.2 ± 2.0 points at 3 months. The average pain score for patients who received ESWT with local anesthesia (Group II) was 6.7 ± 1.1 points at baseline, and 4.1 ± 1.5 points at 3 months. The mean between-group difference was 1.9 points ($P < .001$ in favor of Group II; 95% CI: [1.1–2.7]).

The average pain score during first steps in the morning for patients who received ESWT without local anesthesia (Group I) was 5.0 ± 2.2 points at 3 weeks, and 1.9 ± 1.8 at 12 months. The average score for patients who received ESWT with local anesthesia (Group II) was 3.9 ± 1.9 points at 3 weeks, and 4.1 ± 2.1 points at 12 months. At 3 weeks the mean between-group difference was -1.1 points ($P = .015$ in favor of Group II 95% CI: [-2.0 to -0.2]). At 12 months the mean between-group difference was 2.2 points ($P < .001$ in favor of Group I; 95% CI: [1.4–3.1]).

Secondary outcome measures

At 3 weeks, 13/45 (29%, Group I) versus 24/41 (59%, Group II) of patients reached a $\geqslant 50\%$ improvement. The difference between groups was -0.3 ± 0.1 ($P = 0.009$ in favor of Group II; 95% CI: [-0.5 to 0.1]; on intention-to-treat). At 3 months in Group I 30 of 45 (67%) patients achieved at least a 50% reduction of pain, compared with 12 of 41 (29%) patients in Group II. The difference between groups was 0.4 ± 0.1 ($P < .001$ in favor of Group I; 95% CI: [0.5–0.8]; on intention-to-treat). At 12 months 27/45 (60%) versus 10/41 (24%) of patients reached a $\geqslant 50\%$ improvement. The difference between groups was 0.4 ± 0.1 ($P = 0.001$ in favor of Group I; 95% CI: [0.2–0.6]; on intention-to-treat).

Another secondary efficacy endpoint was defined as number of patients reaching 80 points on the AOFAS Ankle–Hindfoot-Scale. On an intention to treat basis, at 3 weeks in Group I 6 of 39 (13%) patients achieved at least 80 of 100 points, compared with 16 of 41 (39%) patients in Group II. The difference between groups was 0.3 ± 0.1 ($P = .012$ in favor of Group II; 95% CI: [0.1–0.4]). At 3 months in Group I 27 of 45 (60%) patients achieved at least 80 of 100 points, compared with 12 of 41 (29%) patients in Group II. The difference between groups was 0.3 ± 0.1 ($P = .005$ in favor of Group I; 95% CI: [0.1–0.5]). At 12 months in Group I 27 of 45 (60%) patients achieved at least 80 of 100 points, compared with 11 of 41 (27%) patients in Group II. The difference between groups was 0.3 ± 0.1 ($P = .003$ in favor of Group I; 95% CI: [0.1–0.5]).

Another secondary efficacy endpoint was defined as number of patients reaching excellent or good outcome on a subjective 4-step rating scale. On an intention to treat basis, at 3 weeks in Group I 14 of 45 (31%) patients achieved an excellent or good result, compared with 24 of 41 (59%) patients in Group II. The difference between

groups was 0.3 ± 0.1 ($P = .016$ in favor of Group II; 95% CI: [0.1–0.5]). At 3 months in Group I 30 of 45 (67%) patients achieved an excellent or good result, compared with 10 of 41 (24%) patients in Group II. The difference between groups was 0.4 ± 0.1 ($P < .001$ in favor of Group I; 95% CI: [0.2–0.6]). At 12 months in Group I 29 of 45 (64%) patients achieved an excellent or good result, compared with 11 of 41 (27%) patients in Group II. The difference between groups was 0.4 ± 0.1 ($P < .001$ in favor of Group I; 95% CI: [0.2–0.6]).

Between-group differences of improvement are given in Table 4. Proportion of patients achieving ⩾50% improvement on NRS for pain at first steps, of patients achieving ⩾50% improvement on a subjective 4-step rating scale, and of patients achieving ⩾80 points in the AOFAS Ankle–Hindfoot-Score are given in Table 5.

Side effects

In all patients transient reddening occurred after low-energy shock wave application. Twenty-four of 45 patients receiving active ESWT without local anesthesia (Group I) reported pain during ESWT ⩾5 on the NRS, and 3 of 41 patients receiving active ESWT with

Table 4
Mean changes from baseline at 3 weeks, 3 months, and 12 months

Outcome measure	3-Week mean change[a] from Baseline (95% CI)		Between-group difference[b] (95% CI)	
	Group I Active ESWT without LA	Group II Active ESWT with LA	Group I vs Group II	*P* value
Pain at first steps [0–10]	1.9 (1.2–2.7)	2.8 (2.1–3.4)	−0.9 (−1.8–0.1)	.079
Ankle–Hindfoot-Score [0–100]	8.3 (2.8–13.8)	13.0 (5.3–20.6)	−4.6 (−13.9–4.6)	.321
Subjective rating scale [1–4]	1.2 (1.0–1.5)	1.4 (1.1–1.7)	−0.2 (−0.6–0.3)	.488
	3-Month mean change[a] from baseline (95% CI)		Between-group difference[b] (95% CI)	
Pain at first steps [0–10]	4.7 (4.0–5.4)	2.6 (1.9–2.9)	2.1 (1.3–3.0)	<.001
Ankle–Hindfoot-Score [0–100]	30.4 (22.5–38.3)	20.3 (14.9–25.7)	10.1 (0.63–19.5)	.037
Subjective rating scale [1–4]	1.9 (1.6–2.1)	1.2 (0.9–1.4)	0.7 (0.3–1.1)	<.001
	12-Month mean change[a] from baseline (95% CI)		Between-group difference[b] (95% CI)	
Pain at first steps [0–10]	5.0 (4.3–5.7)	2.6 (1.9–3.3)	2.4 (1.4–3.3)	<.001
Ankle–Hindfoot-Score [0–100]	16.1 (3.8–28.5)	9.9 (−0.2–19.9)	6.3 (9.4–21.9)	.429
Subjective rating scale [1–4]	1.9 (1.6–2.2)	1.2 (0.9–1.5)	0.7 (0.3–1.1)	<.001

Missing responses were imputed as the last observation carried forward. ESWT, extracorporeal shock wave treatment; LA, local anesthesia; SD, standard deviation; CI, confidence interval.

[a] Positive change indicates improvement, negative change worsening.

[b] Positive difference in mean change indicates Group I improved more than Group II. Because of rounding, some between-group differences may differ from values obtained by substracting mean change (Group II) from mean change (Group I).

Table 5
Proportion of patient reaching successful outcome at 3 weeks, 3 months, and 12 months

Outcome measure	3 weeks (95% CI)		Between-group difference (95% CI)	
	Group I Active ESWT without LA	Group II Active ESWT with LA	Group I vs Group II	*P* value
Pain at first steps [0–10][a]	0.29 (0.16–0.44)	0.59 (0.42–0.74)	−0.30 (−0.51–0.09)	.009
Ankle–Hindfoot-Score [0–100][b]	0.13 (0.05–0.27)	0.39 (0.24–0.55)	−0.26 (−0.44–0.07)	.012
Subjective rating scale [1–4][a]	0.31 (0.18–0.47)	0.59 (0.42–0.74)	−0.27 (−0.48–0.06)	.016
	3 months (95% CI)		Between-group difference (95% CI)	
Pain at first steps [0–10][a]	0.67 (0.52–0.81)	0.29 (0.15–0.44)	0.37 (0.17–0.58)	<.001
Ankle–Hindfoot-Score [0–100][b]	0.60 (0.44–0.74)	0.29 (0.160–0.46)	0.31 (0.10–0.52)	.005
Subjective rating scale [1–4][a]	0.67 (0.51–0.80)	0.24 (0.12–0.40)	0.43 (0.21–0.63)	<.001
	12 months (95% CI)		Between-group difference (95% CI)	
Pain at first steps [0–10][a]	0.60 (0.44–0.74)	0.24 (0.12–0.40)	0.36 (0.16–0.59)	.001
Ankle–Hindfoot-Score [0–100][b]	0.60 (0.44–0.74)	0.27 (0.14–0.43)	0.33 (0.12–0.54)	.003
Subjective rating scale [1–4][a]	0.64 (0.49–0.78)	0.27 (0.14–0.43)	0.38 (0.17–0.59)	<.001

Calculation on intention-to-treat. A positive between-group difference indicates Group I improved more than Group II. Because of rounding, some between-group differences may differ from values obtained by substracting proportions (Group II) from proportions (Group I).

[a] Proportion of patients with >50% improvement.

[b] Proportion of patients with >80 points.

Table 6
Pain score measured immediately after ESWT (Group I and Group II), and after injection of local anesthetic (Group II)

Outcome measure	Mean (95% CI)		Between-group difference (95% CI)	
	Group I Active ESWT without LA	Group II Active ESWT with LA	Group I vs Group II	*P* value
Pain during 1. ESWT	4.9 (4.5–5.3)	2.2 (1.7–2.6)	−2.7 (−3.3 to 2.1)	<.001
Pain during 2. ESWT	4.4 (4.0–4.7)	1.5 (1.1–1.8)	−2.9 (−3.4 to 2.4)	<.001
Pain during 3. ESWT	2.7 (2.3–3.0)	1.5 (1.2–1.8)	−1.1 (−1.6 to 0.7)	<.001
Pain during 1. injection	–	7.3 (6.8–7.8)	–	–
Pain during 2. injection	–	6.9 (6.5–7.3)	–	–
Pain during 3. injection	–	6.3 (5.9–6.7)	–	–

A positive between-group difference indicates Group I improved more than Group II. Because of rounding, some between-group differences may differ from values obtained by substracting mean (Group II) from mean (Group I).

local anesthesia (Group II). 40 of 41 patients receiving an injection of the local anesthetic reported pain during injection $\geqslant 5$ on the NRS (Table 6). Apart from these minor findings, no clinical relevant side effect was found. No device-related complications occurred.

Discussion

Recently repetitive low-energy extracorporeal shock wave treatment (ESWT) has been widely used to treat a number of musculoskeletal conditions, including insertional disorders such as plantar fasciitis.

In clinical practice, the application of a local anesthesia prior to low-energy ESWT became subject to criticism [4,12,47], therefore calling in question the negative results of a multicenter trial [16] on ESWT in patients suffering from chronic plantar fasciitis. In this trial local anesthesia had been applied for reason of blinding.

Auersperg et al. [4] reported they had enrolled 60 patients with a chronic plantar fasciitis in a triple-arm (20 patients per group), prospective randomized and observer-blinded pilot trial. Patients were randomly assigned to receive either active ESWT without local anesthesia, given daily for three days (Group I, 3×1500 pulses, total energy flux density per shock 0.09 mJ/mm^2), or ESWT with local anesthesia (Group II, 3×1500 pulses, total energy flux density per shock 0.18 mJ/mm^2) or ESWT with local anesthesia (Group III, 3×1500 pulses, total energy flux density per shock 0.09 mJ/mm^2). Main outcome measures were: Pain during first step in the morning (measured on a 0–10 point visual analog scale) and number of patients with >50% reduction of pain and no further therapy needed, measured at six weeks after the last ESWT. At six weeks, there was significant improvement in pain during first steps in the morning in all groups, by 4.2 points in Group I, by 2.6 points in Group II, and by 2.4 points in Group III. The mean between-group difference of improvement was statistically significant, between Group I and Group II, and between Group I and Group III. A reduction of pain of at least 50% was achieved in 60% of patients of Group I, in 36% of patients of Group II, and in 29% of patients of Group III. In conclusion, at six weeks success rates after low-energy ESWT with local anesthesia were significantly lower than after identical low-energy ESWT without local anesthesia.

The current study confirmed their observation. The average pain score for patients who received ESWT without local anesthesia (Group I) was 6.9 points at baseline, and 2.2 points at 3 months. The average pain score for patients who received ESWT with local anesthesia (Group II) was 6.7 points at baseline, and 4.1 points at 3 months. At 3 months in Group I 67% of patients achieved at least a 50% reduction of pain, compared with 29% of patients in Group II. At 3 months in Group I 67% of patients achieved an excellent or good result, compared with 24% patients in Group II. Not all patients were satisfied, of course, in Group I. But with two-third of them presenting with either no pain, full movement, and full activity, or with only occasional discomfort, full movement, and full activity, the results were not only statistically impressing. The results were clinically significant as well.

Obviously, accurate targeting of the pathology at the spot of maximal point tenderness, as described to the examiner by the patient, is crucial for optimal application of low-energy shock waves [12]. Although a randomized and controlled trial, the current study suffers from limitations. First, it is a monocenter study, and treatment was performed by one expert team of orthopaedic surgeons. A selection and treatment bias cannot be ruled out completely though a standardized randomization procedure was used. Second, patients were not matched for activity level before treatment. Third, no placebo group was included in this trial which would help to differentiate more clearly between the treatment effect of ESWT and local anesthesia. All patients enrolled in this trial were fully aware that they were receiving active ESWT. Fourth, the primary outcome measure focused at the 3-month follow-up. Long-term results should be addressed in a separate prospective trial, for ethical reasons then without a placebo-treated control group. Fifth, results of the current trial cannot be

extrapolated to other ESWT treatment regimens or devices.

What may be the reasons for the treatment effect of low-energy ESWT as applied in the current trial?

The rationale for ESWT in clinical use is stimulation of soft tissue healing and inhibition of pain receptors. Ogden et al. [36] postulated shock waves lead to controlled internal fascial tissue microdisruption that initiated a more appropriate healing response within the fascia and a better long-term capacity to adapt to biologic and biomechanical demands.

Haake et al. repeatedly failed to provide evidence for a specific biological response when evaluating changes in the activity of spinal cord neurones in a rat model after shock wave application (1000 impulses, Energy Flux Density (EFD) = 0.13–0.33 mJ/mm^2). The authors concluded that it was unlikely that ESWT could trigger stimulation-induced analgesic response via activation of peripheral nerves, and that analgesic effects of ESWT were endogenous opioid-dependent. The authors further negated that ESWT could trigger the endogenous pain control system [17–19].

The negative results of these experiments were contradicted by recent studies using a more sophisticated technique. To investigate the analgesic properties of low-energy shock wave application, Ohtori et al. [37] demonstrated that low-energy shock waves (1000 impulses, EFD = 0.08 mJ/mm^2) produced morphologic changes in cutaneous nerve fibres. The number of sensory fibers decreased significantly following shock wave application as indicated by the loss of immunoreactivity for calcitonin gene related peptide (CGRP) compared to the untreated skin. CGRP is a marker of sensory neurons, regarded as the primary afferent peptide with the strongest evidence of a role in pain perception [24], and has immunohistochemically been co-localized with substance P [5,14]. Reinnervation of the epidermis started 2 weeks after treatment. Ohtori concluded that low-energy ESWT was able to temporarily destroy the sensory free nerve endings in the rat skin. When repeating shock wave application after 14 days in another experiment, the same authors described delay of reinnervation for as long as 42 days, significantly longer than after single shock wave application [54]. Takahashi et al. [53] investigated the analgesic properties of low-energy shock wave application (1000 impulses, EFD = 0.08 mJ/mm^2). They analyzed changes in CGRP-immunoreactive (ir) neurons in the dorsal root ganglion (DRG). In the non-treated group, 61% of fluorogold-labeled dorsal root ganglion neurons innervating the most middle foot pad of hind paw were CGRP-ir. However, in the shock wave-treated group, the percentage decreased to 18%. Maier et al. [32] showed that high-energy ESWT (1500 impulses, EFD = 0.90 mJ/mm^2) to the distal rabbit femur resulted in a reduced concentration of substance P in the femoral periosteum 6 weeks after shock wave application. Substance P is concentrated in unmyelinated C-fibers and a subpopulation of slowly conducting, lightly myelinated A-δ nerve fibers, and is released at central and peripheral terminals of sensory nociceptive neurons after stimulation. Recently the same group [33] showed that high-energy ESWT (1500 impulses, EFD = 0.90 mJ/mm^2) applied to the ventral side of the distal rabbit femur after 6 weeks resulted in a significant loss of unmyelinated fibers as well as in a pronounced loss of small myelinated fibers within the femoral nerve (facing the shock wave source), while the sciatic nerve (protected from ventrally applied shock waves by the femur) did not suffer reduction of fiber density or reduction of the total number fibers. ESWT as applied furthermore led to a slight but significant reduction in the number of neurons immunopositive for substance P within the lower lumbar DRG, without reducing the total number of neurons within these ganglia.

These studies [32,33,37,53,54] indicate that shock waves may selectively lead to dysfunction of peripheral sensory unmyelinated nerve fibers without affecting nerve fibers responsible for motor function (large myelinated fibers). For high-energy treatment, this selective destruction of unmyelinated sensory nerve fibers within the focal zone of ESWT may contribute to clinically evident long-term analgesia. For low-energy application, analgesia may be a result of a shock wave-induced release of neuropeptides, such as CGRP, resulting in a local neurogenic inflammation in the focal area with subsequent prevention of sensory nerve endings from reinnervating this area. Takahashi [54] hypothesized that a second application accentuated these inflammatory changes and therefore prevented reinnervation.

Centrally, the findings of a reduction in the number of neurons immunoreactive to CGRP and substance P without a reduction of the total number of neurons within the lower lumbar DRG probably are a secondary effect following the (primarily induced) decrease of the number of sensory nerve fibers in the focal zone of shock wave application. Similar results were reported for neurons immunoreactive for CGRP within the DRG of the mouse after transection of the sciatic nerve [50]. So the peripheral and central nervous system may both play a pivotal role in mediating shock wave induced long-term analgesia.

Furthermore, Wang et al. [60] investigated the effect of low-energy shock wave therapy on neovascularization at the tendon–bone junction in rabbits. The results showed that low-energy shock wave treatment (500 impulses, EFD = 0.12 mJ/mm^2) produced a significantly higher number of neo-vessels and angiogenesis-related markers including endothelial nitric oxide synthase (eNOS), vessel endothelial growth factor (VEGF) and proliferating cell nuclear antigen (PCNA) than the

control without shock wave treatment. Chen et al. [10] reported that only an optimal ESW treatment promoted healing of Achilles tendinitis by inducing TGF-beta1 and IGF-I. Rats with the collagenease-induced Achilles tendinitis were given a single shock wave treatment (EFD = 0.16 mJ/mm^2) with 0, 200, 500 and 1000 impulses. 200 impulses restored biomechanical and biochemical characteristics of healing tendons 12 weeks after treatment. However, ESW treatments with 500 and 1000 impulses elicited inhibitory effects on tendinitis repair. Histological observation demonstrated that ESW treatment resolved edema, swelling, and inflammatory cell infiltration in injured tendons. The proliferation of tenocytes adjunct to hypertrophied cell aggregate and newly formed tendon tissue coincided with intensive TGF-beta1 and IGF-I expression. Together, low-energy shock wave effectively promoted tendon healing.

What may be the reasons for the effect of local anesthesia on the clinical outcome after repetitive low-energy ESWT as applied in the current trial?

Lately it has become evident that neuropeptides may play a role in insertional tendonitis [2,30,42,57]. Most recently, Ljung et al. [31] demonstrated findings of a general (PGP 9.5) as well as a sensory innervation (substance P, CGRP) of the tendon–bone junction in subjects suffering from symptomatic lateral epicondylitis. They concluded that this was a direct morphological correlate for the occurrence of nerve-mediated effects in this region. Indicating a sensitization of sensory afferents (nociceptors) to mechanical stimuli, local pain may persist even after the initial irritation has disappeared [56]. Use of a local anesthetic has been shown to alter local release of neuropeptides [5,29,39,49]. This alteration may well interfere with the neurogenic inflammatory response supposed to be provoked by low-energy shock wave application in animal experiments [37,53,54]. Use of local anesthesia has also been shown to be associated with a reduction of the local hyperemic response on neurogenic inflammation [13] which on its part may interfere with the production of neo-vessels and release of angiogenesis-related markers after low-energy ESWT [60].

In recent PET studies pain-related increases and decreases of regional cerebral blood flow have been identified specifically in the anterior cingulate cortex as part of a pain processing network—the pain matrix. Different parts of this matrix represent different components of pain [25] and may interact and be modulated by cognitive or hyperstimulating interventions [41,62]. Repetitive low-energy ESWT might hyperstimulate specific cerebral areas and lead to local changes of regional cerebral blood flow that modulate memory pain cortex [15,40,62]. Together with the effects shown on afferent neurons in animal experiments [32,33,37,53,54] these central neurophysiological modulations secondary to ESWT may lead to a prolonged reduction of the local pain stimulus and eventually to complete extinction of chronic heel pain.

Infiltration of a local anesthetic prior to the application of low-energy ESWT—which focuses the therapeutic energy at a small and localized area—precludes an accurate targeting on the area of maximal discomfort and may therefore prevent the above mentioned central neuromodulation.

Based on the present clinical and experimental knowledge, there remain some interesting points to be addressed in future trials: Does local anesthesia really have adverse influences on effects after low-energy ESWT in animal experiments and what biochemical changes occur with or without LA? Is there a difference between applying the LA directly to the area of interest compared to remote application (block)? Further clinical trials will also have to analyse if the above mentioned central neuromodulating effects can be detected after different modalities of ESWT.

Conclusions

We conclude that there is a positive treatment effect of repetitive low-energy ESWT *as applied* at 3-month follow-up in subjects with chronic plantar fasciitis. This positive treatment effect may be reduced by application of a local anesthetic to the painful area prior to low-energy ESWT. Until further experimental and clinical research has developed evidence for this effect, a local anesthetic should not be used for blinding in randomized-controlled trials evaluating the clinical efficacy of repetitive low-energy ESWT for musculoskeletal disorders.

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