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REVIEW ARTICLE

ELECTROTHERAPY FOR THE TREATMENT OF PAINFUL DIABETIC PERIPHERAL NEUROPATHY: A REVIEW*

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Objective: **To review different types of electrotherapy for the treatment of painful diabetic peripheral neuropathy.**
Methods: **A structured search of the electronic database MEDLINE was performed from the time of its initiation to July 2009. Articles in English and German were selected.**
Results: **The efficacy of different types of electrotherapy for painful diabetic peripheral neuropathy has been evaluated in 15 studies; the effects of transcutaneous electrical nerve stimulation are consistent. The beneficial effects of prolonged use have been reported in three large studies and one small study. The effects of frequency-modulated electromagnetic neural stimulation were assessed in one large study, and a significant reduction in pain was reported. Treatment with pulsed and static electromagnetic fields has been investigated in two small and three large studies, and analgesic benefits have been reported. In one large study focusing on pulsed electromagnetic fields, no beneficial effect on pain was registered. Only small studies were found concerning other types of electrotherapy, such as pulsed-dose electrical stimulation, high-frequency external muscle stimulation or high-tone external muscle stimulation. The conclusions drawn in these articles are diverse. Shortcomings and problems, including a poor study design, were observed in some.**
Conclusion: **Further randomized, double-blind, placebo-controlled studies comprising larger sample sizes, a longer duration of treatment, and longer follow-up assessments are required.**

Key words: review; electrotherapy; painful diabetic peripheral neuropathy.

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INTRODUCTION

Peripheral neuropathy (PN) is a common complication of diabetes mellitus (1). Up to 36% of individuals with non-insulin-dependent diabetes mellitus are affected by this condition, which is believed to be progressive and irreversible (2). The characteristics of diabetic peripheral neuropathy include numbness, diminished sensation, and/or pain. Painful symptoms, such as burning, pins and needles, shooting pain and hyperaesthesia, have also been reported (3). Pain is usually worst at night and may disrupt the patient's sleep (4). Diabetic patients with PN may be unable to maintain their posture, as evidenced by their exaggerated body sway (5). Postural control can be treated by exercise therapy, especially balance training (6). Aerobic exercise training may prevent the onset, or modify the natural history of, diabetic PN (7). PN is also a risk factor for foot ulcers, infection and even amputation (8). Neuropathic ulcers frequently occur at the forefoot beneath the metatarsal heads (9). PN is associated with hyperextension of the metatarsophalangeal joints, clawing of the toes, and reduced plantar tissue thickness (10). This may increase foot pressure and lead to foot ulcers (11). Neither multidisciplinary management of diabetic foot disease nor exercise therapy is a part of this review.

As the aetiology and pathogenesis of the painful symptoms induced by PN are poorly understood, treatment is largely symptomatic, consisting of analgesics, anticonvulsants, opioids and tricyclic antidepressants (12). Suggested aetiological factors include acute and chronic hyperglycaemia, microvascular abnormalities, nitric oxide deficiency, genetic and environmental variables, and nerve compression (13). The pathogenesis appears to be multifactorial. Pathological changes in the endoneural capillaries appear to correlate with the severity of neuropathy (14). Fisher et al. (15) endorse the notion that ischaemia may be an important factor in the pathogenesis of diabetic neuropathies. He found improvements in nerve function, as evaluated by electrophysiological parameters, after 24 weeks of moderate exercise training in patients with type II diabetes mellitus (15). Based on the suspected pathogenesis of ischaemia, the treatment is focused on improving circulation and oxygenation. Due to their numerous comorbidities, patients with diabetes mellitus may find it difficult to perform exercise training and therefore require other treatments. One method is electrotherapy (16–18), which has been shown to enhance microcirculation and endoneural blood flow (18). Electrotherapy could be effective in view of the impaired microcirculation in the peripheral nerves of patients with diabetic PN. An increase in the muscle's oxidative capacity (which is a metabolic effect of electrotherapy) is

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also of interest. Martin et al. (19) found electrical stimulation to exert an effect on the morphological and metabolic properties of paralysed muscles. Local release of neurotransmitters such as serotonin (20), increased production of mitochondrial adenosine triphosphate (ATP) (21), release of endorphins (22), or anti-inflammatory effects (23) may also trigger the analgesic effect of electrotherapy. Activation of the dorsal column is discussed as a further potential mechanism of the effect of electrotherapy. The input of pain is interrupted by the inhibition of C fibres (thus interrupting/gating the input of pain) (24). Mima et al. (25) registered a reduction in the excitability of the human motor cortex by the use of high-frequency transcutaneous electrical nerve stimulation (TENS); the results of this study suggest that short-term TENS might exert an inhibitory effect on the sensory as well as the motor system.

Various types of electrotherapy, such as transcutaneous electrical nerve stimulation (TENS) (26–30), pulsed-dose electrical stimulation applied by stocking electrodes (31–32), pulsed (electro-)magnetic fields (33–36), static magnetic field therapy (37), external muscle stimulation (38–40) and frequency-modulated electromagnetic neural stimulation (FREMS) (41), have been reported, but to our knowledge have not been reviewed thus far.

A structured review of different types of electrotherapy and their effectiveness for the treatment of painful diabetic peripheral neuropathy was therefore performed.

METHODS

Search strategy

A structured literature search was performed using the electronic database MEDLINE from its start to July 2009. Only trials published in English and German were selected. Studies investigating the use of different electrotherapies as a treatment of painful diabetic peripheral neuropathy were chosen. Invasive techniques, such as electrical spinal cord stimulation, were not included.

The following key words were used in different combinations. "Painful diabetic polyneuropathy", "diabetic polyneuropathy", "diabetic neuropathy" and "painful diabetic peripheral neuropathy" were each combined with the following treatment options: physical treatment, physical modalities, electrotherapy, electrical stimulation, magnetic field, pulsed electromagnetic fields, PEMF, pulsed magnetic field therapy, static magnetic field, transcutaneous electrostimulation, transcutaneous electrical nerve stimulation, TENS, NMES, high-frequency external muscle stimulation, external muscle stimulation, high-tone external muscle stimulation, HF, and frequency-modulated electromagnetic neural stimulation, FREMS.

The search produced a total of 3801 hits. Articles concerning spinal cord stimulation, percutaneous electrostimulation, gastric stimulation, ulcers, wounds, animal studies and case reports were excluded. Duplicates were removed. References in the included studies and in reviews of the literature were also screened. A total of 15 articles met the search criteria. Two authors selected the studies and the following data were extracted from each trial: author, design, number of patients included, intervention (type, number of sessions, treatment period) and results with reference to the effectiveness of the intervention (Table I).

The grading of the quality of evidence of the articles was based on the grading system suggested by the evidence based medicine Guidelines, adapted from the GRADE Working Group (42).

RESULTS

The results were differentiated by the applied treatment, as shown in Table I.

Transcutaneous electrical nerve stimulation

Kumar & Marshall (26) evaluated the efficacy of TENS for the management of PN in patients with type 2 diabetes. Thirty-one patients were randomized to TENS or sham treatment. TENS was applied as a home treatment for 4 weeks, 30 min daily, using a portable device. The patients were instructed on the use of the device and the placement of electrodes. The device generated a biphasic exponentially decaying waveform with pulse widths of 4 ms, $\geq$2 Hz, $\leq$35 mA and 25–35 V. Four self-adhesive electrodes were positioned (3 inches (7.5 cm) above the patella and 3 inches medially over the vastus medialis oblique, 3 inches above the patella and 3 inches lateral over the vastus lateralis, on the neck of fibula, and on the gastrocnemius muscle approximately 3 inches below the centre of popliteal fossa). The sham treatment group received devices that had inactive output terminals. In this study, TENS produced a transient reduction in pain and discomfort in 83% of the patients. The symptoms reappeared approximately 1 month after termination of TENS.

In a single-blind, placebo-controlled, randomized, 2-arm study, Kumar et al. (27) evaluated the efficacy of TENS in combination with amitriptyline for the management of PN in patients with type 2 diabetes. Twenty-six patients were included in the trial. All participants were prescribed amitriptyline throughout the 20-week study period. After 4 weeks, those who failed to respond to amitriptyline were randomized to the treatment group (TENS) or the sham treatment group (control). TENS was applied as home treatment for 12 weeks, 30 min daily, using a portable device. The patients were instructed on the use of the device and the placement of electrodes. The devices and the position of the electrodes were the same as those in the afore-mentioned study. The last visit was scheduled to be held 4 weeks after termination of TENS treatment. TENS was effective in reducing pain in patients who failed to respond to amitriptyline, and provided better symptomatic relief in combination with amitriptyline. Nearly 85% of the participants experienced beneficial effects and 36% became asymptomatic. The effect of combining TENS and amitriptyline appears to be superior to that of TENS alone. The authors concluded that the treatment should be continued in responders because their symptoms recurred after termination of TENS, although amitriptyline therapy had been continued.

In a further article, the same study group used the above-mentioned stimulation device to determine the long-term efficacy of TENS on neuropathic symptoms in diabetic patients (28). For the retrospective analysis the authors used a detailed questionnaire concerning symptoms of painful feet (for example pain, discomfort, ulcers, swelling in the lower extremities) before and after TENS, and experience with this form of treatment, including questions concerning the duration and frequency of treatment sessions, period of use each time, who had recom-

Table I. *Electrotherapy for the treatment of painful diabetic peripheral neuropathy*

Author	Design	Level of evidence	*n*	Intervention	Results
Kumar & Marshall (26)	Randomized, controlled	B	31	TENS or sham treatment, 4 weeks, 30 min daily	Transient reduction in pain and discomfort in 83% of patients
Kumar et al. (27)	Randomized, controlled, 2 arm		26	TENS or sham treatment in combination with amitriptyline, 12 weeks, 30 min daily	85% of patients beneficial effect, 36% asymptomatic, recurrence after termination of TENS
Julka et al. (28)	Retrospective analysis		54	TENS long-term use (average: 1.7 years)	Treatment remains effective even with prolonged use
Forst et al. (30)	Randomized, controlled, double-blinded		19	TENS or sham treatment, 12 weeks, at least 30 min daily	After 6 weeks significant improvements in VAS, sign. improvements in NTSS-6-score after 6 and 12 weeks
Armstrong et al. (31)	Pilot study	D	10	Pulsed-dose electrical stimulation by stocking electrodes, 4 weeks active treatment, 8 h/day, nightly	Therapy may be effective in patients with grossly intact protective sensation and relatively good distal vascular perfusion
Oyibo et al. (32)	Controlled		30	Pulsed-dose electrical stimulation by stocking electrodes, 6 weeks active treatment, 8 h/day, nightly	No evidence, poor compliance
Weintraub & Cole (33)	Pilot study	C	24	PEMF, 1 h on 9 consecutive days	Short-term analgesic effect in more than 50% of patients
Musaev et al. (34)			121	PEMF at different frequencies (100 Hz, 10 Hz), 10 days, 10–15 min., + massage and exercise	Reduction in pain, significant regression of major subjective symptoms and improvements in the conductive functions of peripheral nerves
Wróbel et al. (35)	Randomized, placebo-controlled, double-blinded		61	Low-frequency pulsed magnetic field, 15 days, 20 min	Positive impact on pain, quality of life and sleep, but not better than placebo
Weintraub et al. (36)	Randomized, double-blinded, placebo-controlled		225	PEMF, 3 months, 2 h/day	No significant reduction in pain and sleep disturbance, but neurobiological changes in skin biopsy
Weintraub et al. (37)	Multicentre, randomized, placebo-controlled, double-blinded		375	Static magnetic field, shoe insoles for 4 months (24 h/day)	Significant reduction in pain pronounced during the third and fourth month
Reichstein et al. (38)	Randomized, controlled, prospective pilot study	D	41	High-frequency external muscle stimulation or TENS, 30 min daily for 3 consecutive days	Amelioration of symptoms and pain, more effective than TENS
Klassen et al. (39)	Prospective, non-randomized pilot study		40	High-tone external muscle stimulation, 1 h, 3×/week, 1–3 months	Significant improvements of discomfort, pain and sleep disorders
Humpert et al. (40)	Prospective, uncontrolled		92	External muscle stimulation 4 weeks, 60 min, 2×/week	EMS seems to be effective for symptomatic neuropathy, especially in patients with strong symptoms
Bosi et al. (41)	Randomized, cross-over, double-blinded, placebo-controlled	C	31	Frequency-modulated electromagnetic neural stimulation, 20 treatments, 30 min/treatment	Significant reduction in pain, significant increase in sensory tactile perception, increase in motor nerve conduction velocity for at least 4 months

NTSS-6-score: New Total Symptom Score; VAS: visual analogue scale; TENS: transcutaneous electrical nerve stimulation; EMS: external muscle stimulation. A (high): several high-quality studies with consistent results; B (moderate): one high-quality study, several studies with some limitations; C (low): one or more studies with severe limitations; D (very low): expert opinion, one or more studies with very severe limitations (43).

mended the treatment, and whether any adverse effects had been encountered. Fifty-four patients were included in the trial. Thirty-four patients returned the questionnaires. Twenty patients were selected randomly from those who did not return the questionnaires, and telephone interviews were conducted. The device was used 1.9 times per day for 34.7 min and the period of treatment was, on average, 1.7 years. Seventy-six percent of the patients reported a 44 ± 4% subjective improvement in neuropathic pain. This self-reported data suggested that the treatment remains effective even with prolonged use.

A German working group performed a double-blind, randomized study comprising 19 patients with mild to moderate symptomatic diabetic neuropathy, and evaluated the treatment of TENS in comparison with placebo treatment (30). Electrical simulation was performed with skin electrodes placed over the common peroneal nerve using the low-frequency mode (4 Hz), and the intensity was set individually at between 5 and 70 mA. Patients were advised to stimulate both legs for at least half an hour per day. After 6 weeks of treatment, significant improvements in the intensity of pain were seen on

visual analogue scale (VAS); after 6 and 12 weeks, significant improvements in the New Total Symptom Score (NTSS-6 score) were observed.

Pulsed-dose electrical stimulation applied by stocking electrodes

In a pilot study, Armstrong et al. (31) evaluated pulsed-dose electrical stimulation as an analgesic modality in 10 patients with painful nocturnal diabetic neuropathy. The stimulation was administered through a knitted silver-plated nylon/Dacron stocking electrode. A dose of 50 V of pulsed direct current at 100 pulses/s for 10 min, then 10 pulses/s for 10 min, was delivered each hour over an 8-h period nightly for 1 month. Pain was measured by VAS. A significant reduction in pain was noted after 4 weeks of treatment and at the follow-up evaluation 4 weeks after discontinuation of therapy. The authors concluded that the treatment may be effective in alleviating subjective pain due to diabetic neuropathy in a population consisting of patients with grossly intact protective sensation and relatively good distal vascular perfusion. The authors drew attention to the absence of a control group as a shortcoming of the study.

A few years later, a similar study was performed by Oyibo et al. (32) who also used silver-plated nylon/Dacron stocking electrodes, but studied a control group in addition to 30 patients. The active treatment phase lasted for 6 weeks. Fifty volts of pulsed direct current at 80 Hz for the first 10 min, then 8 Hz for the next 10 min each hour over an 8-h period, were delivered by microstimulator units. The stockings used by the control group delivered an insignificant current (5 V). Pain and sleep disturbance were scored on a 10-cm VAS. Only 14 patients completed the study. No significant reduction in pain was observed in either group and no difference was registered between groups. Compliance with the use of the stockings was poor and the drop-out rate was rather high.

Pulsed (electro-)magnetic fields (PEMF/PMF) and static magnetic fields

In a study by Weintraub & Cole (33), 24 patients with refractory neuropathic pain due to PN were treated with PEMF. PN was caused by diabetes (6 patients), pernicious anaemia (2 patients), chronic inflammatory demyelinating polyneuropathy (2 patients) or other conditions (14 patients). The device generated a pure magnetic field with a frequency below 30 Hz and a field strength below 2 mT. The most symptomatic foot was treated for 1 h on 9 consecutive days with a closed circuit coil. A short-term analgesic effect was achieved in more than 50% of the participants. Patients with more severe symptoms achieved greater benefits. The effect of placebo was not tested. The authors propose randomized, double-blind, placebo-controlled studies with larger sample size and longer stimulation times.

Musaev et al. (34) evaluated the effects of PEMF at different frequencies on the state of the segmental peripheral neuromotor apparatus in 121 patients with diabetic PN. The therapy was directed to the upper and lower limbs, corresponding to segmental zones, for 10 days. Each field was applied for 10–15 min. One group received PEMF with a carrier frequency of 100 Hz and a modulation frequency of 1 Hz; the second group received 10 Hz modulated at 0.5 Hz. The intensity of magnetic induction ranged to 8 mT in both groups. Additionally, the participants were given massages and exercise therapy. At the end of the treatment, the intensity of pain was reduced in both groups, and a significant alleviation of the major subjective symptoms of PN was noted. In addition, improvements in the conductive functions of peripheral nerves, and increases in the amplitudes of muscle potentials and the number of functioning motor units were found. Comparative analysis of clinical and electroneuromyographic measures in the 2 groups demonstrated the advantages of a frequency of 10 Hz.

Wróbel et al. (35) studied the impact of low-frequency pulsed magnetic fields on the intensity of pain, quality of life, and sleep in patients with painful diabetic PN. Sixty-one patients were included in a randomized, placebo-controlled, double-blind trial. The treatment group received low-frequency pulsed magnetic fields ranging up to 100 μT at a frequency of approximately 180–195 Hz. The placebo group was treated with sham exposure. The treatment was administered for 20 min per day, 5 days a week, for a period of 3 weeks. Both groups experienced a significant reduction in pain as measured on the VAS, but exposure to the magnetic field was in no way superior to sham therapy.

In a randomized, double-blind, placebo-controlled parallel study, Weintraub et al. (36) used PEMF in 225 patients with symptomatic diabetic peripheral neuropathy. A device delivering 1800 G by 6 individual magnetic sphere units (3 under each foot) was used for 2 h per day (in divided sessions of 10–30 min) over 3 months. The placebo group was treated with an inert, non-active demagnetized sham device. Outcome measures were VAS for pain, Neuropathy Pain Scale (NPS), Patient's Global Impression of Change (PGIC), VAS for sleep disruption, and electroneurography (motor and sensory). Additionally, a sub-study comprised 35 patients who underwent skin biopsies before and after PEMF treatment. The results showed no significant differences between the PEMF and the sham group with regard to the intensity of NP on the NPS or VAS for pain and sleep scores. Diabetic peripheral neuropathy symptoms were found to be slightly reduced on the PGIC, favouring the PEMF group. The data suggested neurobiological changes in epidermal innervation in the exploratory sub-study. The author concluded that PEMF at this dosage was not effective in reducing neuropathic pain.

In a further randomized, double-blind, placebo-controlled trial, Weintraub et al. (37) registered analgesic benefits of static magnetic field therapy in 375 patients with diabetic neuropathy. The treatment was applied by multipolar static magnetic shoe insoles, worn constantly for 4 months (24 h/day). The strength of the magnetic field was 450 G, measured on the surface of the insoles. The control group wore similar non-magnetized shoe insoles. The outcome measures were pain (VAS) and quality of life (exercise-induced foot pain by VAS, sleep interruption by VAS). A significant reduction in neuropathic pain (VAS) was observed. The anti-nociceptive effect was pronounced during the third and the fourth month.

The data suggest that the treatment may be used as adjunctive therapy or as monotherapy. The authors suggested a longer follow-up period for future studies.

High-frequency external muscle stimulation, high-tone external muscle stimulation and external muscle stimulation (HF/HTEMS/EMS)

Reichstein et al. (38) compared the effects of high-frequency external muscle stimulation with those of TENS in 41 patients with diabetic PN. Both lower extremities were treated for 30 min daily on 3 consecutive days. The electrodes for HF treatment were placed on the femoral muscles. Stimulation was performed using a device which generated pulse widths of ≤350 mA, ≤70 V. The initial frequency of 4.096 Hz was increased to 32.768 Hz within 3 s. The maximum frequency was used for 3 s and then down-modulated from 32.768 to 4.096 Hz. In the TENS treatment group, the electrodes were placed on the lower extremities as described above (26). The device generated a biphasic, exponentially decaying waveform with pulse widths of 4 ms, ≤35 mA and 25–35 V and 180 Hz. The intensity ranged from 20 to 30 mA. Pain, numbness, burning, paraesthesia and dysaesthesia were measured by VAS. A significant reduction in pain and non-painful symptoms were noted in the HF group compared with the TENS group. In conclusion, HF could ameliorate symptoms and pain in patients with diabetic PN and is considered to be more effective than TENS. The authors mention the short duration of the study as one of its limitations and recommend long-term investigations in the future.

Klassen et al. (39) aimed to determine whether HTEMS is effective in diabetic end-stage renal disease patients (25 patients) with symptomatic PN, and whether uraemic PN (15 patients) is similarly modulated. Fourteen patients who had received haemodialysis were enrolled. For HTEMS the electrodes were placed on the femoral muscles, and in some cases on the calves as well. The stimulation parameters were similar to those used by Reichstein et al. (38). All subjects were treated for 1 h during the haemodialysis session, 3 times a week. Twelve patients were followed for 1 month, and the others for a treatment period of 3 months. The neuropathic symptoms of pain and discomfort, as well as sleep disorders, all measured on Galer & Jensen's 10-point Neuropathic Pain Scale, were significantly improved. The response was significant in both uraemic and diabetic PN. The response rate was clearly dependent on the duration of HTEMS treatment; the best results were observed after more than 4 weeks. The greatest shortcoming of this study was the absence of a control group, as stated by the authors.

In a prospective, uncontrolled trial Humpert et al. (40) evaluated the effect of external muscle stimulation (EMS) in patients with type 2 diabetes and diabetic neuropathy. The symptoms were graded at baseline on the Neuropathy Disability Score (NDS) and the Neuropathy Symptoms Score (NSS). Ninety-two patients received EMS therapy with electrodes placed on the thighs. Stimulation was performed as described previously by Reichstein et al. (38). Eight treatments were performed (60 min, twice a week for 4 weeks). EMS was shown to be of some benefit in 40–70% of type 2 diabetes patients with reference to the Neuropathy Symptom Score (especially burning sensations and sleep disorders). The authors noted that the weakness of this study was its uncontrolled design.

Frequency-modulated electromagnetic neural stimulation (FREMS)

In a randomized, double-blind, crossover study, Bosi et al. (41) examined the effects of FREMS in 31 patients with painful diabetic neuropathy. Each patient received 2 series of 10 treatments, with each series lasting no more than 3 weeks. FREMS was performed using sequences of monophase-compensated negative potential electrical pulses, characterized by a sharp spike and an asymmetrical shape (peak amplitude variable from 0 to 255 V, pulse frequency varying from 1 to 50 Hz, pulse duration varying between 10 and 40 μs). The therapy was applied to the lower extremities via 4 electrodes. Each session lasted for 30 min. Placebo treatment consisted of no electrical current transmission. FREMS induced a significant reduction in pain (VAS), a significant increase in sensory tactile perception, a decrease in foot vibration perception threshold, and an increase in motor nerve conduction velocity for at least 4 months. The treatment was found to be safe and effective, and was able to modify some parameters of peripheral nerve function.

Summary of the result

The efficacy of different electrotherapies in patients with painful diabetic peripheral neuropathy was evaluated in these 15 studies. The authors' findings concerning the effects of TENS are consistent. Three large studies and one small study reported beneficial effects even with prolonged use over an average period of 1.7 years.

Two small studies evaluated the effect of pulsed-dose electrical stimulation by stocking electrodes. In the first study the authors found no evidence of effectiveness, while the authors of the second study reported a potential effect in patients with grossly intact protective sensation and relatively good distal vascular perfusion.

Treatment with pulsed and static electromagnetic fields was investigated in 3 large and 2 small studies. The results are conflicting. In 2 of the large studies using PEMF, no significant reduction in pain or better efficacy than placebo was registered. Anti-nociceptive effects were registered in one large study, in which the authors used static magnetic fields for 4 months in 259 patients with diabetic PN. A short-term analgesic effect was observed in the 2 small studies.

Of 3 small studies in which the effect of external muscle stimulation (high-tone, high-frequency) was investigated, potential effects were reported for symptomatic neuropathy, especially in patients with strong symptoms. In the remaining 2 studies, improvements in symptoms and pain were registered when using high-frequency and high-tone external muscle stimulation, respectively.

In one large study, FREMS caused a significant reduction in pain, a significant increase in sensory tactile perception, and enhanced motor nerve conduction velocity.

DISCUSSION

The reviewed articles present data concerning electrotherapy for the treatment of painful diabetic PN. As the results are generally poor with reference to evidence-based quality factors, it is difficult to issue recommendations for the use of the individual treatment options. The conclusions derived by the authors are diverse and the shortcomings of the studies are worthy of mention. In the large majority of studies, the follow-up investigation was performed at the end of the treatment. Further follow-up evaluations in the long term were only mentioned in studies dealing with TENS and FREMS. In nearly 50% of the reviewed articles, the study design was poor, mainly because of the lack of a control or placebo group and the absence of randomization. In particular, controls and placebo groups are needed to rule out procedure-related placebo effects and spontaneous remission of symptoms. The sample sizes of the studies were satisfactory: only 4 studies included less than 30 patients. The stimulation parameters used in the studies dealing with the same therapy modality are comparable, with the exception of PEMF. This is a well-known phenomenon in connection with PEMF. In the majority of studies, the duration of treatment was appropriate and consistent with daily routine. Understandably, the use of stockings for more than 8 h or insoles for 24 h a day was associated with a high drop-out rate and poor compliance.

TENS may be recommended for the treatment of PN. External muscle stimulation is a promising option. However, a final positive statement cannot be issued because of the poor study design and the absence of long-term follow-up. The study dealing with FREMS was well designed and reported a significant reduction in pain. Further studies will be needed to confirm these findings.

The articles concerning PEMF cannot be compared because of different study designs, varying stimulation parameters, and inconsistent findings. The studies concerning pulsed-dose electrical stimulation suffered from poor study design, small sample sizes, high drop-out rates, and short follow-up evaluations. In 13 of the 15 studies, the samples were homogenous and the inclusion criteria well described. A more specific description of the exclusion criteria may have been desirable. Clinical experience shows that patients with vertebrostenosis have similar symptoms as those with PN. Therefore, this differential diagnosis should be considered and included in the exclusion criteria. Interestingly, we found no articles describing the use of constant galvanization, which is commonly used to treat patients with PN.

Further randomized, double-blind, placebo-controlled studies with larger sample sizes and longer follow-up periods are needed. Multicentre studies would be helpful to achieve more homogenous sample sizes.

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