# Electrotherapy as an adjunct therapy in the treatment of diabetic ulcers and related complications of diabetes affecting the lower limbs

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**This article is written primarily to discuss the application of electrical stimulation as an adjunct therapy in the treatment of diabetic ulcers and related complications of diabetes affecting the lower limbs. The incidence and prevalence of diabetes and its related co-morbidities continues to grow. Ulceration and its progression through infection into amputation is no exception. Even if amputation can be avoided an unhealed ulcer remains an extremely debilitating condition. The first section considers the healing of diabetic ulcers using several different forms of electrical stimulation and identifies muscle stimulation as a principal mechanism of action in enhancing tissue perfusion and oxygenation. The second section specifically considers the use of a particular form of electrotherapy devices, which are referred to as neuromuscular electronic Stimulators in treating many of the conditions associated with diabetes affecting the lower leg. Much of this research is relatively recent and the positive clinical results achieved have, as yet, only minimally entered medical practice in the UK.**

Recent years have seen the prevalence and incidence of diabetes grow to epidemic proportions in many parts of the world. In England, the prevalence of obesity among adults rose from 14.9% to 26.9% between 1993 and 2015. The rate of increase has slowed since 2001, although the trend is still upwards (Diabetes UK, 2016a). In the UK, obesity levels have more than trebled over the past 30 years and, on current estimates, more than half the population could be obese by 2050 (Health and Social Care Information Centre, 2016).

When diabetes is of long duration and with poor glycaemic control it is usually accompanied by related comorbidities, typically neuropathy, oedema, ischaemia, and peripheral arterial disease (PAD) and, of course, ulceration.

Electrotherapy is not widely used in general medical practice in the UK, which is surprising given its strong and growing clinical trial evidence base in treating dermal wounds of all aetiology and in the absence of clinically proven alternative adjunct therapies. This paper will describe the use of electrotherapy, primarily high voltage pulsed current (HVPC) in treating diabetic ulceration. It will also examine the current evidence supporting the use of neuromuscular electronic stimulation in treating its related complications noted above.

Ulceration is estimated to occur in 10–15% of people with diabetes at least once in their lives. In a detailed piece of research undertaken in 2012 (Kerr, 2012), Marion Kerr of Insight Health Economics, states: "Around 61,000 people with diabetes are thought to have foot ulcers at any given time, approximately 2.5% of the diabetes population. Ulceration and amputation substantially reduce quality of life, and are associated with high mortality. Studies suggest that only 50% of patients with diabetes who have had an amputation survive for a further two years. Even without amputation, the prognosis is poor. Only around 56% of people with diabetes who have had ulcers survive for five years."

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### Article points

1. This paper discusses the application of electrotherapy (particularly NMES) in accelerating the healing of diabetic ulcers and to treating other complications of diabetes, particularly those which are not resolved by pharmaceutical interventions.
2. In treating the comorbities/complications of diabetes, an effective therapy will ideally act on underlying causes rather than symptoms and the clinical evidence here presented demonstrates that electrotherapy is at least as effective as the more commonly used pharmaceuticals.

### Key words

- Electrotherapy
- Neuromusclar electronic Stimulators

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**Page points**

1. The accelerating prevalence of Diabetes and its comorbidities and complications is imposing an ever-increasing burden on heath authorities.
2. Compromised circulation is a complication of diabetes and even recent onset otherwise uncomplicated diabetic ulcers heal slowly and are prone to recur.
3. Evidence suggests that NMES devices, which can improve local circulation via muscle simulation, may be an important addition to standard care in healing complex ulcers.

Kerr estimates that around 40% of ulcers fall into the 'hard to heal' category, which tend to be relatively unresponsive to conventional wound care and are largely the group that may subsequently require fairly radical surgery, which will occasionally include amputation.

In more recent data (Diabetes UK, 2016b), the number of amputations associated with diabetes in the UK now exceeds 7,000 per annum and the number of diagnosed diabetics now approaches 4 million so if the 2.5% suffering ulceration holds true then there are currently likely to be around 100,000 active ulcers at any time. In a recent report entitled "National Diabetes Report: Complications and Mortality" (NHS Digital, 2016), it is noted that approximately one fifth of all hospital admissions in the UK have complications linked to diabetes.

## Electrotheraphy and diabetic ulcers

From the Kerr paper it can be concluded that approximately 60% of diabetic ulcers will heal under conventional treatment but, in most cases, healing may take several months (Margolis et al, 2000). Of the 40% of wounds with more complex aetiology, the prospects for healing are far more uncertain since treatment on the conventional pathway may not effect a cure (Damir, 2011).

Many adjunct therapies have been considered in this application, but none have been adopted with a NICE endorsement. Electrotherapy has been considered by NICE, but the present recommendation is that it should be used with diabetic ulcers only within a clinical trial. Clinical trials of electrotherapy and dermal wounds have generally been carried out on patient cohorts of mixed ulcer aetiology and although they often include a small number of diabetic ulcers, this has usually been insufficient for a convincing stratification of results.

Lundeberg et al (1992) calculated that electrical stimulation (ES) improved the healing rate of diabetic ulcers by 33% and concluded that the principal mechanism of action is improved blood flow, which is consistent with other similar studies. Baker et al (1997) showed a nearly 60% improvement in healing rate in one of two protocols used. Peters et al (2001) used a stimulation device set at "sub-sensory " levels for continuous overnight stimulation and found that in the compliant treatment group 71% healed, whereas only 29% non-compliants in the control (placebo) group healed.

A retrospective study by Burdge et al (2009) used an HVPC device to treat a cohort of people with diabetes with a mean age of 66 years and ulcer duration of 25 weeks. Ulcers fell into the 1C, 2C, or 3D categories and patients had varying comorbidities. In total, 45 wounds were treated and 35 healed over a mean period of 14 weeks, during which time a mean of 23 treatments per patient were delivered. Follow-up at a mean of 40 weeks, revealed that 31 remained healed and two recurrencies were successfully treated with further HVPC. This study, while not a randomised controlled trial (RCT), is a valuable contribution to the literature since it demonstrates that in a limb salvage situation, this form of HVPC uses higher voltage amplitude than previous methods and causes deep-layered, fused muscle contraction, which may facilitate muscle contraction and relaxation, thereby enhancing blood flow." This is allied to the fact that "the wounds comprising this study population were complex limb salvage cases — most were ischemic and neuropathic ulcers and occurred in patients with a history of severe diabetes and previous amputation. Despite this complexity, 33 of the 45 wounds (73.3%) healed and no amputations were needed in 66.7% of patients."

The device used in this study has many similarities with the Neurocare NC2000 (Neurocare) primarily in causing full muscle contraction. The waveform, pulse width and frequency are similar, as are the on/off cycle and the 45 minute treatment episodes that are recommended.

In 2013, Kwan et al undertook a systematic review of RCTs on the use of ES in treating diabetic ulcers. They encountered a lack of homogeneity among the trials searched and, having excluded all but three trials, concluded: "The pooled estimate of the number of healed ulcers of the three studies on electrical stimulation compared to the control or sham electrical stimulation showed statistical significance in favour of electrical stimulation."

## Summary

There are few clinical studies that have evaluated ES to treat a population of ulcers solely of diabetic aetiology. However, such ulcers are frequently included in studies of ulcers of mixed aetiology where the healing rates of diabetic ulcers treated with

electrotherapy appear similar to ulcers of different aetiology. Those studies treating diabetic ulcers only show similar positive results, but a lack of homogeneity in outcome measures impedes inter study comparison. To the author's knowledge only the Burdge study has included complex later-stage diabetic ulceration.

This study appears to demonstrate the combined effect of the multiple mechanisms of action which many attribute to electrotherapy in the wound healing application. In this form of therapy the positioning of the electrodes causes the electrical signal to pass through the damaged tissue of the wound, thereby positively influencing cellular and bio-chemical activity while enhancing blood flow by inducing muscle contractions if the signal is of sufficient strength.

## Related diabetic conditions

Before continuing to consider the application of NMES in the treatment of conditions related to diabetes it may be useful to revisit the US Food and Drug Administration (FDA) indications for NMES. Those which are particularly relevant in treating the conditions described below are highlighted. The FDA indications are:

- Increase local circulation
- Muscle re-education
- Relaxation of muscle spasms
- Maintaining or increasing range of motion
- Prevention or retardation of disuse atrophy
- Immediate post-surgical stimulation of calf muscles to prevent venous thrombosis.

## Neuropathy, oedema, circulation, peripheral artery disease/claudication, and venous disease

In terms of diabetes, ulceration is but one consequence of the condition and, although

arguably potentially one of the most serious, is not of the highest incidence. Ischaemia and neuropathy, which usually pre-exist and are prime causes of ulceration are a debilitating consequence of the condition. Peripheral arterial disease and claudication are often diagnosed. Pain is also a consequence of both neuropathy and the ulcer itself, and poor lymph drainage conditions are common.

## Neuropathy

Neuropathy is a chronic condition that affects 20–50% of the diabetic population (Tesfaye and Selvarajah, 2012) The symptoms, which tend to be progressive, are pain, mainly in the feet and loss of sensitivity.

Peripheral neuropathy is largely treated by pharmaceutical interventions (prescription painkillers) which, in most patients, will only bring relief that is partial and temporary. The degree of amelioration of symptoms that painkillers bring rarely make either sleeping or ambulation pain-free events. Pharmaceutical interventions do not restore dermal sensitivity, but to be fair, do not claim to do so.

Habituation is a feature of pharmaceutical interventions and transcutaneous electrical nerve stimulation (TENS) and in order to bring about any particular degree of relief dosage tends to need to increase over time, which increases the treatment risk profile and will in some patients bring about addiction. Electrotherapy that can improve circulation may, therefore, reduce risk and be more effective as treatment for pain.

There is not an extensive body of research evidence on the use of electrotherapy in treating the pain consequences of diabetic neuropathy. TENS devices are extensively used and for many people bring some relief. However, the clinical evidence for TENS is not entirely convincing. (Crucco et al, 2007; Dubinsky and Miyasaki, 2010; Johnson et al, 2015).

In 2005, Reichstein et al compared muscle stimulation (NMES) with TENS and concluded: "This pilot study shows, for the first time, that NMES can ameliorate the discomfort and pain associated with DSP (Diabetic Symptomatic Polyneuropathy), and suggests that NMES is more effective than TENS" and that "external muscle stimulation offers a new therapeutic option for DSP".

Thakral et al, 2013 compared eight studies wherein different forms of ES were used in treating diabetic neuropathy. Four of the devices used were NMES. Most of these studies showed statistically significant improvements in dermal sensitivity and six of the eight painful neuropathy studies identified significant improvement in symptoms.

Humpert et al (2009) conducted an uncontrolled trial in which 92 diabetic patients with different neuropathic symptoms were treated for 1 month and 73% of the participants reported marked improvement. Patients in the upper tertile of symptom intensity showed significant improvement of paresthesia, pain, numbness and most pronounced for burning sensations and sleeping disturbances.

It may be that these trials with NMES are providing further evidence of the possible multiple mechanisms of action of NMES and are also illustrating that in comparing NMES with both pharmaceutical interventions and TENS that NMES in improving muscle condition and accelerating blood flow is operating at the level of underlying cause rather than symptom and may, therefore, be capable of achieving long-lasting improvements in the patient condition.

The studies cited above may have certain limitations in terms of sample sizes and longer term follow up but they demonstrate that muscle stimulation may be an effective treatment both in terms of pain management and the recovery of some degree of dermal sensitivity. It is generally accepted (though by no means clinically proven) that TENS may bring pain relief in the short term, but it is also acknowledged that TENS acts on the symptom (as do pharmaceutical interventions in pain relief), rather than the underlying cause.

In the author's experience, pain relief can be relatively permanent and a significant degree of dermal sensitivity can be recovered. However, although consistent, this evidence is not yet clinically established.

## Oedema

In treating oedema, the activation of the calf muscle pump appears to be the dominant mechanism of action (Williams et al, 2017). Neurocare advises patients to void their bladders before commencing treatment on the lower limbs since re-activating relatively dormant musculature can rapidly dislodge fluid.

Outside the UK, clinicians in many disciplines routinely use electrotherapy to treat oedema, despite

the fact that supporting clinical evidence has been sparse. However, a recent publication (Williams et al, 2017) has assembled evidence of NMES in treating venous disease and this article is reported at length below since it presents a powerful rationale for the use of NMES in these applications

Williams et al (2017) conducted an evidence review of the use of NMES in the prevention and management of venous disease and noted that all studies showed substantial improvements in venous haemodynamics with stimulation of the calf muscle pump compared to rest. In trials on patients with venous disease, 20 minutes of treatment over a 30-day period resolved evening oedema in 59.4% of cases, reduced it in 34.4%, and remained unchanged in 6.2% of cases. This resulted in a significant reduction in group average supramalleolar circumference, reduced pain score and improved quality of life.

They also noted that "one of the benefits of electrical stimulation over intermittent pneumatic compression (IPC) is that the action increases the activity of the users own muscles, as opposed to a passive compression system. An RCT of intensive care patients demonstrated an improvement in muscle strength with electrical stimulation."

They further observed that NMES may be successful in this area due to the fact that orthostatic oedema can be reversed with NMES and the calf muscle pump can be trained over time. They added: "This evidence is consistent with and supported by two further studies carried out as review articles of clinical studies which have used animal subjects."

One of the two studies mentioned was carried out in 1993 by Mendel and Fish who carried out studies on animal models with ES, mostly using HVPC and concluded that, dependant on the protocol chosen, acute oedema was curbed by HVPC.

## Peripheral arterial disease/claudication

There is as yet a limited body of clinical evidence concerning the use of NMES in treating PAD and claudication. However, that which exists is encouraging. Anderson et al (2004) concluded that "chronic transcutaneous electrical stimulation of calf muscles improves functional capacity without inducing systemic inflammation in claudicants".

In a 2007 review, de Oliveira Medieros et al concluded that electrostimulation increased the capillary bed and blood flow, while activating muscle fibre and, thus, retarded the onset of fatigue in the studied population of PAD patients. These mechanisms could possibly prevent disease progression and aided walking or provided an exercise substitute for walking and reduced the need for revascularisation and amputation, as well as improving health-related quality of life.

The conclusions from the two trials above were recently confirmed in a 2017 study by Williams et al who noted that despite the existence of established proven therapies for PAD, mortality rates were increasing and suggested that these trends could be reversed by the use of simple medical electronic devices, which did not appear to cause adverse side effects.

## Local circulation/deep vein thrombosis

One of the first clinical trials of NMES in the avoidance of DVT was that conducted by Browse and Negus (1970). The two surgeons who conducted this research noted that "though the method of stimulation that we used significantly reduced the incidence of deep vein thrombosis it did not completely abolish it". They explained that the equipment available and the means of transmitting the electrical signal to the calf muscles of the patients presented some logistical difficulties.

Since this trial there have been several more that have confirmed the effect of stimulation by NMES devices in this application (Czyrny et al, 2010: Tucker et al, 2010) and this application of NMES is currently under review by the Cochrane Collaboration (Hajibandeh et al, 2015).

## Conclusion

It is acknowledged that the almost infinite variety of electrical signals that can be developed for clinical purposes can be confusing and also that for many reasons both logistical and technical the design of clinical studies often makes the understanding of measured outcomes and subsequent inter-trial comparison technically challenging.

In the case of wound healing, the evidence supporting the use of electrical/electronic modalities has been slowly accumulating over the past 35 years. In certain medical jurisdictions (eg USA), it is now an established part of wound healing therapy. In many other applications where the therapeutic imperative is to improve muscle capability and blood circulation,

its use is rapidly expanding. RCTs have shown that the therapy is safe, inexpensive and can easily be self-administered. Most importantly, it can dramatically reduce healing and recovery timescales.

As a nation, the British are proud of the NHS in most of its achievements, but the lack of timeliness and efficiency in adopting innovation for which it is notorious (Liddell et al, 2008) undermines the patient experience of care and prevents readily achievable cost-reduction opportunities being accessed.

In considering HVPC, NMES, multiple mechanisms of action suggest multiple simultaneous treatment effects. To take diabetic foot ulceration as an example, the treatment protocol, which defines electrode placement, signal intensity and duration of each treatment episode, will affect the rate of ulcer healing and, simultaneously, relieve much of the pain associated with neuropathy, restore some measure of dermal sensitivity and reduce oedema.

NMES devices vary considerably in performance. Generally, the 'console' (ie mains-powered devices) are the most effective. The important therapeutic objective is to achieve full recruitment of local musculature in comfort. Patients thereby become compliant and active participants in their own treatment programmes and rapid improvements in their medical condition reinforces this experience.

Researchers have sometimes noted that certain electrotherapy devices that were capable of increased signal intensity were experienced as painful at higher output settings which meant that the full potential of treatment could not be realised. This is a characteristic of direct current (DC) devices where amperage varies directly with voltage and many DC devices at close to maximum output will be producing in excess of 40 milliamps. Amperage is the painful part of electrotherapy.

The Neurocare 2000 device overcomes this significant disadvantage by its alternating current (AC) output, which allows up to 300 volts to be delivered at less than 10 milliamps, thus allowing full, pain-free, muscle activation. ■


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