Eur J Vasc Endovasc Surg **31**, 300–305 (2006)
doi:10.1016/j.ejvs.2005.08.003, available online at http://www.sciencedirect.com on SCIENCE DIRECT

Haemodynamic Study Examining the Response of Venous Blood Flow to Electrical Stimulation of the Gastrocnemius Muscle in Patients with Chronic Venous Disease

M. Clarke Moloney,[1]* G.M. Lyons,[2] P. Breen,[2] P.E. Burke[1] and P.A. Grace[1]

[1]*Department of Vascular Surgery, Mid-Western Regional Hospital, and* [2]*Biomedical Electronics Laboratory, Department of Electronic and Computer Engineering, University of Limerick, Limerick, Ireland*

Objectives. *The aim of this study was to explore the option of stimulating calf muscle contraction through externally applied neuromuscular electrical stimulation (NMES) and to measure venous blood flow response to this stimulation.*
Methods. *Ten patients with class 6 chronic venous disease (CEAP clinical classification) were recruited. Measurements of peak venous velocities in the popliteal vein were recorded by Duplex scanning in response to six test conditions; 1. Standing, 2. Voluntary calf muscle contraction, 3. Standing with NMES applied, 4. Standing with compression bandaging applied to the leg, 5. Voluntary calf muscle contraction with compression bandaging applied to the leg, 6. Stationary with compression bandaging applied to the leg and NMES applied. Comfort assessment was completed using visual analogue scales at each test stage and on study completion each patient completed a short structured interview to determine comfort and acceptability of NMES.*
Statistical analyses were carried out using SPSS, Version 9. Non-parametric testing was used in all analyses using the Wilcoxon Signed Ranks Test for paired samples.
Results. *There was a significant increase in venous velocities on voluntary contraction of the calf muscle (median resting vel 7.3 cm/s; voluntary contraction median 70 cm/s) and with the introduction of NMES, both with compression (median velocity 15 cm/s,* $p=0.005$ *Wilcoxon) and without compression (median velocity 13 cm/s,* $p=0.005$ *Wilcoxon). The greatest increase with NMES was when combined with compression bandaging. All patients reported the stimulus as an acceptable treatment option with 90% reporting NMES as comfortable.*
Conclusions. *Healing rates in venous ulceration with the application of compression bandaging remain between 50 and 70%. This study shows a positive haemodynamic response to NMES. Further research is needed to quantitatively measure the effect of NMES on ulcer healing.*

Keywords: Venous ulceration; Haemodynamics; Electrical stimulation; Pain.

Introduction

Chronic venous insufficiency (CVI) of the lower limbs is frequently caused by failure of the calf muscle pump; such failure occurs secondary to valve destruction in the deep leg veins. CVI can also be caused by superficial vein reflux, or a combination of superficial and deep reflux, all of which can lead to venous hypertension resulting in leg ulceration. Compression bandaging, which is currently the mainstay treatment for venous ulcers, centres on reducing venous hypertension by applying external pressure to aid the calf muscle pump in assisting venous return. Despite the application of compression bandaging, healing rates remain disappointing at 50–70% after 12 weeks of treatment.[1] There is an obvious need to develop new treatment strategies, which might improve healing rates.

Neuromuscular electrical stimulation (NMES) refers to the application of pulses of electrical current, delivered through surface electrodes, to trigger generation of a neural action-potential-train to induce an artificial muscle contraction.[2] In a previous study we showed that NMES applied to the gastrocnemius muscle significantly increased venous blood flow through the popliteal vein of healthy volunteers with and without leg compression.[3] However, no data exist as to the efficacy of this potential treatment in patients with venous leg ulceration. The present study, therefore, was undertaken to: 1. investigate the changes in popliteal venous blood flow velocities in patients with

*Corresponding author. Mary Clarke Moloney, Department of Vascular Surgery, Mid-Western Regional Hospital, Limerick, Ireland.
E-mail address: mclarkemoloney@mwhb.ie

venous ulceration using NMES over the gastrocnemius muscle, 2. Compare the effect of NMES on venous blood flow with and without compression bandaging, 3. Assess the acceptability of NMES as a treatment option for patients with venous ulcers.

Methods

Ten patients classified as class-6 on the Clinical–Etiology–Anatomy–Pathophysiology (CEAP) classification system for chronic venous disorders consented to participate in this study. Each patient attended the hospital vascular laboratory for testing. Two round (5 cm diameter) neurostimulation hypoallergenic skin surface electrodes (PALS® Nidd Valley Medical) were applied to the back of each patient's calf and NMES was applied (Fig. 1) as described previously by us.[3]

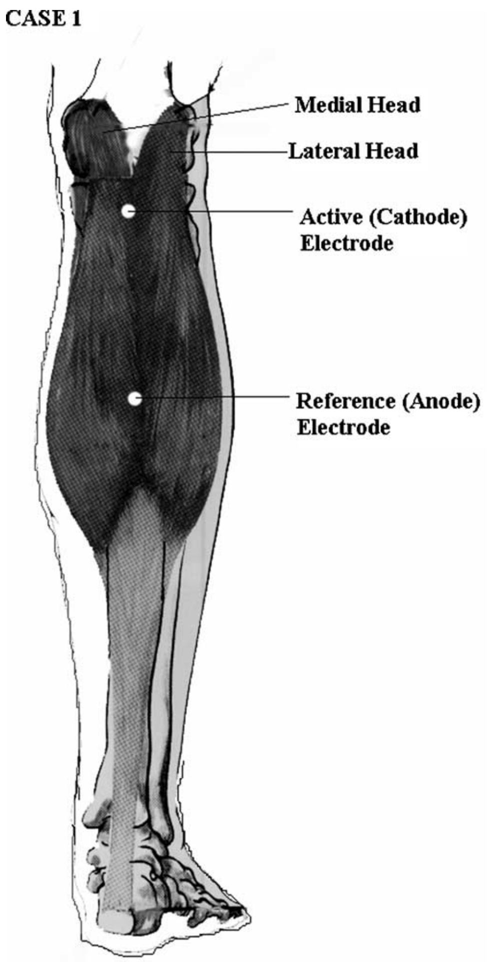

Fig. 1. Placement of the electrodes. The cathode electrode placed high on the calf, distally about 1.25 cm below the proximal end of the muscle heads and the anode electrode placed well above the Achilles tendon, towards the end of the muscle belly.

The choice of positioning of the electrodes was based on a earlier study that established the pattern of electrode positions that would produce the maximum muscle contraction in response to electrical stimulation.[3] A BMR NeuroTech NT2000™ (BMR Ltd, Galway, Ireland) muscle stimulator was used to stimulate the calf muscle. The stimulator was set to deliver a pulse duration of 300 μs, a pulse frequency of 35 Hz, a contraction time of 2 s, a relaxation time of 6 s, a ramp-up time of 0.5 s and a ramp-down time of 0.2 s; we have previously shown that these parameters produce the most efficient muscle contraction with the minimum of discomfort.[3,4]

Prior to conducting the experiment, NMES was applied for a period of 10 min to allow the subject to become accustomed to the sensation of NMES. Stimulation amplitude was gradually increased, the patient was asked to report at what level they felt the amplitude was uncomfortable (pain threshold) and at what level the discomfort became unbearable (pain tolerance level). For all test measurements, stimulus amplitude was set just below the pain threshold level for each individual patient.

Peak venous velocities in the popliteal vein were measured using Doppler ultrasound as previously described.[3] The popliteal vein was identified and measurements of peak venous velocities at each test stage were taken in triplicate with the mean score calculated. Six tests were performed in the following order:

Test 1. Standing—the patient was in the upright standing position. Venous flow velocities were measured and three peak measurements recorded.
Test 2. Voluntary contraction—the patient changed from the standing position to a 'tip-toe' position, this movement causing an exaggerated calf muscle contraction, peak velocities were recorded. This test was repeated three times and the mean velocity score calculated.
Test 3. Standing with NMES applied—the patient resumed the standing position and NMES was applied using the parameters already discussed. NMES elicited a muscle contraction and the peak velocity from each contraction was recorded, again the mean score from three contractions was calculated.
Test 4. Standing with compression bandaging—four layer compression bandaging (Profore™) was applied to the patients leg (from toe to below knee) and Test 1 was repeated.
Test 5. Voluntary contraction with compression bandaging—Test 2 was repeated with compression bandaging.

Test 6. Standing with compression bandaging and NMES applied—Test 3 was repeated with compression bandaging and NMES.

Comfort was assessed using a 100 mm, non-hatched visual analogue scale (VAS) where the patients were asked to mark the level of their pain after each test.[5,6] It was pre-defined that VAS pain scores of 30 mm or less would be categorised as mild pain, between 31 and 69 mm as moderate pain and scores of 70 mm or greater as severe pain, as categorised by Kelly (2001).[7] The minimum clinically significant difference (MCSD) in VAS scores was calculated as an increase in scores between test stages of 12 mm.[7] At the end of the study each patient completed a short structured interview during which they were asked to give a verbal categorical rating of the discomfort caused by NMES, as 'very comfortable', 'comfortable', 'bearable' or 'unbearable'.They were also asked to give a numerical rating of their discomfort using a pain scale ranging from 1 (no pain at all) to 10 (worst imaginable pain). Patients were also asked if they would consider NMES an acceptable treatment option if it were shown to promote ulcer healing.

Statistical analyses were carried out using SPSS, Version 9. Non-parametric testing was used in all analyses using the Wilcoxon Signed Ranks Test for paired samples. Results are given as medians and range. A p value of <0.05 was considered statistically significant.

Ethical approval was obtained from the Research Ethics Committees at the Mid-Western Regional Hospital, Limerick and at the University of Limerick.

Results

The median (and range) results for all tests are given in Table 1. There was no statistical difference in the median popliteal vein venous velocity when patients were standing without (Test 1) or with (Test 4) compression (7.3 *vs* 5.8 cm/s, $p>0.05$). A voluntary muscle contraction (Tests 2 and 5) showed approximately a 10-fold increase in blood flow over standing both without (70 *vs* 7.3 cm/s, $p=0.005$) and with compression (73 *vs* 5.8 cm/s, $p=0.005$).

The introduction of NMES produced a significant increase in velocities (Table 1). There was a significant 82% increase in median venous velocity when NMES was applied when patients were standing (Test 3) compared to the median velocity during standing without NMES or compression (Test 1) (13 *vs* 7.3, $p=0.005$). This increase was also significant when compression and NMES were combined (Test 6) compared to standing with compression (Test 4) (15 *vs* 5.8 cm/s, $p=0.005$). There was no statistical difference in the median velocity when NMES was applied without (Test 3) or with (Test 6) compression (13 *vs* 15 cm/s, $p=0.88$).

Visual analogue scale scores from each patient compared comfort levels without NMES and with NMES at all test stages. Baseline stationary VAS categorical scores in Test 1 without stimulation indicated mild pain in eight patients and moderate in two. When NMES was applied in Test 3 VAS categorical scores remained unchanged in nine patients with one patient reporting an increase from mild to moderate pain. This patient's increased VAS score was greater than the MCSD with a reported increase of 33 mm. (Table 2 for individual VAS scores). Baseline scores in Test 4 (stationary with compression) reported mild pain in eight patients, moderate in two. When NMES was applied (Test 6) pain increased in two patients from mild to moderate (Table 2). MCSD in VAS scores between Tests 4 and 6 was recorded in two patients with increased scores of 25 and 38 mm (Table 3). The numerical pain score at the end of the study period showed a mean score of 2.3 (SD 1.3). Two patients reported the use of NMES as 'very comfortable', seven as 'comfortable', and one as 'bearable'. All 10 patients stated that they would find NMES acceptable as a treatment.

Table 1. Median score (and range) for peak venous velocities at each test stage

Test	Median (range) peak venous velocity (cm/s) in the popliteal vein
Stationary	7.3 (4.0–15)
Voluntary contraction	70* (29–206)
Stationary with NMES	13† (9.4–27)
Stationary with compression	5.8 (3.0–14)
Voluntary contraction with compression	73‡ (27–213)
NMES and compression	15§ (7.2–49)

* $p<0.005$.
† $p<0.005$ *vs* Test 1, stationary (Wilcoxon).
‡ $p<0.005$.
§ $p<0.005$ *vs* Test 4, stationary with compression (Wilcoxon).

Table 2. VAS scores, pain category and the difference in scores between Test 1 (standing) and Test 3 (standing with NMES applied)

Patient No.	VAS scores (mm) Test 1	Pain category	VAS scores (mm) Test 3 (NMES)	Pain category	Difference in VAS scores (mm)
1	20	Mild	20	Mild	0
2	10	Mild	15	Mild	5
3	33	Moderate	40	Moderate	7
4	15	Mild	20	Mild	5
5	3	Mild	4	Mild	1
6	4	Mild	9	Mild	5
7	10	Mild	21	Mild	11
8	45	Moderate	45	Moderate	0
9	3	Mild	5	Mild	2
10	30	Mild	63	Moderate	33 (>MCSD)

No compression applied.

Discussion

In this study we have shown that the application of NMES to the gastrocnemius muscle significantly increases standing popliteal venous blood flow in patients with venous ulceration. However, this increase was only one tenth the increase induced by a voluntary contraction of the calf muscles. Compression had no significant impact on venous blood flow and 90% of our patients found NMES comfortable; all considered it acceptable as a potential treatment for venous ulcers.

The significant finding from this study is the increase in venous velocities produced by the application of NMES; 82% without compression (Test 3) and 155% with compression (Test 6) compared to baseline stationary results (Tests 1 and 4, respectively). Although we did not measure venous pressure directly in our study, we speculate that NMES by increasing popliteal venous blood flow may reduce venous hypertension in patients with venous ulceration. Treatment with NMES might be of greatest value in immobile or reduced mobility patients with venous ulceration who do not use their calf muscle pump optimally. As increased blood flow velocities of 82–155% can be elicited using NMES while patients are immobile, NMES may thus be used to artificially increase the levels of calf muscle activity towards normal to improve venous return and reduce venous pressure.

In our study, very large increases in blood flow velocities were achieved during voluntary calf contraction as seen in Tests 2 and 5. We believe that these results reflect the inseparable and very important link between the ankle joint and the calf muscle pump. These test stages (2 and 5) involved a heel lift motion resulting in exaggerated planter flexion and maximum voluntary calf muscle contraction. The results emphasis the importance of ankle exercises which assist contraction of the calf muscle thereby accelerating venous return. The blood flow velocities generated from voluntary calf muscle contraction seen in Tests 2 and 5, could not practically be artificially generated by NMES; multi-site stimulation would be required to selectively stimulate both the soleus and gastrocnemius muscles and the stimulation intensity levels required to generate such a contraction using surface NMES would be uncomfortable for the patient.

The importance of ankle movement in promoting venous flow has been identified in this and other studies,[8,9] however, ankle arthropathy due either to venous hypertension or other medical conditions such

Table 3. VAS scores, pain category and the difference in scores between Test 4 (standing with compression) and Test 6 (standing with compression and NMES applied)

Patient No.	VAS scores (mm) Test 4	Pain category	VAS scores (mm) Test 6 (NMES)	Pain category	Difference in VAS scores (mm)
1	20	Mild	20	Mild	0
2	10	Mild	15	Mild	5
3	29	Mild	40	Moderate	11
4	10	Mild	35	Moderate	25 (>MCSD)
5	2	Mild	5	Mild	3
6	10	Mild	16	Mild	6
7	20	Mild	26	Mild	6
8	45	Moderate	45	Moderate	0
9	8	Mild	10	Mild	2
10	31	Moderate	69	Moderate	38 (>MCSD)

as arthritis may result in reduced range of ankle mobility in a number of patients, thereby reducing the effect ankle joint movements may have in promoting venous return. Dix *et al.* (2003)[10] investigated the relationship between clinical severity of venous disease, calf muscle pump dysfunction and range of ankle movements. Dix's observed a reduced range of ankle movements in patients with primary varicose veins, which was inversely proportional to the severity of venous disease. He concluded that calf muscle pump dysfunction is associated with reduced range of ankle movements. In addition, reduced ankle mobility has been shown to be a risk factor for slow rates of ulcer healing.[11] Barwell *et al.* (2001)[11] reported only 13% of chronic venous ulcers healed in patients with less than 35° ankle mobility after 24 weeks of treatment, compared to 60% healed in patients with greater than 35° of mobility. NMES may prove a useful adjunct in the treatment of those patients with reduced range of ankle movements. It is our opinion that NMES is capable of producing calf muscle contractions without the action of the ankle joint and, therefore, may help to compensate for the reduced effectiveness of the ankle joint by generating artificial calf muscle contractions.

The findings from this study indicate the potential benefit of using NMES to improve venous return. However, there was no significant difference in venous velocities with the introduction of compression in Tests 4–6. This is surprising, as one may reasonably expect greater velocities in a limb when compression has been applied. In our earlier study which looked at the response of healthy subjects to NMES, we noted significantly increased velocities when compression hosiery was applied in conjunction to NMES.[3] However, the previous study differs from this study in that its subjects were very fit healthy young adults with no evidence of venous disease. A possible explanation for the lack of venous velocity increase with compression in the current study is that all patients had chronic venous disease and compression was applied after the patient had participated in voluntary muscle contractions (Test 2) and NMES induced muscle contractions (Test 3). Thus, the volume of pooled blood available to respond to a contraction would have been reduced and random sequencing of tests might have been preferable.

Surface NMES has many existing uses in medicine, however, discomfort has been identified as a factor which limits its use.[12] Surface NMES involves stimulation of neuromuscular structures, which inadvertently results in activation of sensory receptors on the skin surface. This acute sensory excitation can cause discomfort. To minimise discomfort the stimulation parameters chosen for this study were previously shown to be most effective and cause least discomfort.[3,13,14] The results from the various pain assessment tools used indicated that most patients found NMES comfortable with minimal increase in pain scores with the application of NMES, indicating that the parameters chosen may be appropriate for this population group.

Conclusion

The results from this study show a beneficial haemodynamic response to NMES. NMES may prove useful in the treatment of patients with venous ulceration who have reduced mobility or reduced ankle range of movements. NMES was perceived by all trial patients to be an acceptable treatment for venous ulcers, which did not cause extra discomfort. However, this study did not apply NMES at a therapeutic level and greater research needs to be carried out to investigate the effect of NMES on healing rates compared to current best practise.

Acknowledgements

The authors wish to thank the vascular laboratory team, Limerick Regional Hospital, especially Marian Frawley and Fiona Liddy for performing the Doppler untrasound investigations. We would also like to thank Ms Jean Saunders, Manager of the Statistical consulting Unit, University of Limerick for providing statistical advice on this study.

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Accepted 2 August 2005
Available online 20 October 2005