Prevention of diabetic foot using low frequency magnetotherapy

Cecilia Y Webb, Sunny SL Lo, John H Evans

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1 This pilot study explored the potential for incorporation of magnetotherapy (MT) into care programmes for people with diabetic feet.

2 Twenty-six people with type 2 diabetes, foot ischaemia and an ABI <0.85 took part in the study.

3 Systemic blood pressure, Doppler frequency change and transcutaneous partial pressure of oxygen were measured before, during and after MT treatment.

4 After a 30-minute exposure of the diabetic foot to MT the microcirculation in the dorsum of the foot increased, as reflected by higher transcutaneous partial pressure of oxygen measurements.

KEY WORDS

- **Magnetotherapy**
- **Diabetic neuropathy**
- **Ischaemic foot**
- **Pulsed electromagnetic fields**

Cecilia Webb is Associate Professor from the Department of Rehabilitation Sciences, the Hong Kong Polytechnic University; Sunny Lo is a Physiotherapist I from the Physiotherapy Department, Kwong Wah Hospital, Hong Kong; John Evans is Director of the Centre for Rehabilitation Science and Engineering, Queensland University of Technology Australia.

Introduction

People with type 2 diabetes should be educated to address ischaemic foot problems before and as they arise, with interventions aimed at reducing the discomfort and the psychosocial impact and disability caused. This article discusses a pilot study that was undertaken to explore the possibility of incorporating magnetotherapy into prophylactic programmes for patients with diabetic feet. Magnetotherapy was found to improve local circulation and oxygenation in ischaemic feet of participants with type 2 diabetes.

Type 2 diabetes is associated with maturity-onset diminished insulin secretion by the pancreatic beta cells and/or cellular insulin resistance. Its high prevalence in many countries is causing increasing concern.

Nearly 17 million people in the US have type 2 diabetes (American Diabetes Association website, 2003). In 1997, Currie and Peters estimated that 5% of the UK population had diabetes, and 2.4 million people are now estimated to have diabetes (Diabetes UK website, 2003). The number of people with type 2 diabetes in the UK is set to double by 2010. Even mainland China's 3.63% age-adjusted prevalence of diabetes among adults (Pan et al, 1996) is predicted to rise sharply as the result of westernisation of lifestyles (Nash, 2001). Research has also shown that there is a high prevalence of type 2 diabetes in Chinese people living outside China. In Hong Kong, demand for healthcare resources by people with type 2 diabetes (estimated at 7.7% of the population) has increased, with nearly 33% of prescriptions issued from government-funded primary healthcare units and hospital medical clinics containing antidiabetic drugs (Chan and Cockram, 1997).

Cox and Gonder-Frederick (1992) have highlighted the significance of applying interventions that may minimise the psychosocial issues associated with the complications of diabetes. With this in mind, we decided to carry out a pilot study focusing on the use of magnetotherapy (MT) to treat people with type 2 diabetes who are at risk of wound complications from minor trauma to their feet.

People in this group often have distal polyneuropathy, psychomotor slowing, impaired tactile, thermal and pain sensation, autonomic nerve dysfunction, increased arteriovenous shunting, decreased local arterial blood flow, microangiopathy, decreased sweating and tissue hypoxia in their feet (Flynn and Tooke, 1995). These problems, along with peripheral vascular disease (PVD) and cutaneous ischaemia, are associated with the risk of developing slow-healing or even non-healing wounds (Nelzen et al, 1997).

McKenna (1991) found PVD present in 67% of the ulcerated legs in the study. Research has shown that the relative risk of total mortality for a person with an ankle-brachial index (ABI) of <0.85 was 2.36 (95% confidence interval 1.6–3.48) when the average periwound higher mean transcutaneous partial pressure of oxygen ($TcPO_2$) was <25 mm Hg (Kalani et al, 1999). A $TcPO_2$ study of diabetic feet recommended that measures to prevent breakdown of the skin of the feet should be adopted (Boyko et al, 1999).

Aims

Interventions for reducing discomfort, disability and psychosocial impact on patients and families in the management of diabetic neuropathic feet should preferably

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1 Prevention is better than cure, so it would be of substantial relevance to prophylactic care if MT was effective in reducing dermal damage and diabetic foot complications.

2 Low frequency, pulsed MT stimulation induces local electrical fields with biological effects similar to those produced normally during dynamic mechanical deformation of connective tissues.

3 Pulsed MT may induce non-thermal physiological effects that enhance local skin circulation, reduce tissue hypoxia and provide relief of pain caused by the accumulation of metabolites in healthy people.

4 Participants aged 40 years or above and confirmed as having type 2 diabetes were recruited from a diabetic foot clinic of a multispecialty hospital.

5 Participants had to be medically stable with ischaemia of the feet, concomitant peripheral arterial diseases, an ABI <0.85 in the specified lower limb and the ability to understand simple instructions.

be preventive. This study aimed to explore the potential for incorporating low frequency pulsed MT/pulsed electromagnetic fields (PEMF) in prophylactic self-care programmes to improve peripheral circulation without heating the tissues. As ischaemic feet are associated with skin insensitivity, any thermal effect from conventional therapeutic heat modalities is contraindicated.

While studies on the treatment of diabetic foot ulcers are frequently undertaken, there is a dearth of reports in English on the non-heating effect of pulsed MT on the diabetic foot. Research has shown that pulsed MT accelerates soft tissue repair (Stiller et al, 1992; Salzberg et al, 1995; Kenkre, 1996; Lee et al, 1997). The mechanisms by which MT induce the observed biological effects must be further investigated.

Since prevention is better than cure, it would be of substantial relevance to prophylactic care if MT was effective in reducing dermal damage and diabetic foot complications. Also, the simplicity of administering MT would help to reduce the high socioeconomic and treatment costs of managing the diabetic foot (Ng et al, 2001).

Low frequency, pulsed MT/PEMF

Low frequency, pulsed MT stimulation induces local electrical fields with biological effects similar to those produced normally during dynamic mechanical deformation of connective tissues (Stiller et al, 1992; Basset, 1993). Research into the effects of pulsed MT on injured soft tissues has demonstrated positive anti-inflammatory effects such as a decrease in pain and swelling (Navratil et al, 1993), enhanced healing of venous leg ulcers under double-blind conditions (Stiller et al, 1992) and accelerated union in bone healing without adverse effects (Bassett, 1993).

Lau (1987) found that low frequency pulsed MT induced physiological effects including enhancement of local dermal circulation, reduction in tissue hypoxia, and relief of pain caused by the accumulation of metabolites in healthy people. The effect is not thermal as any temperature rise (0.0001 °C) in local tissues is negligible (Walleczek, 1995). Since MT has the potential to improve the peripheral circulation of people with diabetic neuropathy, studies to explore this further, and to examine the effect of MT in anti-inflammatory, ulcer and wound healing advancement in people with type 2 diabetes, are indicated.

MT at 5 x 10^{-4} Tesla, pulsed at 12 Hz for 10 minutes, resulted in 60% of the normal healthy participants' blood flow increasing by 200–400%. There was also a one- to four-fold increase in $TcPO_2$. This suggests that pulsed MT induced non-thermal physiological effects, enhancing local skin circulation, reducing tissue hypoxia and providing relief of pain from the accumulation of metabolites in healthy participants (Lau, 1987).

Hypotheses

The vital determinants that we hypothesised would be augmented following the administration of low frequency pulsed MT were blood flow in the dorsalis pedis artery, and $TcPO_2$ in the dorsal foot. Our hypotheses were that, compared with people receiving sham-MT, people with type 2 diabetes, foot ischaemia and an ABI <0.85 who received low frequency, pulsed MT would exhibit:

- A higher mean change in Doppler frequency (velocity of blood flow) in the dorsalis pedis artery
- A higher mean $TcPO_2$ in the dorsal foot.

Method

Following ethical approval from the relevant medical research committees, suitable participants aged 40 years or above and confirmed as having type 2 diabetes were recruited from a diabetic foot clinic of a multispecialty hospital. Participants had to be medically stable with ischaemia of the feet, concomitant peripheral arterial diseases, an ABI <0.85 in the specified lower limb, and the ability to understand simple instructions.

People were excluded if they had:

- Poor control of their medical conditions (e.g. poorly controlled diabetes, hypertension, heart disease, thrombo-embolism, cerebrovascular accidents, severe pulmonary problems that lead to varying oxygen perfusion of the foot).
- ABI of ≤0.4

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1 Due to a lack of resources for double-blinding, every effort was made to eliminate operator bias in the single-blind trial.

2 Participants were covered by a blanket and wore dark glasses to eliminate possible Hawthorne effects.

3 After 15 minutes rest, baseline values of systemic blood pressure, Doppler blood flow in the dorsalis pedis artery, and transcutaneous oxygen perfusion of the dorsal foot were recorded.

4 The dependent variables were: systemic blood pressure measured by a sphygmomanometer; mean Doppler frequency change (KHz); and $TcPO_2$.

- Metatarsal level amputations
- Severe dementia
- Recent deep X-ray therapy and X-ray and short-wave diathermy
- Previous exposure to low frequency pulsed MT.

A 50% effect size was conservatively selected as the participants in the study would be older and physiologically poorer than the healthy young subjects in Lau's (1987) study, in which an effect size of 400% in peripheral blood flow (PBF) and 200% in $TcPO_2$ were observed. Any treatment effect on PBF and $TcPO_2$ seen in our study would not be as large as that observed in Lau's study.

Measurements were taken at five time points using repeated measures ANOVA as the main analytical method. The sample size required was calculated as 10 participants per group. However, 26 participants were recruited. As this was a preliminary study, the two groups were not matched for gender and age..

The instruments were calibrated before each patient trial. The pulsed magnetic field (5×10^{-4} Tesla [5 Gauss] at 12 Hz) magneto-pulse (Magnetopulse International, Australia) was calibrated using a standard axial search coil (Griffin, XKC-660-W and XKC-680-Y). Calibration of the Doppler 8 MHz probe (HNE Diagnostics) for determining ABI was carried out (McNeely et al, 1995). Cutaneous perfusion was measured on the dorsal foot by the $TcPO_2$ monitor. $TcPO_2$ was determined using a Clarke's electrode oximeter (heated to 44°C). Its $TcPO_2$ measurement is directly proportional to arterial oxygen tension (PaO_2) and calibration of the cutaneous PO_2 monitor was as described (Gilbey et al,1989).

Owing to a lack of resources for double-blinding, every effort was made to eliminate operator bias in the single-blind trial. Before testing, each participant rested on a plinth for 15 minutes in a dedicated, quiet room under controlled temperature (22–25°C) and humidity (50–70%). The foot to be tested was thoroughly cleansed and placed inside a specially designed, cushioned brace. The participant lay supine, as extreme flexion of the hip and knee would result in a decrease in arterial flow of the ankle. A blanket covered the participant,

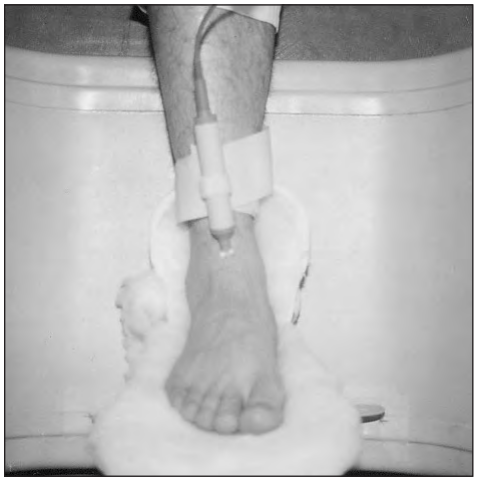

Figure 1. The position of the foot during MT treatment. The Doppler probe is fastened over the dorsalis pedis artery.

who wore dark glasses to eliminate possible Hawthorne effects (psychological effects caused by participants observing the treatment taking place, which affect the parameters being measured). The procedure was re-explained to ensure full compliance. Magnetic shielding from the $TcPO_2$ and Doppler ultrasonic probes was applied to eliminate any noise from the MT unit. See *Figure 1* for the standardised position of the foot during treatment.

After 15 minutes rest, the baseline values of systemic blood pressure, Doppler blood flow in the dorsalis pedis artery, and transcutaneous oxygen perfusion of the dorsal foot were recorded. Systemic blood pressure was recorded pre-test and post-test (at the last post-intervention data collection time). The treatment group received MT stimulation of 5×10^{-4} Tesla at a low frequency of 12 Hz, for an application time of 30 minutes (parameters similar to those used by Lau, 1987). The dependent variables were:

- Systemic blood pressure (mmHg) measured by sphygmomanometer
- Mean Doppler frequency change (kHz); the shift in Doppler frequency would be directly proportional to the velocity of blood flow (ms^{-1})
- $TcPO_2$ (mmHg).

Four pre-intervention measurements were taken from 15, 10, 5 and 0 minutes before the treatment commenced. Participants were blind to the allocation of treatment or control group; the sound emitted at the start of the treatment was engineered to be identical for both groups.

Measurements were recorded at 5-minute intervals from the commencement of MT (at 5, 10, 15, 20, 25 and 30 minutes). Recording was continued for another 20 minutes after MT treatment, giving four sets of post-intervention data (35, 40, 45 and 50 minutes). A total of 14 measurements were therefore made. For each set, mean Doppler frequency change (kHz) and $TcPO_2$ (mmHg) were recorded within a 1-minute period, following the same sequence each time.

A total of 26 patients (11 male, 15 female) were studied. The age range was 53–80 years and the mean age was 72.23 years. Random allocation resulted in 14 participants (aged 72.64 ± 4.11 years) receiving MT (treatment group) and 12 participants (aged 71.75 ± 8.65 years) receiving sham-MT (control group).

Measurements were taken from the right foot of 12 patients and the left foot of 14 patients. Baseline demographic differences between the two groups were compared using appropriate independent t-tests and chi-square tests, but were not significant. The mean duration of diabetes since diagnosis among participants was 7 years (treatment group 7.14 ± 5.27 years; control group 6.58 ± 3.26 years). Seven patients smoked and eight reported that they drank alcohol.

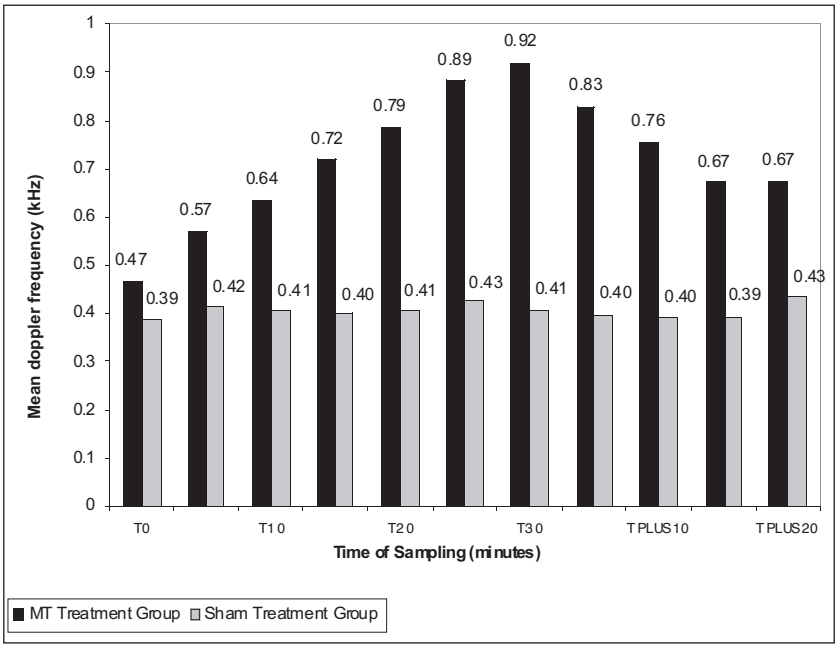

Figure 2. Time trends in mean Doppler frequency (blood flow) data from initiation of treatment through to 20 minutes post-intervention.

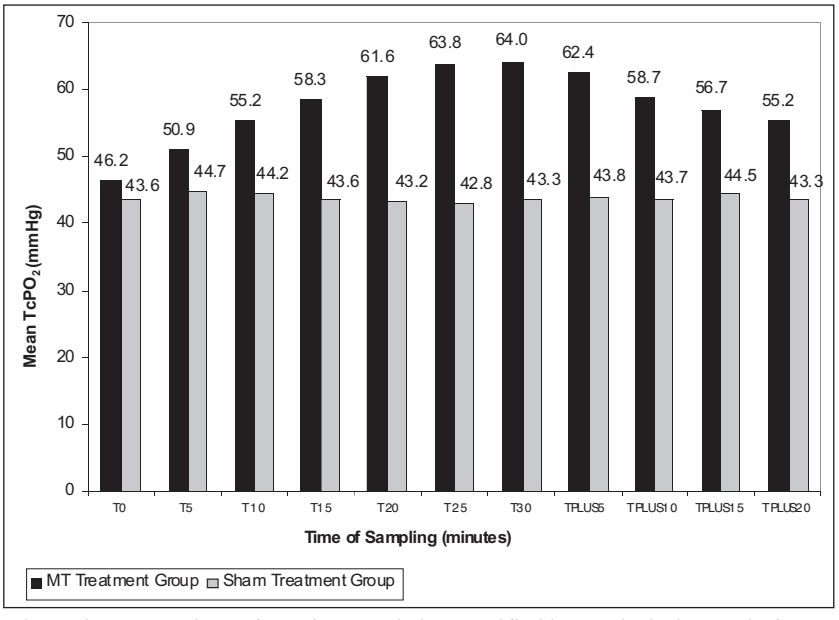

Figure 3. Mean values of $TcPO_2$ recorded at specified intervals during and after treatment.

Results

No significant differences in baseline characteristics were found between the treatment and control groups. Repeat measures ANOVA (RmANOVA) were used to compare the differences between the four data sets recorded before MT commenced, for intragroup and intergroup comparisons. There were no significant differences between measurement times of $TcPO_2$ data ($P = 0.469$) and PBF data ($P = 0.177$). There were no interaction effects when considering group effects (treatment and control group).

Figures 2 and *3* show the mean values of the two dependent variables from the beginning of treatment until 20 minutes after completion.

Both variables increased after the start of treatment in the treatment group. Values gradually increased from the start of treatment (0 minutes) to the end of treatment (30 minutes) and decreased at a similar rate until the end of data collection (50 minutes). The mean values of Doppler frequency (PBF) increased from 0.47 kHz at commencement of MT to 0.92 kHz at 30 minutes (highest or peak increment was 97%). Doppler frequency then decreased to 0.67 kHz at 50 minutes, giving a net increase of 44%. The mean values of $TcPO_2$ increased from 46.21 mmHg at commencement of MT to 64 mmHg at 30 minutes (peak increment of 38.5%). $TcPO_2$ then gradually decreased to 55.21 mmHg at 50 minutes (a net increase of 19.5%). No significant changes in Doppler frequency or

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1 There were statistically significant differences in peripheral blood flow and $TcPO_2$ compared from baseline to the 30th minute.

2 Our results supported the hypotheses that both dorsalis pedis artery blood flow and transcutaneous oxygen tension increased significantly when low frequency, low intensity pulsed MT was applied.

3 Further studies are needed to determine the time required for the parameters to reach a steady level following MT.

4 Any relationship between the effect of MT and the release of endothelium-derived nitric oxide, an important intermediary in the relaxation of endothelial cells, has not been confirmed.

5 A determined excitation frequency could be specific or almost specific for each ion flux rate through the membrane.

$TcPO_2$ were observed in the control group.

RmANOVA was used to examine the hypotheses. Levene's tests of equality of variance-covariance matrix and Box's m-test were performed. For $TcPO_2$ and PBF data there were no significant differences in the variances in the respective times of sampling. The assumption of homogeneity of variances was met. Box's m-test for equality of dispersion revealed significant differences with $P = 0.001$ for $TcPO_2$ and $P = 0.027$ for PBF, suggesting that there were differences between group values, the treatment and control groups. The compound symmetry assumption was met when Mauchly's test was carried out. Analysis showed $P = 0.152$ for $TcPO_2$ and $P = 0.388$ for PBF. The results did not reject the hypothesis that correlation and variances across time were significantly different. Tests of within-participants effects revealed significant changes between the three times of sampling, with $P = 0.000$ for $TcPO_2$ and $P = 0.000$ for Doppler. Between-groups effects were significant, with $P = 0.000$ for $TcPO_2$ and $P = 0.000$ for Doppler.

As there significant differences were found across the times of sampling, paired t-tests were used to ascertain which pair(s) of values was significantly different. Thus, significant differences between baseline and peak values were found. Also by means of t-tests, persistence of effect was determined by comparing each parameter measured at the start of treatment with that recorded at the final time of data collection. Due to the multiple comparisons, significance was adjusted to the more stringentlevel of $P = 0.01$.

There were statistically significant differences in PBF and $TcPO_2$ compared between baseline values and values obtained at the end of the 30th minute (PBF $P = 0.000$; $TcPO_2$ $P = 0.000$). There were also statistically significant differences between baseline values and values obtained at the end of data collection (PBF $P = 0.000$; $TcPO_2$ $P = 0.001$).

From the t-values collected at the respective measurement times, the difference from baseline to 30th minute was larger than from baseline to the end of data collection for the PBF and the $TcPO_2$ data. These data correspond to a net increase of 44% for PBF and 19.5% for $TcPO_2$.

Discussion

Our results support the hypotheses that both the dorsalis pedis artery blood flow and transcutaneous oxygen tension increased significantly when low frequency, low intensity pulsed MT was applied. Values increased continuously until the end of MT treatment but did not reach a steady value. The data showed that the values of the measured variables gradually declined over the post-treatment period. As participants' available time was a limiting factor, the period of treatment could not be extended to investigate when the highest possible values for $TcPO_2$ and PBF would be reached.

Further studies are needed to determine the time required for the parameters to reach a steady level following MT. Persistence of these effects and any consequent reduction in ischaemic pain and means of reducing the socioeconomic impact deserve investigation.

It is important that variable measurements are recorded using highly accurate instruments and that exclusion criteria are stringent to avoid difficulties in interpretation of the data. None of the participants in this study had venous circulation problems or other venous disorders because of the limitations of $TcPO_2$ measurements on people with such problems.

However, it has been suggested that MT may modify the control in intracellular concentration of calcium ions, modulate blood flow via calcium ion channels and may modify nitric oxide biosynthesis which stimulates various calcium ion channels, bringing about vascular smooth muscle contraction (Bkaily, 1994). Any relationship between the effect of MT and the release of endothelium-derived nitric oxide, an important intermediary in the relaxation of endothelial cells (Christopherson and Bredt, 1997) has not been confirmed.

The activity of Na^+/K^+-ATPase is reduced in diabetic nerve, muscle and blood vessels (Greene et al, 1987) Endothelium normally has a stimulatory action on Na^+/K^+-ATPase in the blood vessel wall, and impaired endothelial cell function may explain the reduced activity in people with diabetes. A determined excitation frequency could be specific or almost specific for each ion flux rate through the membrane (Tenforde, 1987).

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1 The question of possible harm induced by clinically used parameters of MT should be addressed in future studies.

2 Improvement in local circulation may decrease the symptoms of ischaemic syndromes.

3 Psychosocial problems arising from the care of complications of the ischaemic feet of people with type 2 diabetes could be minimised by preventing the soft tissue condition of the diabetic foot from deteriorating.

4 Measurements of quality of life and self-care skills in protecting the neuropathic diabetic foot should be included in future studies.

Warnke (1983) claimed that low intensity MT stimulation at 15 mT could induce a reduction in sympathetic tone. This was thought to be related to the synaptic and post-synaptic gaps of the sympathetic neurons having large time constants that would allow the induced alternating eddy currents of 5–25 Hz pulsed MT to effect hyperpolarisation at their synapses. It is thus believed that the effect of alternating magnetic fields is one of a balance between the frequency of action potential of the sympathetic neuron and the hyperpolarisation by the eddy currents induced.

Another possible mechanism for this non-thermal magnetic field is the generation of reactive nitrogen intermediates and the physiological form, free radical nitric oxide, which is recognised as an endogenous modulator of microvascular permeability (McNeely, 1995).

Most of the participants in our study were over 65 years of age. We found that the increase in $TcPO_2$ ranged from 10.5% to 58% above the baseline values observed in the younger, healthy subjects in Lau's (1987) study (up to a four-fold increase in $TcPO_2$ above the baseline values). The time taken to reach the highest recorded value was also different. This may be due to differences in tissue physiology and/or pathophysiology between healthy adults and people with diabetes and the mechanism by which low frequency, low intensity pulsed MT stimulates tissues to produce the hypothesised physiological responses. Even though the therapeutic application of pulsed magnetic fields in accelerating the healing of wounds, bones and other conditions is commonly documented, the question of possible harm induced by clinically used parameters of MT needs to be addressed. As a therapeutic modality, MT induces electrical fields only in the stimulated tissues and its energy is considered too weak to cause thermal effects or to disintegrate chemical bonds in the treated tissues (Stiller et al, 1992).

MT is postulated to promote local peripheral circulation without raising interstitial temperature (Walleczek, 1995) and eliminates or minimises the risk of burn in patients with reduced thermal sensation. Ambulatory, elderly people with good mental health, who are able to manage most self-care skills can be taught to self-administer MT. It can be speculated that improvement in local circulation by MT may decrease the symptoms of ischaemic syndromes.

However, it is known that multiple factors affect the health of patients with diabetes. The condition of ischaemic foot syndromes and, even more important, prevention of peripheral vascular disease could be favourably influenced by optimum control of blood glucose, hypertension, cholesterol-lowering drugs, appropriate diet and exercise, non-smoking, prevention of trauma and dermal damage to insensitive lower extremities. Psychosocial problems arising from the care of complications of the ischaemic feet of people with type 2 diabetes could be minimised (Delamater et al, 2001) by preventing the condition of the soft tissue of the diabetic foot from deteriorating.

However, before advocating the application of MT to the diabetic foot, it is essential to carry out further large-scale studies. Double-blind, cross-over studies on large numbers of people from different backgrounds are needed. One of the limitations of our study was the non-matching of the participants. This should be addressed in future studies as the age of patients and duration of diabetes are likely to have confounding effects on vascular changes and tissue damage in the diabetic foot.

The complex clinical presentation of people with type 2 diabetes means that the exclusion criteria must also be considered carefully. For example, the ABI criteria employed in this study excluded a number of potential participants, but ABI measurement can be fraught with difficulty in patients with diabetes, because of false high readings. Furthermore, although ABI as an indicator of macrovascular function is an important measurement to include in future studies, more stringent recording of the microvascular function is essential as it influences a host of activities of the soft tissue repair cells (Webb et al, 1998).

Repeated MT dosages or a course of treatment for testing the duration of its effects should be investigated. Measurements of quality of life (Gulliford and Mahabir, 2001) and self-care skills in

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1 The time taken to develop peak peripheral blood flow and duration of the overall effect need to be determined. Guidelines can then be developed so that MT can become an effective treatment modality and incorporated into prophylactic care programmes.

2 To exclude researcher bias, further controlled studies involving a course or repeated treatments, using a double-blind, cross-over design, must be undertaken.

protecting the neuropathic diabetic foot should also be included.

Conclusions

This pilot study found that after a single 30-minute exposure of the diabetic foot with ABI <0.85 to MT of 12 Hz (5×10^{-4} Tesla), there was an increase in the microcirculation in the dorsum of the foot, as reflected by higher $TcPO_2$ measurements. The time taken to develop peak PBF and duration of the overall effect needs to be determined. Guidelines can then be developed so that MT can become an effective treatment modality and be incorporated into prophylactic care programmes. To exclude researcher bias, further controlled studies must involve a course or repeated treatments using a double-blind, cross-over design. Quality of life measurements should also be included.■

ACKNOWLEDGMENTS: *The investigators are grateful to the patients who volunteered for the study and the following people, who have helped to make this study possible: Dr WC Wong, Ms YC Ho, Mr J Carnett, Mr KT Wong and Mr L Fung of Kwong Wah Hospital, and Dr K Kwong of the Hong Kong Polytechnic University.*

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