

Restoring lower limb blood flow improves conduction velocity in diabetic patients

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Summary Human diabetic peripheral neuropathy is believed to have, at least in part, a microvascular basis. This study was designed to examine the effects of restoration of arterial blood supply on peripheral nerve function in six non-insulin-dependent diabetic patients with peripheral occlusive vascular disease. In the revascularised legs, transcutaneous oxygen increased from a median 37.5 (28.5–45.7 interquartile range) mmHg to 55.5 (53.5–62.5) mmHg, $p = 0.036$, mean increase 20.2 (14.8–25.6, 95 % confidence intervals(CI)) mmHg. This was accompanied by a significant improvement in peroneal motor nerve conduction velocity from 31.7 (26.5–36.3) m/s to 33.5 (32.9–

39.4) m/s, $p = 0.04$, mean increase 4.7 (1.7–7.7, 95 % CI) m/s. There was no significant change in transcutaneous oxygen or peroneal nerve motor conduction velocity in the contralateral control limbs. This improvement in conduction velocity with improved tissue oxygenation suggests that studies of agents which might indirectly bring about improvements in microvascular blood flow should be urgently considered. [Diabetologia (1995) 38: 1051–1054]

Key words Peripheral neuropathy, peripheral vascular disease.

Evidence that microvascular disease is implicated in the pathogenesis of diabetic peripheral neuropathy can be drawn from histopathological and physiological studies in animals and humans [1]. Observations of the effects of proximal arterio-venous shunts on nerve function in the distal limb have suggested that a reduction in macrovascular blood flow can result in peripheral nerve dysfunction in non-diabetic subjects [2–4]. A recent study demonstrated that peripheral nerve function was inversely correlated to transcutaneous oxygenation in diabetic patients [5]. This is in keeping with experimental work which shows reduced endoneurial oxygenation [6], impaired nerve blood flow and increased arterio-venous shunting

[7], and laser Doppler flux in the nerves of animals and humans [8], and the clinical observation of reduced nerve function in diabetic patients with peripheral vascular disease [9,10]. The previous study also examined the effect of revascularisation on nerve function in non-diabetic patients and demonstrated a significant improvement in nerve function with restoration of limb blood flow [5]. The current study was designed to examine the effects of arterial reconstructive surgery on peripheral nerve function in diabetic patients and to act as a possible model for future therapeutic modalities.

Subjects and methods

All subjects gave informed consent prior to participation in the study, which was performed with the approval of the ethical committee of the Central Manchester Hospitals National Health Service Trust.

Six consecutive NIDDM (non-insulin-dependent) diabetic patients, three male and three female, with symptomatic angiographically-proven femoral artery thromboses suitable for uni-

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Abbreviations: NIDDM, Non-insulin-dependent diabetes mellitus; MCV, motor conduction velocity; TcPO₂, transcutaneous oxygen.

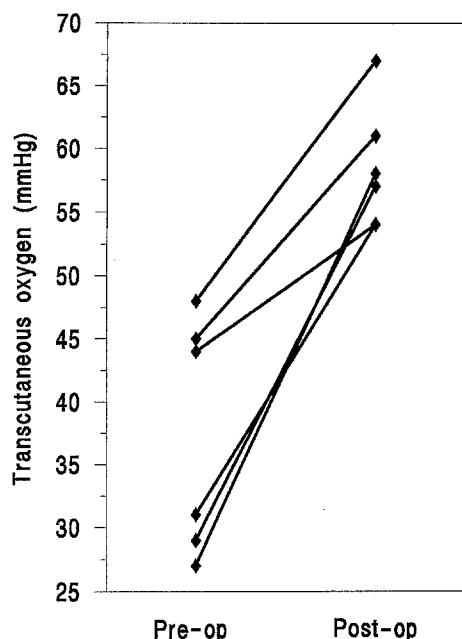


Fig. 1. The change in transcutaneous oxygen tension in the revascularised leg of each subject pre- and post-arterial reconstructive surgery (median 37.5 (28.5–45.7 interquartile range) mmHg to 55.5 (53.5–62.5) mmHg, $p = 0.036$)

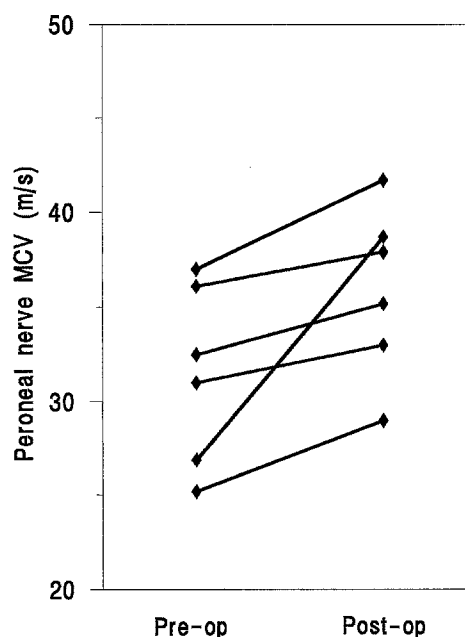


Fig. 3. Changes in peroneal nerve MCV in the revascularised leg of each subject pre- and post-arterial reconstructive surgery (median 31.7 (26.5–36.3 interquartile range) m/s to 33.5 (32.9–39.4) m/s, $p = 0.04$)

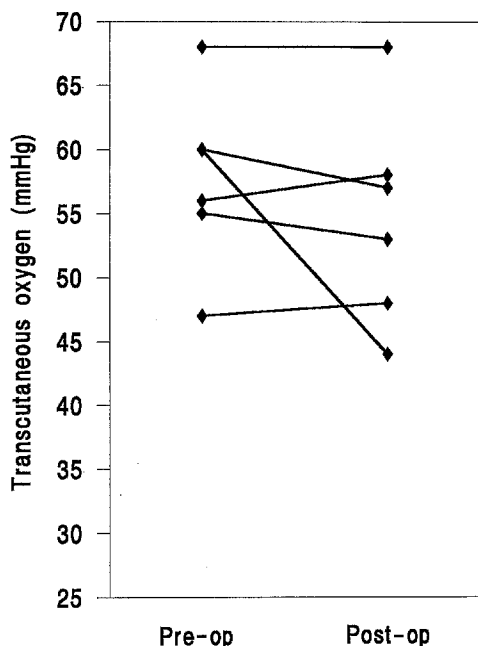


Fig. 2. The change in transcutaneous oxygen tension in the control leg of each subject pre- and post-arterial reconstructive surgery (median 58.0 (49.2–66.0 interquartile range) mmHg to 53.0 (45.0–65.5) mmHg, $p = 1.0$)

lateral bypass surgery were included in the study. The operations were not performed for reasons of limb salvage or critical ischaemia. Their median age was 64 (58–72) years (interquartile range), and duration of diabetes was 7 (3–14) years. All were smokers and none changed their smoking habit during the study. No patient was taking vasoactive drugs. All were treated with aspirin.

Peroneal nerve motor conduction velocity (MCV) and transcutaneous oxygen tension were measured in both lower limbs on the day before, and 6–8 weeks after, bypass surgery. The limb which did not undergo surgery was used as a control for possible changes in the physiological milieu pre- and post-operatively. Blood glucose level was measured in all patients at the time of peroneal nerve MCV to ensure that they were not hypoglycaemic. Peroneal nerve MCV was used as this correlates well with sural sensory nerve conduction velocity, and sural nerve latency is often absent in patients with reduced peroneal MCV [11].

The methods used have been described in detail in a previous paper [5]. Peroneal nerve MCV was measured after equilibration with the patient lying semi-supine in a warm room ($> 25^{\circ}\text{C}$), using standard surface electrodes and a Medelec MS92a neurophysiology system (Medelec, Old Woking, Surrey, UK). Printouts were made of the latencies and these were then measured independently, without knowledge of the patient's identity, or indication of which limb had been measured. Transcutaneous oxygen (TcPO_2) was measured at the site of the extensor digitorum brevis using a TINA TCM3 Oxygen monitor (Radiometer, Copenhagen, Denmark) with an electrode temperature of 44°C . The recorded TcPO_2 was the stable oxygen level after the monitor was attached for at least 20 min to the patient.

Statistical analysis

All results were analysed using Minitab statistical software (Minitab Inc., State College, Pa., USA) and all comparisons were performed as paired Wilcoxon rank sum tests.

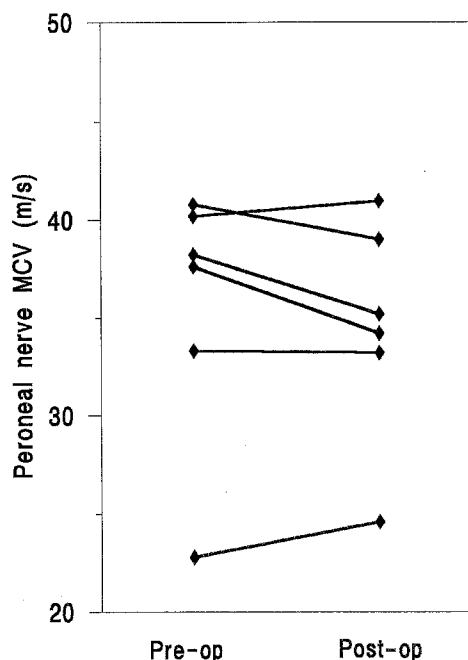


Fig. 4. Changes in peroneal nerve MCV in the control leg of each subject pre- and post-arterial reconstructive surgery (median 35.5 (25.5–39.5 interquartile range) m/s to 34.2 (26.7–40.3) m/s, $p = 0.83$)

Results

The results are displayed graphically in Figures 1–4.

In the revascularised legs, transcutaneous oxygen increased from a median 37.5 (28.5–45.7 interquartile range) mmHg to 55.5 (53.5–62.5) mmHg, $p = 0.036$, mean increase 20.2 (14.8–25.6 95 % confidence intervals) mmHg. This was accompanied by a significant improvement in peroneal motor nerve conduction velocity from median 31.7 (26.5–36.3) m/s to 33.5 (32.9–39.4) m/s, $p = 0.04$, mean increase 4.7 (1.7–7.7, 95 % confidence intervals) m/s.

There was no significant change in transcutaneous oxygen or peroneal nerve motor conduction velocity in the contralateral control limb; median TcPO₂ pre-surgery 58.0 (49.2–66.0) mmHg, post-surgery 53.0 (45.0–65.5) mmHg; median peroneal motor nerve conduction velocity, pre-surgery 35.5 (25.5–39.5) m/s, post-surgery 34.2 (26.7–40.3) m/s, $p = 0.83$ and $p = 1.0$ respectively.

Discussion

This study demonstrates that improving tissue oxygenation can improve nerve conduction velocity in diabetic patients. It extends the findings of our previous study which demonstrated improvement in non-diabetic patients [5]. The mean increase in peroneal MCV of around 15 % is greater than that reported in trials with gamma-linolenic acid (Scotia Pharmaceu-

ticals, Guildford, Surrey, UK), an open labelled study of the use of lisinopril (Zeneca pharmaceuticals, Macclesfield, UK), both of which have, in part, been thought to contribute to improved microvascular blood flow [12,13], or in trials of the aldose reductase inhibitor Tolrestat (Wyeth Laboratories, Taplow, Berks., UK) [14], which is now a prescribable therapy for peripheral neuropathy in many countries around the world. Although such improvements have not been demonstrated in double-blind controlled studies in man, vasodilator and other therapies believed to improve peripheral blood flow have been successful in preventing peripheral neuropathy in experimental diabetes [15]. Improvements in microvascular haemodynamics have been described in patients following vascular reconstructive surgery in association with increases in TcPO₂ of the same magnitude to those seen in this study [16]. In view of these results [16], and the results of the past [5], and present studies, which show improvement in nerve conduction follow up a direct improvement in tissue oxygenation, studies of agents which might indirectly bring about improvements in microvascular blood flow should be urgently considered.

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