

Nerve Blood Flow in Diabetic Peripheral Neuropathy: Revisiting the 'Vasa nervorum' Hypothesis

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Abstract

The aim of this short communication article was to highlight the role of altered nerve blood flow as a patho-anatomical manifestation in diabetic peripheral neuropathy (DPN), a common microvascular complication of globally prevalent metabolic disorder, diabetes mellitus. Limited evidence suggested that higher epineurial blood flow was present in DPN, which indirectly influenced impairments in exercise-induced nerve conduction increments. Newer methods like Nerve photography and fluorescein angiography provide useful objective information on nerve blood flow in terms of epineurial vessel pathology score, epineurial arteriovenous shunting, nerve fluorescein appearance time and intensity of fluorescence. Treatments using Adenosine and adenosine A2A receptor agonist, and alpha-lipoic acid administration were shown to be beneficial, with dose-dependent effects on nerve blood flow.

Keywords: Neuroanatomy; Vascular neurology; Epineurial circulation; Neural hemodynamics.

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Eaton *et al*[1] compared epineurial haemodynamics (epineurial intravascular oxygen saturation and blood flow) in patients with 11 chronic painful and eight painless neuropathy subjects. Intravascular oxygen saturation was found to be higher in the painful neuropathy group compared to those without pain. Faster Fluorescein rise time in those with painful symptoms also indicated higher epineurial blood flow in those subjects.

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Nerve photography and fluorescein angiography: Tesfaye *et al*[2] developed newer techniques of sural nerve photography and fluorescein angiography as an index of nerve blood flow and studied 13 subjects with chronic sensory motor neuropathy, five non-neuropathic diabetic and nine normal control subjects. The study had following findings; "The mean epineurial vessel pathology score of the neuropathic group was significantly higher than the combined normal control and non-neuropathic diabetic groups. Direct epineurial arteriovenous shunting was observed in six neuropathic and one non-neuropathic diabetic patients and not in any of the normal control subjects. The nerve fluorescein appearance time was significantly delayed in subjects with chronic sensory motor neuropathy compared to both normal and non-neuropathic diabetic subjects. The mean intensity of fluorescence at 96, 252 and 576s, was significantly lower in subjects with chronic sensory motor neuropathy compared with other two groups."

Exercise-induced Responses

Tesfaye *et al*[3] recorded sural sensory conduction velocity in 12 non-neuropathic

diabetic subjects, 15 diabetic subjects with established neuropathy and 16 age-matched normal control subjects, before and after exercise to 80% age/sex predicted maximum heart rate, and concluded that the impairment of exercise-induced nerve conduction increment in diabetic neuropathy indirectly implicated impaired nerve blood flow in diabetic neuropathy.

Adenosine and Adenosine A2A Receptor Agonist

Kumar *et al*[4] examined the effects of chronic administration of adenosine and CGS 21680 hydrochloride (adenosine A_{2A} receptor agonist) on motor nerve conduction velocity (MNCV), nerve blood flow (NBF) and histology of sciatic nerve in DPN rats. Adenosine (10 mg/kg, i.p.) Showed improvements in sciatic MNCV and NBF in diabetic rats while CGS 21680 (0.1 mg/kg, i.p.) significantly improved NBF; but not MNCV.

Lipoic Acid

Nagamatsu *et al*[5] studied the effects of lipoic acid (LA) on oxidative stress in diabetic peripheral nerves of rats by measuring nerve blood flow (NBF), electrophysiology, and indexes of oxidative stress. LA was shown to have dose-dependent influence on NBF in diabetic nerves, but not on normal nerves.

Stevens *et al*[6] reported therapeutic effects of administration of the antioxidant DL-alpha-lipoic acid (LA) to streptozotocin-injected diabetic rats, as follows; "LA improved digital sensory but not sciatic-tibial motor NCV, corrected endoneurial nutritive but not composite NBF, increased the mitochondrial oxidative state without correcting nerve energy depletion, and enhanced the accumulation of polyol pathway intermediates without worsening myo-inositol or taurine depletion."

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fluorescein angiography provide useful objective information on nerve blood flow in terms of epineurial vessel pathology score, epineurial arteriovenous shunting, nerve fluorescein appearance time and intensity of fluorescence. Treatments using Adenosine and adenosine A_{2A} receptor agonist, and alpha-lipoic acid administration were shown to be beneficial, with dose-dependent effects on nerve blood flow.

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Note: In this research no any own findings of authors study & results, there is only focus on previous studies.