Short Communication

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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, epineurialarteriovenous shunting, nerve fluorescein appearance time and intensity of fluorescence. Treatments using Adenosine and adenosine A2A receptor agonist, and alpha-lipoic acid administration were shown o be beneficial, with dose-dependent effects on nerve blood flow.

Keywords: Neuroanatomy; Vascular Neurology; Epineurial Circulation; Neural Hemodynamics.

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.

Eatonet al [1] comparedepineurialhaemodynamics (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.

Nerve photography and fluorescein angiography: Tesfayeet al [2] developed newer techniques of sural nerve photography and fluorescein angiography as an index of nerve blood flow and stuided 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 epineurialarteriovenous 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 576 s, 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

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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 insciatic MNCV and NBF in diabetic ratswhile CGS 21680 (0.1 mg/kg, i.p.) significantly improved NBF; but notMNCV.

Lipoic acid:Nagamatsuet 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] reportedtherapeutic 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."

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, epineurialarteriovenous shunting, nerve fluorescein appearance time and intensity of fluorescence. Treatments using Adenosine and adenosine A2A receptor agonist, and alpha-lipoic acidadministration were shown o be beneficial, with dose-dependent effects on nerve blood flow.

References

1. Eaton SE, Harris ND, Ibrahim S, Patel KA, Selmi F, Radatz M, et al.Increased sural nerve epineurial blood flow in human subjects with painful diabetic neuropathy. Diabetologia. 2003; 46(7): 934-9.
2. Tesfaye S, Harris N, Jakubowski JJ, Mody C, Wilson RM, Rennie IG, et al. Impaired blood flow and arterio-venous shunting in human diabetic neuropathy: a novel technique of nerve photography and fluorescein angiography. Diabetologia. 1993; 36(12): 1266-74.
3. Tesfaye S, Harris ND, Wilson RM, Ward JD. Exercise-induced conduction velocity increment: a marker of impaired peripheral nerve blood flow in diabetic neuropathy. Diabetologia. 1992; 35(2): 155-9.
4. Kumar S, Arun KH, Kaul CL, Sharma SS.Effects of adenosine and adenosine A2A receptor agonist on motor nerve conduction velocity and nerve blood flow in experimental diabetic neuropathy.Neurol Res. 2005; 27(1): 60-6.
5. Nagamatsu M, Nickander KK, Schmelzer JD, Raya A, Wittrock DA, Tritschler H, et al.Lipoic acid improves nerve blood flow, reduces oxidative stress, and improves distal nerve conduction in experimental diabetic neuropathy.Diabetes Care. 1995; 18(8): 1160-7.
6. Stevens MJ, Obrosova I, Cao X, Van Huysen C, Greene DA. Effects of DL-alpha-lipoic acid on peripheral nerve conduction, blood flow, energy metabolism, and oxidative stress in experimental diabetic neuropathy. Diabetes. 2000; 49(6): 1006-15.