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Primary and Secondary Prevention of Diabetic Peripheral Neuropathy: An Update

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Abstract

Diabetic neuropathy (DN) is a debilitating disorder that occurs in nearly 50 percent of patients with diabetes, causing motor deficits, silent cardiac ischemia, orthostatic hypotension, vasomotor instability, hyperhidrosis, gastroparesis, bladder dysfunction, and sexual dysfunction. The objective of his short communication was to provide an insightful overview of prevention of diabetic peripheral neuropathy (DPN), a common disabling microvascular complication of diabetes and its associated foot complications. Glycemic control is an essential intervention shown to be beneficial in both type-1 and type-2 diabetes patients in preventing microvascular and neuropathic foot complications. Medical management comprising of acetyl-L-carnitine, Aldose reductase inhibitors, antioxidants, essential fatty acids, chromium, ginkgolides, and pentoxifylline, Ciliary neurotrophic factor, coenzyme Q10, edaravone, Erythropoietin and its carbamylated derivative, gamma linolenic acid, gangliosides, GCPII (NAALADase) inhibitor, glutathione, IGF1, methylcobalamin, Olive (Oleaeuropaea L.) leaf extract, oxygen supplementation and Tolrestat (Giugliano et al, 1995) were reported for preventing DPN. Flexor tenotomy, insoles, Podikon digital silicone padding, tibial neurolysis, surgical decompression of lower extremity peripheral nerves were reported for their efficacy to prevent diabetes-related neuropathic foot complications.

Keywords: Preventive medicine; Preventive endocrinology; Preventive neurology; Diabetic neuropathy; Primary and secondary prevention.

Diabetic neuropathy (DN) is a debilitating disorder that occurs in nearly 50 percent of patients with diabetes, causing motor deficits, silent cardiac ischemia, orthostatic hypotension, vasomotor instability, hyperhidrosis, gastroparesis, bladder dysfunction, and sexual dysfunction.[1] The objective of his short communication was to provide an insightful overview of prevention of diabetic peripheral neuropathy (DPN), a common disabling microvascular complication of diabetes.

Pathogenetic biochemical mechanisms of DN involved sorbitol andmyo-inositol (MI) metabolism, phosphoinositides, protein kinase C, and the (Na,K)-ATPase,[2] and among these, "a rise in tissue sorbitol secondary to concentration-dependent activation of polyol pathway activity by glucose, and an accompanying fall in tissue myo-inositol and Na-K-ATPase activity have recently been linked to a self-reinforcing cyclic metabolic defect that accounts for rapidly reversible slowing of conduction in peripheral nerve in diabetes.

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Impaired Na-K-ATPase activity also appears to be responsible for intracellular Na+ accumulation and resultant localized axonal paranodal swelling that characterizes diabetic neuropathy in both humans and laboratory animals."[3]

Glycemic control is an essential intervention shown to be beneficial in both type-1 and type-2 diabetes patients in preventing microvascular and neuropathic complications.[4] Animal models had shown alpha 1-adrenoreceptor antagonists, calcium channel blockers, agents that inhibit the renin-angiotensin system, and vasomodulatorprostanoids, omega-6 essential fatty acids, aldose reductase inhibitors, aminoguanidine prevented the formation of advanced glycation end-products.[5]

Current recommendations include optimisation of glycaemic and HbA1c values and correct use of tricyclic antidepressants, none of the other substances tested has proven to be efficacious for PDN. Gangliosides, aldose-reductase inhibitors, including tolrestat, gamma-linolenic acid, levacecarnine (acetyl-L-carnitine) and antioxidants, were all shown to be of poor efficacy and often with significant adverse effects.[6]

Medical management comprising of acetyl-L-carnitine,[7] Aldose reductase inhibitors,[8,9,10] antioxidants, essential fatty acids, chromium, ginkgolides, and pentoxifylline,[11] Ciliary neurotrophic factor,[12] coenzyme Q10,[13] edaravone,[14] Erythropoietin[15] and its carbamylated derivative,[16] gamma linolenic acid,[17] gangliosides,[18] GCPII (NAALADase) inhibitor,[19] glutathione,[20] IGF1,[21] methylcobalamin,[22] Olive (Oleaeuropaea L.) leaf extract,[23] oxygen supplementation,[24] and Tolrestat[25] were reported for preventing DPN.

Futuristic emphasis on a novel conjugate of gamma-linolenic acid and alpha-lipoic acid[26] is essential for preventive practice and Dyckand O'Brien[27] suggested that in controlled clinical trials, a mean change of 2 points on the neurologic disability score, corresponding to a change of motor nerve conduction velocity of the average ulnar median and peroneal nerves of 2.9 m/s and peroneal nerve of 2.2 m/s and corresponding changes of amplitude of 1.2 and 0.7 mV, respectively were to be considered clinically detectable and meaningful.

Ongoing patient and family education can emphasize the importance of preventive self-care measures, with referrals for specialist care and therapeutic footwear if begun early, can prevent foot ulcers from diabetic neuropathy, thereby improving the quality of life and reducing healthcare costs for this chronic disease.[28] Flexor tenotomy,[29] insoles[30] Podikon digital silicone padding,[31] tibial neurolysis,[32] surgical decompression of lower extremity peripheral nerves[33,34] were reported for their efficacy to prevent diabetes-related neuropathic foot complications.

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