Treatment of Painful Diabetic Neuropathy

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Peripheral neuropathy is one of the commonest long term complications of diabetes mellitus which has been reported to be prevalent in 22% of diabetic cohort.1 Painful diabetic neuropathy (PDN) occurs in 6% of the patients with diabetic peripheral neuropathy (DPN) and this is most distressing symptom which impairs quality of life.2 Patients seek advice to get relief but unfortunately treatment has been inadequate. Mechanisms of PDN involve many biological, structural and electrophysiological alterations of nervous tissues. They can be enlisted as-

A. Peripheral mechanisms which include changes in sodium channel distribution and expression, changes in calcium channel distribution and expression, altered neuropeptide expression, sympathetic sprouting, loss of spinal inhibitory control, altered peripheral blood flow, axonal atrophy, degeneration, or regeneration, damage to small fibres and increased glycaemic flux.3

B. Central mechanisms which include, Central sensitisation, changes in the balance of facilitation/inhibition within descending pathways and increased thalamic vascularity.

Myriad of pathogenetic mechanisms of PDN is a challenge to develop a drug that can be definitive treatment to alleviate miseries of the condition. It is also not certain which of the mechanisms is overtly mediating the pain in one individual. Several pharmacological treatments have been proved effective in the management of painful PDN to certain extent. It is efficacy and safety that is considered while choosing pharmacological agents. Many times, a principle of “hit trial” help selection of the drug for PDN.

Though few drugs are very commonly used for pain management in PDN, only duloxetine and pregabalin are approved for the treatment of neuropathic pain in diabetes by both the Food and Drugs Administration of the U.S. and the European Medicines Agency. This indicates we should take care in using other drugs of various classes. However, some of the topical agents might be very useful in relieving pain and not having any systemic untoward effect.

Search for a topical agent will need the knowledge of the mediators of pain in PDN. Impaired nitric oxide production changing the nerve excitation threshold (shown in animal experiment) and causing hypoxia due to inadequate vasodilatation have been described. In our own study we demonstrated adequate nitric oxide synthase activity in diabetic foot tissue which indicated over expression of the enzyme in an attempt to generate NO but the NO production was reported to be diminished.3,5

The idea of using topical agent that can donate NO to the tissue has led to study effect of isosorbide dinitrate and glyceryl dinitrate (GTN) spray in PDN with some encouraging outcome.6-8 It may be useful to relieve pain in patients who have sleepless night due to agony of pain without major side effects and to buy time till the benefit of glycaemic control sets in.

We must try such formulation that is easily available and convenient to administer topically in PDN for the merits described above. Nitrosense Derma Protect, a nitric oxide eluting patch appears promising and study published in this issue of the journal should be replicated to accumulate more information on this device.

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References


