Diabetic Peripheral Neuropathy: Therapeutic Options

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Abstract

Diabetes poses neurological damages and result in diabetic peripheral neuropathy (DPN). The prevalence of DPN varies from 10-90%. The persistent hyperglycemia, microvascular insufficiency, oxidative and nitrosative stress, defective neurotrophism, and autoimmune nerve destruction are the important factors of DPN. Peripheral nerve conduction velocities (NCV) are considered one of the most sensitive indices of the severity of neuropathy in DPN. Control of hyperglycemia is only the best treatment exists for DPN. Besides glucose lowering therapy, antidepressants, anticonvulsants, opioid analgesics, anti arrhythmics, and NMDA receptor antagonists are commonly used, though all these drugs have adverse actions. Recent researches are focused on the development of neurotrophic factors (NTFs), nitrate sprays and topical capsaicin for the treatment of DPN.

Keywords: Diabetes; Diabetic peripheral neuropathy; Nerve conduction velocity; Neurotrophic factors; Nitrate sprays; Topical capsaicin

Introduction

At present, diabetes and its associate complications are owed global health burden and risk to silent death. In 2015, WHO estimated diabetes killed 1.6 million people globally and expected to double within 10 years [1]. The number of people with diabetes worldwide was estimated in 2011 were 366 million and is expected to rise to 522 million in 2030 [2]. The estimated worldwide prevalence of diabetes in 2010 was 6.4% and this value is predicted to rise to around 7.7% in 2030 [3]. The highest prevalence of diabetes in adult population noted in North America 7.9% followed by Europe 7.8% and South America 5.6% [4]. The top ten countries with diabetes population are China, India, USA, Brazil, Russian Federation, Mexico, Indonesia, Germany and Egypt [5].

Diabetic peripheral neuropathy

Diabetic peripheral neuropathy (DPN) is the most common and troublesome complication of diabetes leading to great morbidity and resulting in a huge economic burden for diabetes care. DPN was defined by the presence of at least two of the following three characteristics: (a) pain, paresthesias, or numbness; (b) absence of tendon reflexes; (c) abnormal malleolar vibration perception threshold. Diabetic patients due to DPN have 12 times higher risk of amputations when compared with non-diabetic subjects [6]. The exact prevalence of DPN is not known and reports vary from 10-90% in diabetic patients depending on the criteria and methods used to define neuropathy [7]. In United States, about 60-70% of people with diabetes have some form of DPN. People with diabetes can develop nerve problems at any time, but risk rises with age and longer duration of diabetes. The highest rates of DPN are among people who have had diabetes for at least 25 years [8].

Mechanisms involved in DPN

Mechanisms involved behind DPN are persistent hyperglycemia, microvascular insufficiency, oxidative and nitrosative stress, defective neurotrophism, and autoimmune nerve destruction [9]. One of the consequences of hyperglycemia is increased metabolism of glucose by the sorbitol pathway. This involves the reduction of glucose to sorbitol catalyzed by aldose reductase and the oxidation of sorbitol to fructose by sorbitol dehydrogenase. Aldose reductase is present in human brain, nerves, aorta, muscle, erythrocytes and ocular lens [10]. Sorbitol does not cross cell membranes and thereby accumulates in the nervous tissue, thus generating osmotic stress. Osmotic stress increases the intracellular fluid molarities as well as water influx, Schwann cell damage and nerve fiber degeneration [11]. Another hypothesis suggests neuro immune interactions actively contribute to the onset and persistence of pain in diabetes [12]. In experimental study, it has been observed that up regulation of the NADPH oxidase complex results in oxidative stress through reduced glutathione production, decreased nitric oxide concentrations and increased reactive oxygen species concentrations [13]. Free radicals, oxidants, and some unidentified metabolic factors activate the nuclear enzyme poly (ADP-ribose) polymerase that is a fundamental mechanism in the development of...
Capsaicin is commercially available as isosorbide dinitrate or glyceryl trinitrate. Both isosorbide dinitrate as well as glyceryl trinitrate act as potent nitric oxide donor and have similar pharmacological activity compared to endothelial derived relaxing factor-a nitric oxide dependent enzyme with vasodilator capacity. The basis of nitrate spray use is based on the theory that impaired nitric oxide generation which is involve in the progression of pathogenesis of DPN [32-35].

Topical capsaicin: Capsaicin is commercially available as 0.025%, 0.075%, and 0.1% creams. Topical capsaicin has shown analgesic benefits in postherpetic neuralgia, painful polyneuropathies including DPN. Capsaicin causes reversible depletion of substance P from the sensory nerve endings by activity of vanilloid-receptor and possibly through a reversible decrease in the number of epidermal nerve fibre. FDA approved 8% Capsaicin patch for postherpetic neuralgia. A major adverse effect is a burning discomfort potentially leading to poor patient adherence.

Conclusion

DPN is most common complication of diabetes that can be result early, if hyperglycemia is not properly controlled. Substantial evidences supports that only early detection and diagnosis can resist DPN from major neuronal damage. Therapeutic treatments for DPN are limited. Besides oral therapy, topical agents are now also showed effectiveness in the management of pain in DPN with minimum side effects.

References

1. WHO Fact sheets.


