Mini Review

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Diabetic neuropathic pain: Neurogenic Diabetic problems

Abstract

Over 90% of diabetics suffer from diabetic neuropathy, a common complication of both type 1 and type 2 diabetes. Although pain is one of the most common signs of diabetic neuropathy, the pathophysiological mechanisms underlying it are still poorly understood. Although a number of other hypotheses have been proposed, it is generally agreed that the harmful effects of hyperglycaemia are a major cause of this complication. Diabetic neuropathic pain is mostly treated by excluding other causes of painful peripheral neuropathy, improving glycaemic control as a preventative measure, and taking painkillers. Anticonvulsants like pregabalin and gabapentin, as well as antidepressants that block the reuptake of serotonin and noradrenaline are the first-line treatments for pain. Additionally, there is experimental and clinical evidence to suggest that opioids can aid in pain management, particularly when used in conjunction with first-line medications. Capsaicin cream and lidocaine patches, both of which can be applied topically, have also been suggested as potential adjuvants for the treatment of diabetic neuropathic pain, but there is insufficient clinical evidence to support their use. In conclusion, gaining a deeper comprehension of the mechanisms that lie behind diabetic neuropathic pain will not only aid in the search for brand-new treatments but also in the development of better guidelines for maximizing pain management with the medications that are currently available.

Keywords: Diabetes • Neuropathic pain • Hyperglycaemia • Anticonvulsants • Antidepressants

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Introduction

Diabetes, one of the most common causes of neuropathy, currently affects 382 million people worldwide, according to the International Diabetes Federation [1]. The most prevalent clinical form of diabetic neuropathy, affecting more than 90% of patients, is distal symmetrical polyneuropathy. DSPN typically affects the toes and distal foot, but it gradually spreads proximally to involve the legs and feet in a stocking pattern. Additionally, diabetic retinopathy and nephropathy can develop as a result of the progressive loss of nerve fibres that affect the autonomic and somatic divisions. The most common clinical effects of DSPN, which are associated with increased mortality and morbidity, are painful neuropathy in the feet and foot ulcers. Patients typically only seek medical attention when they experience pain, which affects 10% to 26% of this population [2].

Diabetic neuropathies include a wide variety of nerve abnormalities and are common. According to the diagnostic criteria, prevalence rates range from 5 to 100 present. Both Type 1 and Type 2 diabetics suffer from significant morbidity and mortality as a result of diabetic neuropathies, which affect both the autonomic and peripheral nervous systems. The majority of neuropathies are caused by diabetes; they cause between 50 and 75 percent of non-traumatic amputations and cause more hospitalizations than all other diabetic complications combined. Peripheral neuropathies have a particularly negative impact on stability, sensorimotor function, gait, and activities of daily living in diabetic older adults. Based on a straightforward screen for decreased foot sensation, peripheral neuropathy was found in 28% of adults between the ages of 70 and 79 and 35% of adults under the age of 80 in the United States in 1999 and 2000. The most recent treatments for common diabetic neuropathies, such as symmetric, focal, and diffuse neuropathies, are presented and discussed in this review. In addition, we will provide the reader with algorithms for identifying and treating common pain and entrapment syndromes as well as a global strategy for identifying syndromes that call for specialized treatments thanks to our improved

comprehension of their etiopathogenesis. This review cannot provide a comprehensive analysis of autonomic neuropathy; however, the reader is referred to two excellent reviews on the subject [3].

Diabetic neuropathy is mostly caused by metabolic disorders. The polyol pathway's increased activity can be attributed to hyperglycaemia caused by insulin resistance or decreased insulin secretion. Aldose reductase is the first enzyme in this pathway that limits the rate of sorbitol formation from glucose by oxidizing NADPH to NADP+. By sorbitol dehydrogenase, sorbitol is further oxidized to fructose and nicotinamide adenine dinucleotide (NAD+) is reduced to NADH [4]. Aldose reductase's affinity for glucose increases in hyperglycaemic states, causing sorbitol accumulation and intracellular osmotic stress due to its inability to cross cell membranes. It's interesting that there have been reports of insignificant sorbitol concentrations in the nerves of diabetic patients, suggesting that the nerve damage that occurs as a result of diabetes is not caused by this osmotic stress. The current accepted hypothesis, on the other hand, states that polyol pathway hyperactivity is primarily caused by an increase in the turnover of cofactors like NADPH and NAD+. This decreases the reduction and regeneration of glutathione and increases the production of advanced glycation end products (AGEs) and the activation of triacylglycerol and PKC isoforms. The accumulation of harmful species may be linked to glutathione depletion, which may be the primary cause of oxidative stress.

Neuropathic pain in diabetes

Although our knowledge of the pathophysiological mechanisms that lead to diabetic complications has greatly improved, there is still no plausible explanation for why some patients develop the painful form of the disease while others do not. In general, researchers look at the underlying mechanisms of neuropathy as a larger event and consider pain and other sensory manifestations to be direct outcomes of neuropathy [5]. Intriguingly, however, pain intensity can occur even in the absence of nerve injuries and is typically unrelated to the severity of neuropathy. The pathophysiological mechanisms that are currently believed to promote the DNP will be discussed in this review.

Micro vascular changes

DNP is frequently linked to damage to the micro arteries. A significant physiological sign of a change in the microvasculature was found in clinical and preclinical studies to be a reduction in peripheral perfusion in the skin as well as the nervous tissue [6]. A rise in wall thickness, hyalinization of the basal lamina of vessels that nourish peripheral nerves, and a decrease in luminal volume all result in nerve ischemia. Plasma protein scape from the capillary membrane to the endometrium causes these changes, leading to nerve swelling and increased interstitial pressure, as well as increased capillary pressure, fibrin deposition, and thrombus formation [7]. Nerve hypoxia can be triggered by hyperglycaemia itself, particularly in sensory nerves, affecting their electrical stability. Data from clinical studies that appeared to be controversial stated that diabetic patients with the DNP had increased blood flow in the lower limbs and higher levels of intravascular oxygen than patients without pain. However, the authors continue to consider the endometrium to be hypoxic. Alternately, increased blood flow may be the result of a potential sympathetic dysfunction [8].

It's also important to note that DNP patients also have altered endothelial function. Acetylcholine caused less vaso dilatation in diabetic patients' dermal vessels than it did in healthy volunteers. Additionally, vasoconstriction mediate by the sympathetic system was defective, which may also be associated with the DNP and its pathophysiology. Since treatment with antioxidants can maintain regular perfusion and restore sensory transmission in a type 1 diabetes model, it is believed that oxidative stress may be one potential cause of the aforementioned micro vascular changes.

Treatment of DNP

Because its pathophysiology is still poorly understood and its pain relief is still insufficient, DNP remains a therapeutic challenge [9]. Except for those that focus on glycaemic control, pharmacological treatments are symptomatic, do not address pathophysiological mechanisms, and are constrained by side effects and tolerance.

In randomized controlled trials, a wide range of drugs, either alone or in combination, have been shown to significantly reduce

neuropathic pain in comparison to placebo, but most patients still don't get enough relief. In clinical trials, treatment is typically deemed successful if patients experience a 50% reduction in pain along with additional positive effects on quality of life, sleep, fatigue, and depression. As a result, the treatment for this condition essentially consists of eliminating other potential causes of painful peripheral neuropathy, enhancing glycaemic control as a preventative measure, and taking painkillers [10].

Conclusion

Diabetic neuropathy is a multifaceted condition with numerous pathologies. The first step in finding the right kind of treatment is recognizing the clinical equivalent of these pathological processes. The particular manifestation and underlying pathogenesis of each patient's individual clinical presentation should be taken into consideration when tailoring treatment. A special attention should be paid to pain management in older adults in order to maximize daily function and mobility while minimizing medication side effects. Due to instability, weakness, and the need for strength and coordination training, older adults are particularly vulnerable to falls and fractures. If we are to lessen the severe impairment of quality of life (QoL) and ability to perform daily activities (ADLs) that diabetic neuropathy causes, ultimately medications that target large fiber dysfunction will be required.

Acknowledgement

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Conflict of Interest

None

References

1. Schellenberg ES, Dryden DM, Vandermeer B *et al.* Lifestyle interventions for patients with and at risk for type 2 diabetes: a systematic review and meta-analysis. *Ann Intern Med.* 159: 543-551 (2013).
2. Schwingshackl L, Hoffmann G, Lampousi AM *et al.* Food groups and risk of type 2 diabetes mellitus: a systematic review and meta-analysis of prospective studies. *Eur J Epidemiol* 32: 363-375 (2017).
3. Reynolds A, Mann J, Cummings J *et al.* Carbohydrate quality and human health: a series of systematic reviews and meta-analyses. *Lancet.* 393: 434-445 (2019).
4. Beccuti G, Monagheddu C, Evangelista A *et al.* Timing of food intake: Sounding the alarm about metabolic impairments? A systematic review. *Pharmacological Research.* 125: 132–141 (2017).
5. Anderson JW, Ward K High-carbohydrate, high-fiber diets for insulin-treated men with diabetes mellitus. *Am J Clin Nutr.* 32: 2312-21 (1979).
6. Booth FW, Chakravarthy MV. Physical activity and dietary intervention for chronic diseases: a quick fix after all. *J Appl Physiol.* 100: 1439-40 (2006).
7. Roberts CK, Won D, Pruthi S *et al.* Effect of a short-term diet and exercise intervention on oxidative stress, inflammation, MMP-9, and monocyte chemotactic activity in men with metabolic syndrome factors. *J Appl Physiol.* 100: 1657-65 (2006).
8. Skov J, Eriksson D, Kuja-Halkola R *et al.* Co-aggregation and heritability of organ-specific autoimmunity: a population-based twin study. *Eur J Endocrinol* 182: 473-480 (2020).
9. Hyttinen V, Kaprio J, Kinnunen L *et al.* (2003) Genetic liability of type 1 diabetes and the onset age among 22,650 young Finnish twin pairs: a nationwide follow-up study. *Diabetes.* 52: 1052-1055.
10. Tinajero MG, Malik VS. an Update on the Epidemiology of Type 2 Diabetes: A Global Perspective. *Endocrinol Metab Clin.*50: 337-355 (2021).