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A Review on Diabetic Neuropathy

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Abstract

Diabetic Peripheral Neuropathy (DPN) is a prevalent complication that affects a significant majority of individuals with both type 1 and type 2 diabetes, with a prevalence rate of over 90%. The development of DPN is primarily attributed to the toxic effects of prolonged hyperglycemia on the peripheral nerves. This condition is characterized by notable impairments in tactile sensitivity, vibration sense, lower-limb proprioception and kinesthesia. Painful DPN has been associated with a multitude of adverse consequences, including a substantial decline in overall quality of life, heightened levels of anxiety and depression, sleep disturbances and increased variability in gait. Unfortunately, DPN is often inadequately managed, underscoring the importance of improving glycemic control in diabetes management. To address the symptoms of DPN, major international clinical guidelines recommend several symptomatic treatments. First-line therapies include tricyclic antidepressants, serotonin-noradrenaline reuptake inhibitors and anticonvulsants that target calcium channels. These medications aim to alleviate pain and improve the overall functioning of individuals with DPN. Additionally, opioids and topical agents such as capsaicin and lidocaine are also considered as potential treatment options for DPN. The objectives of the present paper revolve around reviewing the current guidelines for the pharmacological management of DPN. By summarizing and examining these guidelines, healthcare professionals and researchers can gain insights into the recommended approaches for effectively addressing the symptoms of DPN and improving the overall well-being of individuals with diabetes-related neuropathy.

Keywords: Diabetic neuropathy; Epidemiology; Body mass index

Introduction

Diabetic neuropathy is a condition that affects the peripheral nerves in individuals with diabetes mellitus. The prevalence of diabetes has emerged as a major global healthcare concern in the 21st century. In 2015, it was estimated that approximately 415 million people worldwide were afflicted with diabetes and this number is projected to rise to 642 million by 2040. Nearly half of all individuals with diabetes are expected to develop diabetic peripheral neuropathy. Diabetic peripheral neuropathy, characterized by symptoms and signs of peripheral nerve dysfunction in people with diabetes after excluding other causes, significantly impacts the daily lives of patients. The initial manifestation of diabetic neuropathy is often pain in the lower limbs, which can take various forms such as a burning sensation, electric shocks or needle-like pricking. Some patients may also experience a loss of sensation. DPN greatly diminishes the patient's quality of life and has economic implications. Once diagnosed, managing DPN presents new challenges in patient care [1].

Literature Review

Epidemiology

Describing the epidemiology and natural progression of patients with diabetic neuropathy is challenging due to the use of different clinical diagnostic criteria, variability in patient selection (including those with or without pain) and the utilization of diverse physiological techniques. The EURODIAB complications study revealed a baseline prevalence of 28% for diabetic peripheral neuropathy, with glycemic control and duration of diabetes being significant determining factors. Similar findings were observed in the Diabetes Control and Complications Trial (DCCT). In a study involving 4,400 patients, the prevalence of diabetic peripheral neuropathy was approximately 75%among newly diagnosed diabetes cases, which increased to 45% after 25 years of living with diabetes [2].

In North India, a cross-sectional study conducted in 2013 involved 586 participants, among whom 18.4% were newly diagnosed with diabetes (less than 6 months), while 81.6% had known diabetes. The participants had a mean age of 57.1 ± 9.7 years and a mean duration of diabetes of 10.8 ± 7.5 years. The study utilized Semmes-Weinstein Monofilament (SWM) and Vibration Perception Threshold (VPT) to assess Diabetic Peripheral Neuropathy (DPN) prevalence in the population [3].

Similarly, a study conducted in South India included 1000 diabetic patients and employed biothesiometry and assessment of VPT to determine the prevalence of DPN. In this study, the prevalence was found to be 19.1%. A retrospective study conducted in Goa, India, analyzed data from 3261 patients with Type 2 Diabetes Mellitus (T2DM) and established a prevalence rate of 16.3% for DPN. Another study focused on young-onset diabetes, involving 1500 patients with an average age of 34.68 ± 4.23 years. In this study, the prevalence of advanced neuropathy was determined to be 13.1%.

A retrospective study conducted in a tertiary setting with 249 T2DM patients revealed a surprisingly low prevalence of 14.4% for

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DPN. However, the specific method used to diagnose neuropathy in this study was not disclosed. Lastly, a study involving 1319 T2DM patients from four different centers across India reported a prevalence of 15% for SWM insensitivity as an indicator of DPN.

These various studies conducted in different regions of India provide valuable insights into the prevalence of DPN among diabetic populations. The utilization of different assessment methods and the inclusion of patients with varying durations of diabetes contribute to a broader understanding of DPN prevalence in the country. These findings underscore the importance of early detection and management of DPN to mitigate its impact on individuals with diabetes [4].

Discussion

Clinical features

The risk factors associated with Diabetic Peripheral Neuropathy (DPN) were determined in a study conducted by EURODIAB, which followed 1,100 individuals with type 1 diabetes over a span of 7.5 years. These risk factors were found to be similar to those observed in macrovascular diseases, such as hypertension, smoking, elevated lipid levels, duration of diabetes and body mass index. Furthermore, it was discovered that neuropathic pain is also linked to other conditions, such as peripheral arterial disease, even in non-diabetic subjects. This finding underscores the significance of considering neuropathic pain in both the diagnosis and treatment process. The signs of diabetic neuropathy can vary, with neuropathic pain manifesting as deep, aching pain accompanied by burning and stabbing sensations. Research indicates that a substantial percentage of patients, ranging from 25% to 39%, do not receive adequate pain management, resulting in a negative impact on their quality of life. The reported pain has been shown to affect general activity, mood, mobility, work, social relationships, sleep, leisure activities, walking ability and overall enjoyment of life [5].

Pathophysiology

The exact cause of diabetic neuropathy is not fully understood, but it is believed to result from nerve dysfunction and cell damage caused by oxidative stress and inflammation. Various health conditions, including hyperglycemia, dyslipidemia and insulin resistance, contribute to the impairment of metabolic pathways such as the polyol pathway, which leads to excessive formation of reactive oxygen species in the mitochondria and cytosol. These reactive oxygen species cause damage to the axons of peripheral nerves, leading to Diabetic Peripheral Neuropathy (DPN). The pain pathway is also influenced by multiple neurotransmitters. The development of DPN is influenced by multiple factors. Chronic hyperglycemia and ischemic effects on peripheral nerves are considered the two main mechanisms leading to dysfunction and damage. Hyperglycemia has various harmful metabolic effects, including activation of the polyol pathway, generation of reactive oxygen species (oxidative stress), reactive nitrogen species (nitrosative stress) and accumulation of Advanced Glycation End products (AGEs). Excess glucose in the body is metabolized through the polyol pathway, where it is converted to sorbitol by the enzyme aldose reductase before being oxidized to fructose by sorbitol dehydrogenase. This intracellular accumulation of sorbitol leads to a reduction in nerve myoinositol and taurine levels, disrupts the activity of Na^+/K^+-ATPase membrane and causes sodium accumulation in the nerves, ultimately leading to axon dysfunction and structural damage. The glycation of proteins, lipids and nucleic acids with the formation of AGEs leads to glycosylation of the basement membrane of endothelial cells, impairing vasodilation. Furthermore, accumulated AGEs bind to receptor of AGEs on macrophages, triggering the production of inflammatory cytokines (IL-1), tumor necrosis factor, growth factors and adhesion molecules (VCAM-1). Another pathway involved in the complications of diabetes is the activation of the nuclear enzyme Poly (ADP-Ribose) Polymerase (PARP). Increased oxidative stress results in DNA damage and activation of PARP-1, leading to cellular energy failure, which is believed to be significant in the pathogenesis of DPN [6].

Treatment

Diabetic Peripheral Neuropathy (DPN) poses a significant challenge in terms of pharmacological treatment due to the unknown underlying pathophysiology. While a complete cure is currently unattainable, there are ways to prevent and reduce the associated pain. Three main principles contribute to pain management: Glycemic control, foot care and pain management strategies. Glycemic control and foot care primarily focus on preventive measures. In addition, lifestyle interventions such as weight loss and physical activity can be beneficial in treating DPN. Pharmacological treatment is also recommended by the American diabetes association to relieve pain and symptoms associated with diabetic peripheral neuropathy, ultimately improving the patient's quality of life. Medications like duloxetine and pregabalin are approved by the US Food and Drug Administration (FDA) specifically for this purpose. Tricyclic antidepressants are used off-label for pain reduction in DPN, although they are not currently FDA-approved due to significant potential side effects. Opioids can be utilized to alleviate neuropathic pain, but their habit-forming nature makes them unsuitable as first or second-line therapy for DPN [7].

Patients diagnosed with Diabetic Peripheral Neuropathy (DPN) commonly experience distressing symptoms. Although maintaining tight glucose control, engaging in moderate exercise and following a balanced diet are important, they may not be sufficient to reverse the progression of the disease. Therefore, in order to restore function and provide effective treatment, patient education and pharmacological therapy become necessary. The significance of tight glucose control in managing DPN has been demonstrated in studies such as the United Kingdom prospective diabetes study and the Diabetes Control and Complications Trial (DCCT). These studies have shown the positive impact of controlling blood glucose levels on DPN symptoms [8].

Several guidelines recommend the use of pharmacological treatments, both approved and off-label, to alleviate pain and improve the quality of life for patients with DPN. These treatment options encompass various categories, including antidepressants, anticonvulsants, analgesics and topical medications. Using a combination of these drugs or employing them individually has been shown to significantly reduce neuropathic pain [9].

Among the pharmacological agents, three specific medications have received regulatory approval for the treatment of DPN: Pregabalin, duloxetine and tapentadol. These drugs have undergone rigorous evaluation and have been found to provide benefits in managing DPN symptoms. In summary, while tight glucose control, exercise and a balanced diet are important aspects of DPN management, they may not be sufficient on their own. Patient education and pharmacological therapy, including approved medications like pregabalin, duloxetine

and tapentadol, play a crucial role in alleviating pain and improving the quality of life for individuals with DPN [10].

Anticonvulsant

Pregabalin, the first anticonvulsant to receive approval from the Food and Drug Administration (FDA) for the treatment of Diabetic Peripheral Neuropathy (DPN) and neuropathic pain after spinal cord injury, has shown promising results. It is believed that pregabalin improves the trafficking of α2-δ subunits, leading to a decrease in the expression of functional calcium channels. This mechanism contributes to its analgesic effects [11].

In addition to its pain-relieving properties, pregabalin has been found to possess anxiolytic abilities and beneficial effects on sleep quality and overall quality of life. These additional benefits contribute to improving the general condition of patients suffering from DPN. However, it's important to be aware of potential side effects, which may include dizziness, somnolence, peripheral edema, headache and weight gain [12].

Aside from pregabalin, gabapentin is the only other anticonvulsant drug approved for the treatment of DPN. Some clinical trials have suggested that both gabapentin and pregabalin offer better analgesic efficiency compared to tricyclic antidepressants or opioids. Another significant advantage of these drugs is their tolerability and lack of serious toxicity. Overall, pregabalin has gained FDA approval for treating DPN and neuropathic pain after spinal cord injury. Its ability to improve calcium channel trafficking, along with its analgesic effects, anxiolytic properties and positive impact on sleep and quality of life, makes it a valuable therapeutic option. However, it's crucial to monitor and manage potential side effects associated with pregabalin use. Additionally, gabapentin is an alternative anticonvulsant medication that has demonstrated efficacy in DPN treatment, with similar benefits and favorable tolerability.

Antidepressants

The first-line of drug treatment in Diabetic Peripheral Neuropathy (DPN) management involves the use of antidepressants. Duloxetine, a serotonin and norepinephrine reuptake inhibitor, is considered highly effective (rated level A) and is approved in the United States for the treatment of DPN. Its analgesic efficacy in DPN treatment has been observed to be maintained over a period of six months, making it a preferred medication for this condition. Common side effects of duloxetine include nausea, somnolence and dizziness [13].

Additionally, other Tricyclic Antidepressants (TCA) such as amitriptyline and nortriptyline have demonstrated effectiveness in treating DPN. However, it's important to note that these medications have different side effect profiles. Amitriptyline is associated with side effects such as postural hypotension, arrhythmias, congestive impairment, constipation and urinary retention, which may occur more frequently compared to nortriptyline treatment.

Overall, antidepressants, particularly duloxetine, play a crucial role as the first-line pharmacological approach in DPN management. Duloxetine's high efficacy, sustained analgesic effects and its FDA approval for DPN treatment make it a preferred choice. However, it's necessary to be mindful of potential side effects, including nausea, somnolence and dizziness. Other TCAs like amitriptyline and nortriptyline can also be effective, but their side effect profiles differ, with amitriptyline being associated with a higher incidence of certain adverse effects. Therefore, the choice of antidepressant medication should be based on individual patient factors and considerations [14].

Opioids

Opioids are typically considered as second or third-line treatments for Diabetic Peripheral Neuropathy (DPN). Drugs such as morphine and tramadol can be utilized to alleviate DPN-related pain, although they are accompanied by potential side effects including nausea, headache and somnolence [15].

Tapentadol, on the other hand, has demonstrated effectiveness in managing various types of chronic pain, including low back pain and DPN, while maintaining a tolerable safety profile. Clinical trials have reported that tapentadol can lead to a reduction of at least 30% in pain intensity for approximately 50% of patients who received this treatment.

While opioids such as morphine and tramadol can be utilized as alternatives for DPN management, their use is typically considered after other treatment options have been explored. This approach is due to the potential side effects and risks associated with long-term opioid use, such as dependence and addiction. Tapentadol, with its demonstrated efficacy and tolerable safety profile, provides a potential option for patients with DPN who require second or third-line treatment to alleviate their pain.

It is important to note that the decision to use opioids, including tapentadol, should be made in close consultation with a healthcare professional, taking into account the individual patient's specific circumstances, risks and potential benefits [16].

Capsaicin topical cream

The use of topical products offers several advantages, including a lower likelihood of adverse effects. Moreover, the potential for drug interactions is significantly reduced when utilizing topical local treatments, making them favorable options for patients with multiple medical conditions. One such option is capsaicin cream, which has demonstrated effectiveness in treating neuropathic conditions and has received approval for topical pain relief. Capsaicin cream, however, may be associated with certain adverse effects. These can include itching, stinging, erythema (skin redness), a transient burning sensation and initial pain at the site of application. It is important to note that these effects tend to diminish with repeated use [17].

By employing topical treatments like capsaicin cream, patients can experience targeted relief from pain without the systemic side effects often associated with oral medications. The localized application of these treatments minimizes the risk of drug interactions and offers an alternative for individuals with various medical conditions who may be more susceptible to systemic adverse effects. When considering the use of capsaicin cream or any other topical product, it is crucial to carefully follow the instructions provided and consult with a healthcare professional for proper guidance and management of potential adverse effects [18].

Lidocaine and alpha lipoic acid

Lidocaine patches serve as a peripheral analgesic, primarily acting locally with minimal systemic absorption. These patches are often used in combination with other analgesic drugs. Lidocaine functions as a sodium channel blocker, counteracting the hyper excitability of peripheral nociceptors that contributes to neuropathic pain. While

lidocaine patches are generally well-tolerated, some adverse effects may include local irritation, contact dermatitis and itching.

Alpha Lipoic Acid (ALA) acts as an antioxidant, which helps reduce oxidative stress-an important factor in the pathophysiology of diabetic neuropathy. ALA's antioxidant and anti-inflammatory actions contribute to an overall improvement in the symptoms of diabetic neuropathy. Compared to other drugs used for DPN treatment, ALA has relatively few side effects. The most common side effects associated with ALA include nausea and vomiting. The use of lidocaine patches provides localized relief from neuropathic pain while minimizing systemic exposure to the medication. By targeting sodium channels, lidocaine effectively reduces the hyper excitability of peripheral nociceptors. However, it's essential to be aware of potential local adverse effects such as irritation, dermatitis and itching. ALA, on the other hand, offers antioxidant and anti-inflammatory benefits in the management of diabetic neuropathy. By reducing oxidative stress, ALA helps improve symptoms associated with neuropathy. It is known for its favorable tolerability profile, with nausea and vomiting being the most commonly reported side effects. When considering lidocaine patches or ALA as part of the treatment plan for diabetic peripheral neuropathy, it is advisable to consult with a healthcare professional. They can provide guidance on proper usage, potential interactions with other medications and help monitor and manage any side effects that may arise [19].

Nursing care for diabetic neuropathy

It involves a comprehensive approach to managing the symptoms and complications associated with this condition. Here are some key aspects of nursing care for diabetic neuropathy:

Assessment and monitoring

- Regularly assess the patient's neuropathic symptoms, such as tingling, numbness, pain or loss of sensation.
- Monitor the patient's blood glucose levels and help them maintain optimal glycemic control.
- Assess the patient's skin integrity and foot health to identify any signs of ulcers, infections or wounds.

Education and self-care

- Educate the patient about the importance of foot care, including daily inspection, proper cleaning and wearing appropriate footwear.
- Teach the patient about managing blood glucose levels through diet, medication and lifestyle modifications.
- Provide guidance on managing pain and discomfort associated with diabetic neuropathy, including the use of prescribed medications or alternative therapies.

Foot care

- Encourage regular foot inspections and prompt reporting of any abnormalities, such as cuts, blisters or sores.
- Teach the patient proper foot hygiene techniques, including washing and drying feet thoroughly, avoiding hot water and using moisturizers.
- Emphasize the significance of regular podiatry visits and the importance of wearing well-fitting shoes and socks.

Pain management

- Assess the patient's pain level and implement appropriate pain management strategies, such as administering prescribed medications, providing heat or cold therapy or recommending relaxation techniques.
- Educate the patient about non-pharmacological pain management options, such as distraction techniques, relaxation exercises or Transcutaneous Electrical Nerve Stimulation (TENS).

Emotional support

- Offer emotional support and address any concerns or anxieties the patient may have related to their diabetic neuropathy.
- Encourage participation in support groups or counseling services to connect with others facing similar challenges.

Collaboration and referrals

- Collaborate with other healthcare professionals, such as physicians, podiatrists, physical therapists or pain management specialists, to ensure comprehensive care.
- Make appropriate referrals for specialized care, such as wound management or nerve conduction studies.

It is to be remembered that, nursing care for diabetic neuropathy should be individualized to meet the specific needs of each patient. Regular assessment, education and collaboration with the healthcare team are crucial to promoting optimal management and improving the patient's quality of life [20].

Conclusion

Diabetic Peripheral Neuropathy (DPN) continues to be a prevalent and debilitating complication of diabetes. Effective treatment strategies should primarily focus on identifying risk factors, implementing comprehensive diabetic foot care programs, providing symptom relief to enhance the quality of life and emphasizing patient education as a crucial component. However, it is worth noting that advancements in medical research and innovative approaches hold promise for the future management of DPN. Emerging approaches, such as gene therapy and targeted delivery of antioxidant therapy, may present the most favorable potential for reversing this common and disabling complication associated with diabetes. These novel therapeutic avenues offer hope for addressing the underlying mechanisms of DPN and potentially reversing its effects. Given that approximately 50% of adults with diabetes are likely to develop peripheral neuropathy at some point in their lives, it is imperative to implement more rigorous screening protocols and proactive management strategies. By adopting a diligent approach to screening, healthcare professionals can identify DPN at its early stages and initiate timely interventions to mitigate complications. This proactive approach not only improves patient outcomes but also helps reduce the overall burden on healthcare resources associated with managing this complex condition. Efforts to combat DPN should encompass a multidisciplinary approach involving healthcare providers, researchers and patients themselves. By focusing on risk factor identification, comprehensive foot care, symptom relief, patient education and exploring innovative treatment modalities, it is possible to enhance the management of DPN and minimize its impact on individuals with diabetes.

References

1. Guariguata L, Whiting DR, Hambleton I, Beagley J, Linnenkamp U, et al. (2014) Global estimates of diabetes prevalence for 2013 and projections for 2035. Diabetes Res Clin Pract 103: 137-149.

2. Zhou H, Zhang W (2019) Gene expression profiling reveals candidate biomarkers and probable molecular mechanism in diabetic peripheral neuropathy. Diabetes Metab Syndr Obes 12: 1213-1223.
3. Wc K (2002) Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med 346: 393-403.
4. Toeller M, Buyken AE, Heitkamp G, Berg G, Scherbaum WA, et al. (1999) Prevalence of chronic complications, metabolic control and nutritional intake in type 1 diabetes: Comparison between different European regions. Horm Metab Res 31: 680-685.
5. Almuhannadi H, Ponirakis G, Khan A, Malik RA (2018) Diabetic neuropathy and painful diabetic neuropathy: Cinderella complications in South East Asia. J Pak Med Assoc 68: 85-89.
6. Ashok S, Ramu M, Deepa R, Mohan V (2002) Prevalence of neuropathy in type 2 diabetic patients attending a diabetes centre in South India. Japi 50:546-550.
7. Ankush, Dias A, Gomes E, Dessai A (2016) Complications in advanced diabeticsin a tertiary care centre: A retrospective registry-based study. J Clin Diagn Res 10: OC15-OC19.
8. Sosale B, Sosale AR, Mohan AR, Kumar PM, Saboo B, et al. (2016) Cardiovascular risk factors, micro and macrovascular complications at diagnosis in patients with young onset type 2 diabetes in India: CINDI 2. Indian J Endocrinol Metab 20: 114-118.
9. Umamahesh K, Vigneswari A, Thejaswi GS, Satyavani K, Viswanathan V (2014) Incidence of cardiovascular diseases and associated risk factors among subjects with type 2 diabetes–an 11-year follow up study. Indian Heart J 66: 5-10.
10. Viswanathan V, Thomas N, Tandon N, Asirvatham A, Rajasekar S, et al. (2005) Profile of diabetic foot complications and its associated complications-a multicentric study from India. JAPI 53: 933-936.
11. Ziegler D (2008) Treatment of diabetic neuropathy and neuropathic pain: How far have we come? Diabetes Care 31: S255–S261.
12. Armstrong DG, Chappell AS, Le TK, Kajdasz DK, Backonja M, et al. (2007) Duloxetine for the management of diabetic peripheral neuropathic pain: Evaluation of functional outcomes. Pain Med 8: 410-418.
13. Feldman EL, Nave KA, Jensen TS, Bennett DL (2017) New horizons in diabetic neuropathy: Mechanisms, bioenergetics and pain. Neuron 93: 1296-1313.
14. Sajic M (2014) Mitochondrial dynamics in peripheral neuropathies. Antioxid Redox Signal 21: 601-620.
15. Chokroverty S, Reyes MG, Rubino FA, Tonaki H (1977) The syndrome of diabetic amyotrophy. Ann Neurol 2: 181-194.
16. Shakher J, Stevens MJ (2011) Update on the management of diabetic polyneuropathies. Diabetes Metab Syndr Obes 4: 289-305.
17. Brownlee M (2001) Biochemistry and molecular cell biology of diabetic complications. Nature 414: 813-820.
18. Singh RB, Barden A, Mori T, Beilin L (2001) Advanced glycation end-products: A review. Diabetologia 44: 129-146.
19. Vinik AI, Erbas T, Park TS, Stansberry KB, Scanelli JA, et al. (2001) Dermal neurovascular dysfunction in type 2 diabetes. Diabetes Care 24: 1468-1475.
20. Onakpoya IJ, Thomas ET, Lee JJ, Goldacre B, Heneghan CJ (2019) Benefits and harms of pregabalin in the management of neuropathic pain: A rapid review and meta-analysis of randomised clinical trials. BMJ Open 9: e023600.