

Diabetic Peripheral Neuropathy: Evaluation and Management

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ABSTRACT

Diabetes is a leading cause of peripheral neuropathy. Fifty percent of patients with diabetic peripheral neuropathy (DPN) will have pain. All patients with diabetes should be screened annually for neuropathy by performing a neuropathy-specific history and physical examination. The Michigan Neuropathy Screening Instrument can easily be used to screen patients in the primary care setting. Tight glycemic control is the most important intervention for the treatment of DPN. For the patient with painful DPN, tricyclic antidepressants are considered the first line of treatment. Many patients may require a combination of pharmacologic and nonpharmacologic interventions.

Keywords: diabetes, painful diabetic peripheral neuropathy, peripheral neuropathy, screening, treatment

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Diabetes is 1 of the leading causes for the development of peripheral neuropathy.¹ Approximately 50% of patients with diabetes will develop peripheral neuropathy,^{2,3} and 50% of those who develop diabetes peripheral neuropathy (DPN) will have painful symptoms.² DPN is frequently underreported and undertreated and can lead to an increased risk for morbidity and mortality and decreased quality of life.^{1,3} DPN is associated with the development of foot problems and is 1 of the leading causes of amputations and the development of foot ulcers.¹ The health care cost associated with DPN is approximately \$10.9 billion per year in the United States.³ DPN is most prevalent in patients with type 2 diabetes and is frequently underreported and undertreated in this population.^{1,2} Many patients with diabetes will present with nondiabetic neuropathies or be asymptomatic.⁴ It is essential for patients with diabetes to be screened and treated early for DPN in order to minimize complications and improve overall quality of life. The purpose of this article is to discuss what is currently known about DPN as well as outline recommendations for the screening, treatment, and management of patients with DPN.

PATHOPHYSIOLOGY: CLINICAL FEATURES

DPN can be defined as the presence of symptoms and/or signs of peripheral nerve dysfunction after the exclusion of other causes in patients with diabetes.^{4,5} DPN results from progressive nerve fiber loss, and in early stages small nerve fibers are affected, with large fibers being involved later on as the disease progresses.¹ The change in the nerve fibers is what produces the symptoms of paresthesia and pain.¹

Pathogenesis

The exact cause of DPN is unknown. DPN can result from multiple different biochemical changes, with chronic hyperglycemia being the major contributor to the development of the metabolic events that influence these changes.² A combination of axonal injury because of hyperglycemia, insulin resistance, toxic adiposity, endothelial injury, and microvascular dysfunction can lead to nerve ischemia and contribute to the development of DPN.² In addition, changes in vascular factors, neurostructural mechanisms, and metabolic interactions can all contribute to the development of DPN. Metabolic interactions can include 1) changes in sodium and calcium channel distribution and expression, 2) varied

neuropeptide expression, 3) peripheral sensitization, 4) altered blood flow, 5) axonal atrophy, 6) small fiber damage, 7) glycemic flux, 8) an increase in peripheral nerve epineural blood flow, 9) altered foot skin microcirculation, 10) reduced intraepidermal nerve fiber density, 11) increased thalamic vascularity, and 12) autonomic dysfunction.^{2,6}

Presentation

Individuals with DPN usually present with a type of sensory neuropathy, either acute sensory or chronic sensorimotor DPN.^{4,7} Acute sensory neuropathy (ASN) usually develops after an episode of ketoacidosis or when there has been a sudden change in glycemic control.^{4,7} ASN usually has a rapid onset, and patients will present with complaints of severe burning pain and aching with nocturnal exacerbations.^{4,6,7} The severity of symptoms is usually moderate to severe.⁷ Weight loss is commonly observed, and individuals with ASN may have allodynia upon sensory testing and a normal motor examination. Occasionally, these individuals will have decreased ankle reflexes.⁷ Patients who present with ASN will usually have a complete recovery within 12 months. Tight glucose control is essential in the treatment of this condition.⁷

Unlike patients with ASN, chronic sensorimotor neuropathy has a more gradual and insidious onset and is the most common presentation in patients with type 2 diabetes.^{4,7} Symptoms usually start in the toes and gradually move proximally. Once lower limbs are affected, the symptoms may move to the upper limbs.⁵ Symptoms can include burning pain, paresthesia numbness, and possibly weight loss. The severity of symptoms can range from 0 or absent to severe, with most individuals having moderate symptoms. A stocking and glove pattern of sensory loss and absent ankle reflexes may be noted. Symptoms can occur intermittently for several years.⁷

Painful symptoms are experienced by 50% of individuals with chronic DPN.⁶ Individuals will commonly describe pain as a burning sensation, feeling like an electrical shock, stabbing, or knifelike. Pain most commonly appears in the feet (96% of individuals), balls of the feet (69%), toes (67%), dorsum of the foot (54%), hands (37%), calves and

heals (37%), and plantum of the foot (39%).⁸

Individuals with DPN may also report pain with touching or allodynia and/or discomfort with frequent walking described as feeling like they are walking on marbles or walking barefoot on hot sand. Altered temperature perceptions, such as feet feeling very warm or cold, and having nonspecific aching or cramping feelings in feet or legs may also be reported.⁶ Individuals will frequently report an increase in pain at night, which results in an increase in sleep disturbances.⁶

Risk/Contributing Factors

Poor glycemic control is the main factor that contributes to the development of DPN. The risk of developing DPN also increases over time; the longer the person has had diabetes, the more likely they are to develop DPN. Other factors that can contribute to the development of DPN include a history of hypertension, hyperlipidemia, and cigarette smoking.^{2,3} Uncontrolled hypertension can accelerate the onset of DPN and is 1 of the main cardiovascular risk factors for the development of DPN. Hyperlipidemia and smoking increase the risk for the development of microvascular and microvascular complications associated with diabetes.⁹

Health Consequences. Neuropathic pain is the number one negative health consequence that results from DPN. Neuropathic pain negatively impacts the overall quality of life and the ability to function.^{1,10} Many individuals with painful DPN will experience sleep disturbances, anxiety, and/or depression. Overall, individuals with painful DPN will rate their health status as being substantially lower than individuals with nonpainful DPN.¹⁰

DPN has also been identified as 1 of the leading causes of amputations and foot ulcers in individuals with diabetes.¹ Individuals who develop DPN have an increased morbidity and mortality risk.^{3,5} Individuals with DPN are at a greater risk for injuries because of a combination of factors including an impact on functional ability because of loss of foot sensation; poor eyesight, which is sometimes associated with aging and diabetes; and the presence of other comorbidities.¹ Based on this increased risk and the fact that DPN frequently goes underreported

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