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Early Onset Of Diabetes Is Associated With Worse Outcomes Of Diabetes Neuropathy

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Abstract
Diabetes mellitus results from a failure of either the secretion or the action of insulin. An additional factor is an over secretion of glucagon. Diabetic neuropathies are a lineage of nerve illness caused by diabetes. Diabetic neuropathy is a major cause of neuropathy worldwide and may lead to amputations. Diabetic neuropathy damages nerves in legs and feet. Diabetic neuropathy is a serious and common complication of type 1 and type 2 diabetes.Long-term high blood sugar levels causes nerve damageMany diabetics suffer from neuropathy, also referred to as diabetic nerve damage. Higher than normal sugar levels caused by diets high in carbohydrates and incorrect nutrition can lead to diabetic neuropathy. Furthermore, many diabetes medications can make the problems worse. Obesity is the second most risk factor for neuropathy after diabetes.

Keywords: Diabetic neuropathic pain, Plantar soft tissue, Diabetic foot, Plantar pressure, Peripheral neuropathy , Diabetes

Introduction

People with diabetes can gradually lose the protective sensation of pain in their feet due to peripheral neuropathy. (1,2)

Diabetic foot ulcers are open wounds that have limited capacity for healing, they can get infected and even lead to amputation (3)

The main role of plantar soft tissue is to act as a shock absorber, to dampen the effect of ground reaction forces during weight-bearing activities by promoting more even distribution of plantar loads (4)

Mechanical behavior of plantar soft tissue can significantly undermine the tissue's ability to fulfil its mechanical role vulnerable to overload injury and ulceration (5)

People with diabetes and neuropathy who tend to load their feet more heavily also tend to have plantar soft tissues with lower hardness (6)

People with diabetes often have one or more complications, including cardiovascular disease or microvascular disease such as chronic kidney disease, diabetic retinopathy, and neuropathy (7,8). The development of neuropathy was also associated with potentially modifiable cardiovascular risk factors such as serum lipids, hypertension, body mass index, and cigarette smoking (9).

DM and insulin resistance (IR) are associated with the development of cardiovascular and nervous diseases (10)

The development of these disorders reflects complex pathological processes in which the oxidative stress (OS) caused by reactive oxygen species (ROS) (11,12).The prevalence of neuropathy in diabetic patients is about 30%, whereas up to 50% of patients will certainly develop neuropathy during the course of the disease (13,14). Elevated intracellular levels of glucose lead to advanced glycation end-products formation and polyol pathway activation, resulting in subsequent formation of ROS (15) The most common symptom of DPN is neuropathic pain, which occurs in up to 50% of people with DPN and is the most frequent reason for seeking medical care(16) People with DPN are also seven times more likely to develop foot ulcerations (17)

Types

Autonomic nervous system involvement may cause an impaired sympathetic response to hypoglycemia.

As a result of it, the patient no longer experiences the classical warning symptoms.

Motor,sensory autonomic nerves may be involved in different combinations. In diabetes mellitus,different peripheral neuropathies are commonly associated.

Diabetes is the supreme cause of peripheral neuropathy..Uncontrolled diabetes and older in people,the peripheral neuropathy takes upper hand.

The most common form of diabetes neuropathy is distal sensory- motor polyneuropathy. Loss of ankle jerks are observed in uncontrolled diabetes patients.

1. Diabetes amylotrophy or motor neuropathy is mainly a proximal form of neuropathy. This is very common in older diabetic patients.Loss of knee reflexes occur. The patient recovers to normal,after control of diabetes.

2. in sensory neuropathy, patients complain of numbness of the feet,dorsum of the feet and spreading up on legs.and finally to fingers. With the development of sensory ataxia, the patient loses vibration sense .Glove and stocking sensory loss is also common.Trophic lesions,ulcers and Charcot joints developed. Many patients develop pupillary abnormalities.

3. Autonomic neuropathy patients show impotency. Nerve supply is impaired to the intestine and produces diarrhoea. Cardiovascular reflex disturbances are observed in 25 % patients. Tachycardia,burning micturition,sweating are the common manifestations in autonomic neuropathy. The Guillain-Barre Syndrome (Acute postinfectious Polyneuropathy). Immunological pathogenesis resulting in multifocal demyelination in spinal roots and peripheral nerves.The clinical features of this syndrome are,pain in back ache,tingling affecting the distal part of the limbs and ascending proximally. In 50% of patients motor symptoms predominate,with weakness,which may be profound and rapidly progressive and which often affects proximal more than distal limb musculature.

What are the symptoms of diabetes neuropathy?

The common symptoms of diabetes neuropathy are loss of sense and sensitivity of touch, loss of coordination during walking, burning sensation in feet, at night,numbness and pain in hands and feet,weakness of muscle,nausea, vomiting and anorexia,diarrhea ,constipation, dizziness, sweatin,incomplete bladder emptying, erectile dysfunction, dry vagina,visual problems,and increased heart rate.

What causes diabetic neuropathy?

Type-1-Diabetes-- β-cell destruction (mostly immune mediated) and absolute insulin deficiency; onset most common in childhood and early adulthood

Type-2-Diabetes-- Most common type, various degrees of β-cell dysfunction and insulin resistance; commonly associated with overweight and obesity.

Diabetic neuropathy is specifically due to high blood sugar levels constantly holding up over a long period . Other associated reasons are, high cholesterol levels that harm blood vessels, lifestyle factors,like smoking,alcohol and excess fatty junk

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food.Deficiency of vitamin B-12 produce neuropathy. Metformin, can decrease levels of vitamin B-12.

Can you reverse diabetes neuropathy?

Nerve damage in this can't be reversed. The reason is nerve tissue in the body can't be repaired women damaged.

Clinical features of diabetic neuropathy

Persistent burning or dull pain

1. Numbness to feel pain or temperature changes.
2. Tingling or burning sensation.
3. Electrical shock like,stabbing ,evoked pain
4. Sharp pains or cramps.
5. Increased sensitivity to touch — for some people, even a bed sheet's weight can be painful.
6. Serious foot problems, such as ulcers, infections, and bone and joint pain.

Pathogenesis of diabetes neuropathy

The diabetic neuropathies preferentially affect sensory neurons.unmyelinated small sensory axons are chiefly liable to damage. The longest sensory axons are damaged first. The underlying pathogenesis of diabetic neuropathy remains incompletely understood. Persistent hyperglycemia , weakened insulin , hyperlipidemia, and adiposity trigger changes in multiple biochemical pathways that result in damage to mitochondria and an overall increase in oxidative stress and inflammation that ultimately results in nerve injury.

Diabetes is associated with a microangiopathy, and nerve biopsy samples from patients with diabetic neuropathy demonstrate thickened endoneurial blood vessel walls.(18)

The ultimate result is peripheral nerve ischemia owing to endothelial injury and microvascular dysfunction. To compound the ongoing nerve damage, peripheral nerve repair is also impaired in diabetes.

The Diabetes Control and Complications Trial showed that more intensive glucose control prevented the onset and progression of both peripheral and cardiac autonomic neuropathy in patients with T1DM. In fact, there was a 64% reduced risk of peripheral neuropathy and a 45% reduced risk of cardiac autonomic neuropathy over 5 years.(19)

Complications of diabetes neuropathy

The condition usually develops slowly, sometimes over the course of several decades.Hypoglycemia unawareness,Loss of a toe, foot or leg,Urinary tract infections and urinary incontinence,Sharp drops in blood pressure, Digestive problems, Sexual dysfunction and Increased or decreased sweating.In grave peripheral neuropathy, patient may be subjected to infections. Unsatisfactory wound healing can lead to ablation.

How diabetic neuropathy diagnosed?

Fasting plasma glucose and haemoglobin A1c are crucial diabetic neuropathy laboratory screening assays. Imaging tests are rarely useful in diagnosing or treating diabetic neuropathy. In the right clinical situation, an MRI of the cervical, thoracic, and/or lumbar areas might help rule out other causes of symptoms that resemble diabetic neuropathy. Electrophysiologic testing should be included in the assessment of diabetic neuropathy, according to several consensus panels. Both nerve conduction screening and needle EMG of the most distal tissues commonly affected are included in an acceptable array of electrodiagnostic tests.

Sensitivities and specificities of some of the clinical screening tools are as follows:

Hemoglobin A1c values are likely to be high in individuals with chronic diabetic neuropathies, and can be used to ensure that all aspects of recent diabetes treatment. The intensity of the elevation does not strongly coincide with the intensity of the nerve illness, especially in asymmetrical disorders. In borderline circumstances, a 3-hour glucose tolerance test is more sensitive. Screening for kidney and proteinuria can also be done with a urinalysis.

Some additional investigations which are usually advised are electromyography and nerve conduction studies,conventional nerve conduction velocity studies,needle electromyography and electrophysiological studies.

Plexus MRI may be beneficial in patients with radiculoplexus neuropathy syndromes to rule out other issues (such as tumours). CT myelography is an option to MRI for individuals who cannot get an MRI to rule out compressive diseases and other abnormalities in the spinal canal. Brain imaging,

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usually with an MRI, is beneficial in cranial nerve palsies to rule out intracranial aneurysms, compressive diseases, and infarcts.

To detect and quantify cardiac autonomic neuropathy, scintigraphic techniques are performed (for research purposes). Radiolabeled norepinephrine analogues, 123I-metaiodobenzylguanidine (MIBG), and 11C-hydroxyephedrine are among the techniques used. These chemicals are actively taken up by the heart's adrenergic nerve terminals. When this approach is used with single-photon emission computed tomography (SPECT) scanning, it is possible to detect diminished cardiac innervation. Electrocardiography may indicate prolongation of the QT interval. This is actually secondary to disproportion between right and left heart sympathetic innervation. This prolongation is thought to increase risk of arrhythmias. A screening ECG is always advisable for patients with longstanding DM.A nerve biopsy, usually of the sural nerve, can be taken to confirm and aid to define the neuropathic stage (ie, mild, moderate, severe). However, because this is an intrusive treatment, it runs the danger of causing chronic pain, numbness, and cold sensitivity along the sural nerve's distribution. As a result of the availability of NCV/EMG and QST, sural nerve biopsy is no longer required for diagnostic purposes.

Diabetic neuropathy should be managed from the moment diabetes is diagnosed. Because failing to detect diabetic polyneuropathy can result in catastrophic repercussions, including incapacity and amputation, and the primary care physician should be on the lookout for the development of neuropathy, or even its occurrence at the time of initial diabetes diagnosis. Recognize any person with medical evidence of diabetic peripheral neuropathy to be at danger for foot ulcers, and educate them on how to properly care for their feet. Refer the patient to a podiatrist if necessary. Patients with an inflamed diabetic foot ulcer or gangrene should be admitted. Diabetic peripheral neuropathy patients should undergo additional follow-up, with a focus on foot inspection to underline the importance of regular self-care. Several studies have demonstrated that providing frequent foot inspections and reinforcing the educational emphasis on foot care can greatly lower incidence of ulceration and even amputation.

Diabetic Polyneuropathy Biomarkers

The biomarker data showing which cytokines are involved in DPN progression are limited.

High serum uric acid (UA), γ-glutamyltransferase (GGT), C-reactive protein (CRP), fibrinogen levels, which are considered to be predictive of atherosclerosis, have also been associated with DPN **(20,21)**

Uric acid (UA), C-reactive protein (CRP), γ-glutamyltransferase (GGT), erythrocyte sedimentation rate (ESR), and fibrinogen increased levels may affect neuropathy by increasing oxidative stress through mechanisms related to inflammation and vascular impairment in diabetes mellitus (DM) patients, Although levels of UA, CRP, GGT, fibrinogen, and ESR were reported to be elevated in DPN patients, these biochemical parameters were not detected as markers for DPN.

Increased CRP levels in DPN patients with neuropathic pain may reflect the inflammatory mechanisms involved in the pathogenesis of pain associated with DPN. The elevation of serum CRP levels in DPN patients with neuropathic pain is a remarkable finding. This condition indicates that CRP in DPN patients is closely associated with neuropathic pain. **(22)**

How diabetic neuropathy treated?

The most important treatment for reducing the evolution of neuropathy is tight and stable glycemic control. Because fast shifts from hypoglycemia to hyperglycemia have been linked to the onset and aggravation of neuropathic pain, glycemic control stability may be just as significant as the actual level of control in neuropathic pain relief.

Certain B vitamin supplements are found to be effective and are usually prescribed in an attempt to reduce the symptoms of diabetic neuropathy.

Prevention of diabetes neuropathy

Any new drug which is liable to cause diabetes neuropathy must be used with care and industrial hazards should be avoided by protective clothing,exhaust ventilation and other techniques advised by the industrial medical officer.When polyneuropathy has developed as a result of exposure to a toxic substance,the first step is to remove the patient from further exposure.When the cause is neutritional,every effort should be made to restore the

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original body weight,plenty of protein is supplemented by generous doses of the vitamin b complex.If the cause is metabolic the appropriate treatment must be initiated with out delay,eg.diabetes.(23)

Management of Diabetic Neuropathy

Intensive glycemic control is effective for the primary prevention of Neuropathy with type 1 diabetes (24,25).

Insulin treatment persist for over a decade for the primary prevention of neuropathy (26). In type 2 diabetes, BG levels are associated with a reduced frequency of neuropathy (27).

No other clearly efficacious disease-modifying treatments are currently available (28).

There are insufficient comparative studies to recommend which oral medication should be used first line, although the primary use of opioids for PDN, despite clinical trial evidence for pain efficacy (29)

Lifestyle intervention of diabetes neuropathy

Diabetic peripheral neuropathy (DPN) is the alarming aggravation resulting in a enormous economic burden for diabetes care. More than 50% diabetes develop neuropathy. Capsaicin cream, applied to the skin, can reduce pain sensations in some people. Alpha-lipoic acid. Acetyl-L-carnitine can be applied. Take good care of your feet. Check your feet every day. Protect your feet. Get special shoes if needed. Be careful with exercising. Get regular physical activity.Lose weight if you're overweight.Limit or avoid alcohol.Stop smoking or don't start. Follow a healthy eating plan.

Summary

DPN is a common and costly disease. Over the past decade, there have been great strides in understanding the underlying pathophysiology and the interplay of metabolic risk factors. Hostile glycemic control is an effective disease-altering strategy in type 1 diabetes but not in type 2 diabetes.

Conclusion

Research has been focused on mechanisms of diabetic neuropathy,but treatment options to eliminate the initial causes are still be short off. The impaired glucose metabolism in diabetes leads to hypoxia and acidosis, which trigger other abnormalities responsible for mitochondrial and bioenergetic dysfunction by increasing ROS production to cause membrane hyperexcitability and reduction of ATP production."Early onset is associated with worse outcomes".Early and accurate diagnosis allows for adequate treatment, preventing progression of neuropathy and severe complications. exercise and medical and surgical weight loss are all new therapeutic cource of action for neuropathy. New diagnostic tests like (IENFD and CCM) are available, and well accepted as neuropathy research source than as clinically functional devices.

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