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DIABETIC NEUROPATHY: IS A SERIOUS CHALLENGE OR NOT?

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ABSTRACT
Diabetes Mellitus (DM) is one of those threatening problem increasing with modernization, where the current administration of therapeutic options are failing and new therapeutic drugs are required. The prevalence of diabetes has more than tripled over the past 30 years and includes a growing prevalence amongst people residing in low and middle income countries. Despite a large armamentarium of drug therapies for diabetes, the mortality associated with it remains significant. According to the international diabetes federation, 382 million people worldwide are currently affected by diabetes, one of the leading causes of neuropathy. The distal symmetrical polyneuropathy(DSPN) is the commonest clinical form of diabetic neuropathy. Generally, DSPN affects the toes and distal foot, but slowly progresses proximally to involve the feet and legs in a stocking distribution. It is also characterized by a progressive loss of nerve fibers affecting both the autonomic and somatic divisions, thereby diabetic retinopathy and nephropathy can occur. Foot ulceration and painful neuropathy are the main clinical consequences of DSPN, linked with higher morbidity and mortality.

KEYWORDS: Diabetes Mellitus (DM), DSPN.

INTRODUCTION
Diabetes includes a group of metabolic disorder that share the phenotype of kyperglycemia. Diabetes Mellitus defined by any one the following criteria:

1. Common Symptoms of Diabetes (polyuria, polydipsia, weight loss) plus random blood glucose _> 200mg/dl.
2. Fasting plasma glucose_> 126mg/dl (fasting is defined as no calorie intake for at least 8 hrs).
3. Plasma glucose _> 200mg/dl (2 hrs after an oral glucose tolerance test with 75 gm of glucose. Common Symptoms of Diabetes (polyuria, polydipsia, weight loss) plus random blood glucose _> 200mg/dl.
4. Fasting plasma glucose_> 126mg/dl (fasting is defined as no calorie intake for at least 8 hrs).
5. Plasma glucose _> 200mg/dl (2 hrs after an oral glucose tolerance test with 75 gm of glucose.

Normally, insulin allows glucose to travel into cells. There, it is used for energy and stored as glycogen. Insulin also stimulates protein synthesis and free fatty acid storage in adipose tissues. Insulin deficiency blocks tissues access to essential nutrients for fuel and storage. The pathophysiology behind each type of diabetes differs.

Neuropathy refers to any condition that damages nerve cells. These cells play a critical role in touch, sensation, and movement. Diabetic Neuropathy refers to damage of nerves that's caused by diabetes. Neuropathy is one of the common effects of diabetes. Diabetic neuropathies are a family of nerve disorders caused by diabetes. People with diabetes can, over time, develop nerve damage throughout the body. Some people with nerve damage have no symptoms. Others may have symptoms such as pain, tingling, or numbness—loss of feeling—in the hands, arms, feet, and legs. Nerve problems can occur in every organ system, including the digestive tract, heart, and sex organs.

Diabetic neuropathy is a common complication of both type 1 and type 2 diabetes patients, which affects over 90% of the diabetic patients. Although pain is one of the main symptoms of diabetic neuropathy, its pathophysiological mechanisms are fully known. It is widely accepted that the toxic effects of hyperglycemia play an important role in the development of this complication, but several other hypothesis have been postulated. The management of diabetic neuropathic pain consists basically in excluding other causes of painful peripheral neuropathy, improving glycemic control as a prophylactic therapy and using medications to alleviate pain.

Diabetic Neuropathic Pain (DNP) is characterized by tingling, burning, sharp, shooting, and lancinating or even as electric shock sensations. It is usually considered

moderate to severe and often worse at night, causing sleeping disturbs. The pain can be constant and accompanied of cutaneous allodynia, which can substantially affect the quality of the life of patients, impacting the ability to perform daily activities and having a negative influence on mood. The pain may also be a reason of withdrawal of recreational and social activities and may be associated with depression.

DISCUSSION

Diabetic neuropathy can be classified as peripheral, autonomic, proximal, or focal. Each affects different parts of the body in various ways.

Peripheral neuropathy, the most common type of diabetic neuropathy, causes pain or loss of feeling in the toes, feet, legs, hands, and arms.

Autonomic neuropathy causes changes in digestion, bowel and bladder function, sexual response, and perspiration. It can also affect the nerves that serve the heart and control blood pressure, as well as nerves in the lungs and eyes. Autonomic neuropathy can also cause hypoglycemia unawareness, a condition in which people no longer experience the warning symptoms of low blood glucose levels.

Proximal neuropathy causes pain in the thighs, hips, or buttocks and leads to weakness in the legs.

Focal neuropathy results in the sudden weakness of one nerve or a group of nerves, causing muscle weakness or pain. Any nerve in the body can be affected.

Peripheral neuropathy, also called distal symmetric neuropathy or sensorimotor neuropathy, is nerve damage in the arms and legs. Feet and legs are likely to be affected before hands and arms. Many people with diabetes have signs of neuropathy that a doctor could note but no symptoms felt by patient. The symptoms get worse at night.

Autonomic neuropathy affects the nerves that control the heart, regulate blood pressure, and control blood glucose levels. Autonomic neuropathy also affects other internal organs, causing problems with digestion, respiratory function, urination, sexual response, and vision. In addition, the system that restores blood glucose levels to normal after a hypoglycemic episode may be affected, resulting in loss of the warning symptoms of hypoglycemia.

Proximal neuropathy, sometimes called lumbosacral plexus neuropathy, femoral neuropathy, or diabetic amyotrophy, starts with pain in the thighs, hips, buttocks, or legs, usually on one side of the body. This type of neuropathy is more common in those with type 2 diabetes and in older adults with diabetes. Proximal neuropathy causes weakness in the legs and the inability to go from a sitting to a standing position without help. Treatment for weakness or pain is usually needed. The length of the recovery period varies, depending on the type of nerve damage. Focal neuropathy is painful and unpredictable and occurs most often in older adults with diabetes.

However, it tends to improve by itself over weeks or months and does not cause long-term damage. People with diabetes also tend to develop nerve compressions, also called entrapment syndromes. One of the most common is carpal tunnel syndrome, which causes numbness and tingling of the hand and sometimes muscle weakness or pain. Other nerves susceptible to entrapment may cause pain on the outside of the shin or the inside of the foot.

Screening and Tests

128 Hz tuning fork or 10 g monofilament at diagnosis and annually in people with type 2 DM and after 5yr duration of type 1 DM.

Diagnosis Laboratory tests that may be helpful include the following:
Fasting plasma glucose
Hemoglobin A1c and Complete blood count
Complete metabolic panel (electrolytes and liver function panel)
Vitamin B-12 and folate levels
Thyroid function tests
Erythrocyte sedimentation rate
C-reactive protein
Serum protein electrophoresis with immune-fixation electrophoresis
Antinuclear antibody
Anti-SSA and SSB antibodies
Rheumatoid factor
Paraneoplastic antibodies
Genetic screens
Hematology screen (for anemia)
Sequential multiple analysis-7 (renal function and electrolyte imbalances) complete metabolic panel (CMP)

Other diagnostic modalities that may be considered are as follows:
Electromyography and nerve conduction velocity testing
Electro physiologic studies
Magnetic resonance imaging
Computed tomography (including single-photon emission computer tomography)
Nuclear imaging
Doppler imaging
Micro-dialysis
Electrocardiography
Nerve and skin biopsy (now rarely recommended for clinical purpose

Treatment

According to the current guidelines from the American Academy of Neurology, the most effective medications for treating painful diabetic neuropathy (PDN) includes:

Pregabalin (Lyrica)
Gabapentin (Neurontin)
Duloxetine (Cymbalta)
Other suggested treatment may be considered are:
Opioids, also known as narcotics
Topical medications, like Capsaicin(Qutenza)
Electrical nerve stimulation

Glucose management is a highly effective way of reducing symptoms and the progression of neuropathy .Managing glucose levels should always be apart of your treatment plan.

Nerve conduction studies or electromyography are also sometimes used to help determine the type and extent of nerve damage. Nerve conduction studies check the transmission of electrical current through a nerve. Electromyography shows how well muscles respond to electrical signals transmitted by nearby nerves. These tests are rarely needed to diagnose neuropathy.

Management

Key components of the management of diabetic neuropathy include the following:
Foot care, including regular follow-up, patient education, and referral as appropriate
Tight, stable glycemic control (most important for slowing progression of neuropathy)
Pain management (eg, with pregabalin, gabapentin, sodium valproate, dextromethorphan, morphine sulfate, tramadol, oxycodone, duloxetine, topical capsaicin, transdermal lidocaine).

Treatment of diabetic gastroparesis (eg, with erythromycin, cisapride [not available in the United States], metoclopramide, polyethylene glycol 3350, tegaserod [currently available only on an emergency basis]).

Experimental therapies include aldose reductase inhibitors, alpha-lipoic acid, actovegin, and spinal cord stimulators.

Treatment of autonomic dysfunction must address the following:
Erectile dysfunction
Orthostatic hypotension
Gustatory sweating

Surgical treatment may be considered as follows:
Aggressive debridement or amputation for recalcitrant foot necrosis or infection
Jejunostomy for intractable gastroparesis
Implantation of a penile prosthesis for ongoing impotence
Bracing, special boots, or, in some cases, surgery for Charcot foot
Pancreatic transplantation for diabetes with end-stage renal diseases

First line drugs for pain relief include anticonvulsants, such as pregabalin and gabapentin and antidepressants, especially those that act to inhibit the reuptake of serotonin and noradrenaline. In addition, there is experimental and clinical evidence that opioids can be helpful in pain control, mainly if associated with first line drugs. Other agents, including for topical application such as capsaicin cream and lidocaine patches have also been proposed to be useful as adjuvants in control of diabetic neuropathic pain, but the clinical evidence is insufficient to support their use. In conclusion, a better understanding of mechanisms underlying diabetic neuropathic pain will contribute to the search of new therapies, but also to the improvement of the guidelines to optimize pain control with the drugs currently available.

CONCLUSION

Diabetes causes a broad spectrum of neuropathic complications, including acute and chronic forms affecting each level of the peripheral nerve, from the root to the distal axon. Nerve damage from diabetes cannot be reversed. This is because the body cannot naturally repair nerve tissues that have been damaged. However, researchers are investigating methods to treat nerve damage caused by diabetes. Necessary Strategies must be implemented to target these modifiable risk factors to improve major public health initiatives.

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