Review

REHABILITATION IN DIABETIC NEUROPATHY

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DIABETIC NEUROPATHY

Diabetic neuropathy is the most common complication of type 1 and type 2 diabetes. Of all complications of diabetes, neuropathy causes the greatest morbidity and it decreases the patient's quality of life. Diabetic neuropathy is found around the world in 20-30% of individuals with type 2 diabetes. In the United States of America, diabetic neuropathy occurs in 10-20% of patients with newly diagnosed diabetes and its prevalence is up to 50% in the elderly patients with type 2 diabetes.

Classification

Diabetic neuropathy can be classified as follows:

1) Symmetric Polyneuropathy
   a) Sensory neuropathy,
   b) Sensory-motor neuropathy
2) Autonomic Neuropathy
   a) Cardiovascular
   b) Gastrointestinal
   c) Genitourinary
   d) Sudomotor
3) Diabetic Amyotrophy
4) Focal and Multifocal Neuropathies

The onset of sensory neuropathy is usually insidious and shows a stocking and glove distribution in the distal extremities. Sensory-motor neuropathy involves both sensory and motor function where pain, numbness and paresthesias occur along with decreased strength in the lower limb muscles. The decreased sensation in diabetic patients with peripheral neuropathy causes foot ulcers. Frequent multiple trauma to feet leads to Charcot joint due to lack of sensation.

For the purpose of this presentation we will focus on peripheral neuropathy and not on autonomic neuropathy.

PERIPHERAL NERVES

The peripheral nervous system keeps us in touch with the outside world and carries many important functions. Peripheral nerves are made up of bundles of fibers whose cell bodies lie within the ventral gray horns of spinal cord, within the dorsal root ganglion and autonomic ganglion. Peripheral neurons can be categorized broadly as motor, sensory, and autonomic. Two types of nerve fibers have been identified, myelinated and unmyelinated, both are covered by Schwann cells of neuroectoderm origin. The nerve fibers are classified according to their fiber size and speed of conduction. The alpha fibers are 13-20 micrometers in diameter, are myelinated and responsible for limb proprioception. The beta fibers are 6-12 micrometers in diameter; they are also myelinated and responsible for limb proprioception, vibration and pressure sensation. The delta fibers are 1-5 micrometers in diameter; they are also myelinated and responsible for the mechanical and sharp sensation. The C fibers are 0.2-1.5 micrometers in diameter, they are unmyelinated fibers and are responsible for thermal pain and mechanical burning pain.

Pathophysiology

Multiple, clinical and basic science studies have shown that diabetic neuropathy has multifactorial causes and is preventable. Large prospective clinical trials, such as the Diabetes Control and Complication Trial (DCCT) and the United Kingdom Prospective Diabetes Study (UKPDS), have shown that tight control of diabetes and near normal euglycemia can prevent the onset or slow the progression of diabetic neuropathy. Many factors have been recognized in the pathogenesis of the diabetic neuropathy, such as metabolic failure, vascular insufficiency, loss of growth factor "Trophin" and autoimmune destruction of small unmyelinated nerve fibers (C fibers). The poor glycemic control

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can affect several metabolic pathways. Hyperglycemia increases the production of the advanced glycosylated end products. Hyperglycemia can also cause a defect in polyol pathways and the induction of the aldose reductase enzyme leads to conversion of glucose to sorbitol in cells. Excess amount of intracellular accumulation of sorbitol causes swelling of the cell by increasing intracellular osmolality. The increased activity of protein kinase-C is also implicated in the damage of the blood vessels by increasing the basement membrane abnormalities and vascular permeability. Hyperglycemia has been implicated in the impairment of resistance to the oxidative stress and in the causation of neuropathy.

Another factor involved in the pathogenesis of the diabetic neuropathy is need for nerve regeneration after injury. Recent studies have suggested that loss of neurotropic support contributes to the pathogenesis of diabetic neuropathy. The neurotropic factors are proteins that promote the development, survival and maintenance of specific neuronal populations. Finally, autoimmune damage has also been postulated in the development of peripheral neuropathy in diabetic patients.

Symptoms of Peripheral Neuropathy

Patients with diabetic neuropathy complain of a variety of pain and altered sensations. The dysesthetic pain usually occurs in the lower extremities and is of glove and stocking type. The skin tingling and burning sensation in the lower extremities is a common symptom. Sometimes patients complain of painful sensations on contact with something like bed sheets during the nighttime. Abnormally exaggerated response to the painful stimuli is also observed in patients with diabetic neuropathy. The sensation of pins and needles, electric shock-like sensations, numbness and aching, knife-like pain, a sensation that the feet are in ice water, or shooting and lancinating pain are also not uncommon findings. Diabetic neuropathy may cause muscular pain, such as dull aches, night cramps, band-like sensation, deep muscle aches, spasms of muscles, and sometimes toothache-like pain.

Physical Examination

The physical examination of extremities, especially of the feet, reveal that light touch, pinprick, proprioception and vibration sensation are decreased. Inability to feel a monofilament on the plantar surface of the feet is the early findings of diabetic neuropathy. The neuropathy can lead to dryness of feet, cracks, onychomycosis and deformities of feet.

The patients who are unable to feel monofilament on the plantar surfaces of the feet or who have decreased or absent proprioception with a 128 hz tuning fork are at increased risk for developing diabetic ulcers. Approximately 60% of such patients develop foot ulcers within three years. Therefore, routine testing of sensation with monofilament or a 128hz tuning fork is important in all diabetic patients. Physical examination may reveal loss of ankle reflexes. One may find either decreased or absent pedal pulses.

The differential diagnosis of diabetic peripheral neuropathy includes neuropathies secondary to pernicious anemia, uremia, alcoholism, and chemical toxins like isoniazid or any causes of nerve entrapment or compression.

Diagnosis of Peripheral Neuropathy

Laboratory Studies

- Fasting plasma glucose and hemoglobin A_{1c} (HbA_{1c}) represent the most important screening tool. HbA_{1c} can also be used as the follow-up tool for glycemic control.
- Complete blood count screen to check for anemia and infection.
- Sequential Multiple Analysis-7 (SMA7) to check renal function and electrolyte imbalances.
- Electrocardiogram to detect prolongation of QT interval secondary to imbalance between right and left sympathetic innervations. This abnormality is thought to increase risk of arrhythmias.

Electro-diagnosis

Electromyography (EMG), nerve conduction velocity (NCV) studies can be very helpful in the diagnosis and follow-up of peripheral neuropathy. The segmental demyelination can cause a blockage in the propagation of nerve action potentials. The nerve conduction studies show slowing of conduction velocity and temporal dispersion of the evoked potentials. The amplitude of the evoked responses

is diminished if the axonal degeneration is present. Compared to motor nerves, the sensory nerves are usually affected early in the lower extremities. Sural nerve sensory studies may be sensitive in the diagnosis of early diabetic peripheral neuropathy. The EMG may show abnormal spontaneous discharges, such as fibrillations, positive sharp waves, and fasciculations, again indicative of axonal degeneration. The EMG and NCV studies are more useful in the differential diagnosis of focal neuropathies, radiculopathies and entrapment neuropathies.

Treatment of Diabetic Neuropathy

The management of painful diabetic neuropathy is a difficult challenge. The symptoms of this disorder can cause a mild discomfort to an incapacitating situation. Although many remedies have been recommended, none have been consistently effective in all patients. Some drugs have been shown to be beneficial in certain patients while not useful in others.

In diabetic neuropathy, rigid control of hyperglycemia and elimination of infections are necessary as the first line of treatment. It has been shown that early in the course of diabetes, the institution of insulin therapy and control of hyperglycemia results in improvement of motor conduction velocity. However, in chronic diabetic neuropathy, the improvement in the glycemic control has been shown to decrease the pain but may not improve the sensory nerve conduction velocity.

Rehabilitation in Diabetic Neuropathy

The rehabilitation for diabetic neuropathy starts with prevention, altering risk factors and modifying life styles. The risk factors are advanced age, long duration of diabetes, poor glycemic control, hypertension, smoking, dyslipidemia and alcohol intake.

The role of exercise in diabetes management is well studied and well recognized and can be used as preventive measure. Exercise can lower the blood sugar and improve the body's ability to use glucose. With regular exercise, the amount of insulin needed decreases. Exercise can also help reverse the insulin resistance in overweight patients. Exercise improves risk factors for heart disease and decreases the risk of heart problems. Exercise reduces low-density lipoprotein (LDL) cholesterol and increases high-density lipoprotein (HDL) cholesterol, which is protective against heart disease. Exercise has been shown to improve mild to moderate high blood pressure. Exercise, when combined with a meal plan, has the ability to control type 2 diabetes without the need for medications. Regular physical exercise and activity provides an effective way for a person with diabetes to manage their blood sugars.

In addition to the benefits specific to diabetes, a person with diabetes will experience improved physical fitness. Exercise increases the efficiency of the heart, lungs and circulatory system both at rest and with exercise. The body's improved ability to transport oxygen provides increased stamina and endurance. The person has more reserve energy to do leisurely activities.

Exercise can help patients to lose weight or maintain their ideal body weight. Exercise burns excess calories that are stored in the fat cells. Exercise helps in dealing with life's everyday stresses. It also aids in relieving depression and building self-confidence. Through exercise, the person has more energy, is more relaxed, and feels less fatigued.

The exercise routine should consist of aerobic exercises three to five times a week for 20 to 40 minutes in duration and strength training twice a week. In strength training, weight lifting is of eight repetitions in sets of three, with a two minute rest period in between. A consultation with exercise physiologist is very useful. Balance exercises should be added and Ti-che exercises are very good in developing balance.

Exercises should be prescribed with caution in diabetic patients. Routine cardiogram and preferably exercise tolerance should be performed in patients above the age of 40. Diabetic patients should learn usual precautions, and know blood glucose levels before and after exercise. Proper foot care and self checking of feet once a day should be done by patients with neuropathy.

Management of Acute or Advanced Peripheral Neuropathy

The main rehabilitation goal is to teach patients to achieve the maximum functional level possible. Other goals should be to prevent contractures, maintenance of muscle mass, improve muscle

strength and provide proper nutrition to promote recovery from neuronal degeneration.

The range of motion exercises should be carried out at least twice a day to preserve or regain motion. The shoulders, hip, knee flexures, and heel cord have a tendency to develop early contractures. A proper range of motion exercises should be able to prevent such contractures. The swelling of extremities may lead to joint stiffness and, therefore, dependent edema should be corrected with proper positioning. Weakened muscles should be prevented from overstretching. It is important to recognize that mild sustained stretching exercises are believed to be more effective than short duration stretching exercises.

A number of programs have been developed for strength training of weakened muscles. Three main types of exercises, isotonic, isometric and isokinetic exercises are used. During the early stages of recovery, the muscles get easily fatigued and over exercising may cause harm and should be avoided (1). Isometric exercises can strengthen and maintain the muscles mass. Isotonic exercises are progressive resistive exercises, such as weight training, and can be prescribed as tolerated. Low impact aerobic exercises, like walking, should be prescribed, but if a person cannot walk, a stationary bicycle or swimming is recommended. General conditioning exercises and the functional activities that improve coordination and endurance are more beneficial. For example, day-to-day activities, such as washing dishes, doing housework, going to market are more useful that patient can follow long term.

The occupational therapist works with the patients to improve the activities of daily living such as eating, grooming, dressing and bathing, as well as functional transfers which are very useful for using the toilet and getting in and out of the bath tub. They can provide appropriate adaptive equipment and train patients to use this equipment that could be very beneficial in achieving functional independence.

Foot drop and the wrist drop can be prevented with the appropriate positioning orthosis. If a foot drop has already been developed, using ankle-foot orthosis can compensate the dorsiflexion weakness. The ankle-foot orthosis may be molded plastic or metal upright brace with anterior-posterior stop, which is usually attached to the shoes. In diabetic patients, consideration to the sensation and the circulation should be given and, therefore, a custom-fitted poly-propolyne ankle-foot orthosis is recommended. If dorsiflexure is not corrected, the patient tries to compensate by stepage gait, thus developing a poor gait pattern and increased energy expenditure.

Depending upon the severity of the cases, appropriate mobility aids, such as canes, walkers, two-wheeled walkers, crutches, and wheelchair can be prescribed. Canes, walkers and crutches provide a wider base of support and give sensory input through upper extremities, and canes can be useful in exploring the environment. Neuropathic arthopathy, Charcot joint, may occur due to loss of overall sensation including joint sensation and repeated trauma. In such patients, custom molded shoes are prescribed. In chronic diabetic peripheral neuropathy, foot ulcers are common. Sometimes chronic foot ulcers may need absolute non-weight bearing. Under these circumstances, the patient can be fitted with patellar tendon weight bearing braces.

Various physical modalities and medications may be helpful in treating painful neuropathies and hyperesthesias. Mild heating with infrared radiation or a tepid whirlpool bath may be effective in pain reduction. Any form of heating agent should be used very cautiously on insensate areas or in skin areas with vascular compromise. Gentle stroking massage and cold applications are more useful than heat. Transcutaneous electrical nerve stimulation (TENS) units, low frequency, high intensity are useful, especially in radiculopathies.

Use of Drugs

Drugs are commonly used in conjunction with physical therapy. Non-steroidal anti-inflammatory drugs may cause decrease in inflammation and help in reducing pain especially in muscular pain, radiculopathies and focal neuropathies. Ibuprofen and naproxen are commonly used drugs in this category. These drugs should be used with caution in patients with impaired renal functions. Baclofen or other muscle relaxers could be of benefit. The tricyclic antidepressants are good for patients with the feelings of pins and needles, electricity, numbness and aching, and knife-like shooting pains.

Amitriptyline and imipramine are commonly used drugs under this category. The anti-epileptic drugs are also used in the treatment of diabetic neuropathy. These drugs have been found to have analgesic affects in the neuropathic pain. The mode of action of these drugs involves blocking of channels and inhibiting specific neuronal components. Commonly used drugs in this category are gabapentin, which sometimes is very useful in treating patients with dysesthetic pain such as burning or pins and needles. This drug should be used after all first line measures have failed and has not caused relief in the pain of diabetic neuropathy. Another drug in this category, which has been found to be useful, is carbamazepine. This is a third line choice of the agent to be used in diabetic neuropathy to improve symptoms of pain. The next categories of drugs, which can be used in the treatment of diabetic neuropathy, are Selective Serotonin Reuptake Inhibitors (SSRI). Paroxetine in this category has been found to be useful in the treatment of painful diabetic neuropathy, especially in patients who are also depressed. In another category, anti-arrythmic agents such as mexiletine and lidocaine have been used to ameliorate neuropathic pain in diabetic neuropathy.

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