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EVALUATION OF NERVE CONDUCTION STUDIES IN PATIENTS WITH DIABETIC NEUROPATHY: A STUDY ON MEDIAN, ULNAR, PERONEAL AND TIBIAL NERVE

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ABSTRACT

Nerve conduction study (NCS) has its significant importance in the diagnosis of diabetic neuropathy. We evaluated NCS in patients with diabetic neuropathy and also compared these parameters on the basis of their variations between upper and lower limbs, and the progression of the neuropathy with the duration of diabetes**.** We undertook a pilot study of NCS of Median, Ulnar, Peroneal and Tibial nerve in 56 diabetics of age 40 to 50 years with symptoms of neuropathy. The compound muscle action potentials (CMAP) were recorded with surface electrodes. NCS revealed abnormal values of conduction velocity(NCV) in 63% of the total patients. We found decline of Median 27%, Ulnar 26%, Peroneal 29% and Tibial 35% NCV. While rest of 37% patients had normal values for conduction velocity besides having neurological symptoms. We found close association between neurological deficit score and abnormalities in NCS. The values for amplitude were still in normal range. Decrease in conduction velocity of Tibial and Peroneal nerve indicate earlier progression of the disease in lower limbs than upper limbs that further indicated early demyelination in these nerves. The normal amplitude of all four nerves indicated that axonal loss may accompany in later stages of disease.

Key Words: Compound Muscle Action Potential (CMAP), Nerve Conduction Study (NCS), Demyelination, Diabetic Neuropathy.

INTRODUCTION

Neuropathies, the disorders of nerves that ultimately result in sensory deficits in the innervation area & usually affect the hands and feet, causing weakness, numbness, tingling and pain (Robinson, 2000). There are many causes of neuropathy; Glucose control seems to play a role in neuropathy. The causes are probably different for different varieties of diabetic neuropathy. Researchers are studying the effect of glucose on nerves to find out exactly how prolonged exposure to high glucose causes neuropathy. Nerve damage is likely due to a combination of factors such as metabolic factors; high blood glucose, long duration of diabetes, possibly low levels of insulin, and abnormal blood fat levels (Rosenfalck & Rosenfalck, 1975). How the nerves are injured is not entirely clear but research suggests that high blood glucose changes the metabolism of nerve cells and causes reduced blood flow to the nerve (Partanen *et al*., 1995). These conditions are thought to result from diabetic microvascular injury involving small blood vessels that supply nerves. The most common type of diabetic neuropathy affects the nerves in the legs and is usually known as peripheral neuropathy. This is the type of neuropathy that causes foot problems. Bansal *et al*., (2006) found that the distal symmetrical neuropathy is the commonest diabetic neuropathy. Peripheral neuropathy causes either 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. Autonomic neuropathy can also cause hypoglycemia (low blood sugar) unawareness, a condition in which people no longer experience the warning signs of hypoglycemia. While 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 may be affected. Symptoms depend on the type of neuropathy and which nerves are affected. Often, symptoms are minor at first, and since most nerve damage occurs over several years, mild cases may go unnoticed for a long time. Symptoms may involve the sensory or motor nervous system, as well as the involuntary (autonomic) nervous system. In some people, mainly those with focal neuropathy, the onset of pain may be sudden and severe. Once a careful history and a thorough physical examination have established the presence of diabetic neuropathy assessment strategies can help in management (Vinik *et al*., 2003). The development of new treatments to slow or arrest the progression of diabetic polyneuropathy (DPN) has increased the importance of the early and accurate identification of this complication. Accurate diagnosis of DPN is a formidable task because of the diversity of presentations, involvement of different nerve fiber types, and the common dissociation of symptoms from objective measures of neural function (Partanen, 1995). Several diagnostic tools are available or in development, each with strengths and limitations. Electrophysiology is a sensitive, objective, and targeted measure of DPN, but it reflects, almost exclusively, the activity of large-caliber, myelinated axons. Newly refined skin-punch biopsy procedures use morphometric and immunohistochemical methods to examine thinly myelinated and unmyelinated nerve fibers. The integrity, density and distribution of these fibers may provide a sensitive index of small-fiber distal axonopathy. The

existing diagnostic tools and newly emerging methods provide a battery of tests that can be used to assess multiple aspects of neural function and increase sensitivity to detect the onset and progression of DPN (Internet, 1999). Neuropathy can result in two sets of what superficially appear to be contradictory problems. Most patients who have neuropathy have one of these problems but some can be affected by both numbness which leads to ulceration pain and burning sensation due to numbness they exert lot of pressure on feets which forms callus leads to ulceration (Thomas *et al*., 1995). Degeneration in these "small fiber neuropathies" involves the most distal portions of nerve fibers that are found in different organs and tissues (somatic fibers) rather than fibers in major nerves (Lauria *et al*., 2007). There are various methods for the diagnosis of diabetic neuropathy including two most common methods i.e. electromyography and nerve conduction velocity but the most relevant and affordable technique is NCV. Nerve conduction are extremely useful investigative techniques in evaluating the patient in pain, because they satisfy two fundamental steps (Verdugo *et al*., 1992) in the assessment of a neuropathic pain syndrome, prior to any attempt at therapy. First, they rigorously establish the presence or absence of a peripheral nervous system lesion, and secondly, they determine the relevance of an established peripheral lesion to the subjective clinical complaint. Neuromuscular junction disorders, amyotrophic lateral sclerosis, and other anterior horn cell disorders (except poliomyelitis in its acute stage) rarely produce pain. The principle changes in nerve function are related to demyelination, axonal degeneration and conduction block. There are no absolute dividing lines between these situations; they show some overlap and also dynamic changes from one stage to another due to the interaction between Schwann cells and the axonal condition (Tasaki *et al*., 1942). In cases of demyelination, the conduction velocity is reduced. In cases of axonal degeneration, there may be normal velocity in the remaining axons, but a weaker muscle response is evoked. In cases of conduction block, no axonal degeneration occurs and therefore a normal response is obtained when stimulating distal to the lesion. When stimulation is performed proximal to the site of abnormality, a reduced number of axon conducts impulses, and a smaller than normal muscle response is obtained. Longer nerves generally conduct more slowly than shorter nerves (Campbell *et al*., 1981). It has been shown that there is a good correlation between CV and estimated axonal length in the peroneal and sural nerves, but not in the motor or sensory fibers of the median nerve. Based on a good correlation between the height of the patient and the length of the nerve, the CV in lower limbs decreases by 2-3 m/s for10 cm increase in height (Falck *et al*., 1995). Nerve impulses propagate faster in the proximal than in the distal nerve segments (Gilliatt *et al*., 1960). It has been reported that CV is slower in women than that in men (LaFratta *et al*., 1964 & Stetson *et al*., 1992) but the correlation is complex since gender and height are not independent of each other (Falck *et al*., 1995)

OBJECTIVES

The purpose of this study was to investigate the importance of NCV and Amplitude in patients with diabetic neuropathy and how decline in conduction velocity and amplitude could relate the appearance of specific symptoms in diabetic neuropathy e.g. Hyperasthesis and numbness. Moreover to evaluate the decrement in NCV and its amplitude in relation with the progression of demyelination and axonal loss in diabetic Neuropathic patients.

MATERIALS AND METHODS

EQUIPMENT & SETTINGS FOR NCV RECORDING:

Equipment that contain instrument for electrodiagnosis that include an amplifier, an oscilloscope display, gain, and filter controls and stimulator. Electrodes are plugged in to box that transmitsignal to a preamplifier that inturns transmits signals to the main unit by a shielded cable. The signal is amplified, filtered and either display on the oscilloscope. The oscilloscope display divided in to both horizontal and vertical axes. The horizontal axis (time) has ten divisions representing seconds per division (sec/div), the vertical axis (voltage) has eight or ten divisions representing volts per division (volts/divi).

STIMULUS AND RECORDING PARAMETER FOR NCS:

PARAMETER	***MNCV***	***SNCV***	***F WAVE***	***H REFLEX***
Gain	2mv/div	20uv/div	200uv/div	200uv/div
Time base	2ms/div	1ms/div	10ms/div	10ms/div
LFF	10Hz	10Hz	10Hz	10Hz
HFF	32kHz	2kHz	32kHz	32kHz
Stimulus duration	0.2ms	0.1ms	0.2ms	0.2ms

*NCV; nerve conduction velocity, LFF; low frequency filter, HFF; high frequency filter

Surface electrodes are used for routine NCS. The electrodes are stainless steel, silver or gold disk soldered to multi stranded conducting wire. Ring electrodes are tight coils of stainless steel used to record or to stimulate sensory action potentials from fingers. The coil is coated with conducting gel, wrapped around fingers, and cinched with a rubber or plastic fastner. Electrode gel is needed to reduce the impedence and prevent artifact, because skin surface is irregular and hair interferes with conduction. The gel is malleable extension of the electrode, allowing electrical continuity between the ionic milieu of skin and the electrode. Gel is also needed to reduce the impedence of stimulating electrode. The stimulus voltage passing through a high impedence can create sufficient heat to cause local tissue injury.

METHOD OF RECORDING ROUTINE NCS:

Median nerve motor NCV was calculated by placing the active recording electrode(G1) over the belly of the Abductor Pollicis Brevis .The reference electrode(G2) was placed 2cm distally. The cathode for distal stimulation is placed 7 cm proximal to G1 on the median nerve. The anode is placed 2cm proximally. The cathode for proximal stimulation is placed over the median nerve proximal to the Antecubital Fossa. For Ulnar nerve motor NCV the CMAP was recorded from the abductor digiti minimi, G1 is placed over the belly of the abductor digiti minimi, approximately midway between the origin and insertion. G2 is placed 2 cm distal to G1. Distal stimulation was on the ulnar aspect of the wrist, 7cm proximal to G1. Proximal stimulation was developing so that the cathode is just below the ulnar groove. Nerve-conduction velocities are calculated for the nerve segments between the wrist and groove and, across the groove. Peroneal nerve the motor NCV is usually determined by recording from the extensor digitorum brevis. Distal stimulation was in the lower leg, adjacent to the tendon or the tibialis anterior. Proximal stimulation is at the fibular neck. When the nerve is believed to be injured at the fibular neck, more stimulation is then performed in the popliteal fossa. The NCV across the fibular neck is compared to the NCV distal to the neck. For Tibial Motor NCVs are performed by recording from the ABDUCTOR HALLUCIS MUSCLE on the medial aspect of the foot. Distal stimulation is delivered to the nerve as it passes behind the medial epicondyl, and proximal stimulation is delivered in the POPLITIAL FOSSA. The difference in latencies between the two points of stimulation, and the distance between the two points of stimulation, provide the basis for the calculation of the conduction velocity. The conduction velocity by the formula:

NCV (m/sec) = dmm (msec) / pml (msec) – dml (msec).

RESULTS

NERVE	CONDITION	OBSERVED VALUES	% DECLINE
	Normal	49.86±3.53(17)	0%
MEDIAN	Reduced	36.66±8.01(9)	26.80%
	Normal	45.6±0.94(4)	8%
ULNAR	Reduced	37.24±4.72(18)	26%
	Normal	42.35±2.60(6)	12%
PERONEAL	Reduced	33.79±15.7(14)	28.50%
	Normal	40.93±0.44(4)	18%
TIBIAL	Reduced	31.39±5.16(14)	34.80%

Our data reveals the normal and reduced values of nerve conduction velocity in diabetic Neuropathic patients.

Comparison of % decline among Neuropathic patients in upper and lower extremities:

As the data shows that there are differences in % decline in upper and lower extremities. The values of observed Neuropathic patients shows more decline in nerve conduction velocity of lower extremities as mention above which is 28.5% in peroneal and 34.8% in tibial, but less decline in upper extremities as 26% in both the median and ulnar nerves.

DISCUSSION

Patient with diabetes having damaged nerve fibers (neuropathy) are those having diabetic neuropathy. There are many consequences of diabetic neuropathy. Patients with long term diabetes are more prone towards neuropathy, but

its progression depends upon the symptoms, duration of diabetes, life style, age and working habbits. Peripheral neuropathy is a major complication of diabetes mellitus and marked differences can be observed in the types of nerve fibers involved. In contrast, diffuse demyelinating neuropathy is characterized by reduction of conduction velocities, usually more than 40% of the normal range (Albers *et al*., 1985). Distal latencies are also prolonged. The sensory nerve action potentials and compound muscle action potentials usually have low amplitudes and temporal dispersion in a pure demyelinating neuropathy, there is no denervation of muscle fibers. Motor units are decreased in number; decreased recruitment is attributable to conduction block in some fibers. Dyck (1991) proved that 90% of the diabetic patients had sensory and motor symptoms, while autonomic symptoms were positive only in 70%. Reduced or absent excitability of the nerve is observed when conduction block or axonal degeneration becomes severe. This is measured by the need for an increase in duration and intensity of the stimulus. If the conduction block or axonal degeneration is complete, the nerve eventually becomes inexcitable. This is best observed in cases of Wallerian degeneration of all the nerve fibers distal to the lesion when the nerve is severed (Gilliatt *et al*., 1960). In clinical practice certain parameters of CMAP are used to evaluate the specific type of neuropathy. These parameters include Shape of CMAP- NCV, Distal and proximal latencies and amplitude of CMAP (Albers *et al*., 1985). Lambert (1962) was the first one to compare elecrophysiological changes in demyelinating and degenerative neuropathies in diabetic neuropathic patients. Diabetic neuropathy refers to symptoms and signs of neuropathy, or nerve damage, as a result of diabetes. There are many other reasons for nerves to be damaged or harmed. So the symptoms play important role in decreasing the nerve conduction velocity which in turn leads to damage in nerves of lower and upper extremities but there are some other factors like temperature, age, sex body length etc are responsible for the slowing of NCV. Some recent studies have reported that 60 percent of patients with Diabetes have some form of neuropathy, but in most cases (30 to 40 percent), there are no symptoms. About 30 to 40 percent of patients with diabetes have symptoms suggesting neuropathy, compared with 10 percent of people without diabetes. Diabetic neuropathy appears to be more common in smokers.

In symptomatic diabetic neuropathy, there is slowing of nerve conduction velocity owing to demyelination and loss if large myelinated fibers and a decrease in nerve action potentials owing to loss of axons. Purely demyelinative neuropathy is rare in patients with diabetes, and is more suggestive of a demyelinative neuropathy of inflammatory or dysglobulinemic origin (Kimura *et al*., 1983). Systematic electrophysiological testing is not necessary in diabetic patients with typical peripheral neuropathy. Changes in conduction velocity can be detected in asymptomatic patients, but their presence is not predictive of the onset of symptomatic neuropathy. In patients with obvious symptoms of neuropathy conduction slows down due to demyelination and electrophysiological responses in diseased nerves are limited. Responses can be classified in to three groups; (a) conduction slowing; (b) conduction block (c) reduced or absent excitability of the nerves. Nerve conduction slowing is the most important parameter in the nerve conduction study and is seen as prolong latency or conduction time. This slowing is attributed to three factors (a) segmental demyelination; (b) loss of large-diameter fibers and (c) metabolic abnormalities with segmental demyelination, nerve conduction slowing occurs because of lengthen conduction time between the two demyelinated nodes of Ranvier and the loss of saltatory conduction in the relatively thin demyelinated fibers (Bostock. *et al*.,1978). The most common cause of neuropathy in clinical practice is diabetes. Peripheral neuropathy develops in more than half of long-term diabetics. Diabetes causes several types of neuropathy (Lombardi 2007). A prominent finding in diabetic neuropathy is thickening of arterioles due to increased deposition of basement membrane material, similar to changes that occur in brain arterioles and glomerular capillaries. Nonenzymatic Glycation of neural structures and other biochemical changes in diabetes probably play a role also (Lauria, 2007). People, whose average blood glucose levels were higher, have higher rates of neuropathy. It is also clear that People with diabetes can develop nerve problems at any time. Significant clinical neuropathy can develop within the first 10 years after diagnosis of diabetes and the risk of developing neuropathy increases the longer a person has diabetes. High blood glucose also damages blood vessels that carry oxygen and nutrients to the nerves. In addition, inherited factors probably unrelated to diabetes may make some people more susceptible to nerve disease than others. People with diabetes are also prone to developing compression neuropathies. The most common form of compression neuropathy is carpal tunnel syndrome. Asymptomatic carpal Tunnel syndrome occurs in 20 to 30 percent of people with diabetes, and symptomatic carpal tunnel syndrome occurs in 6 to 11 percent. (Bostock *et al*., 1978) Numbness and tingling of the hand are the most common symptoms. Muscle weakness may also develop. At least 5 % of all people with diabetes eventually have a foot ulcer, and 6 out of every 1,000 people with diabetes have an amputation. Causes of neuropathy other than the diabetes itself are relatively common in diabetic patients with distal sensory Polyneuropathy. De Freitas *et al*., 1992 done a retrospective study on patients who are suffering from long-term diabetes and some have recent history of diabetes. They found that the patients who have long-term history of diabetes have damaged nerves (neuropathy) than recent one. This proved that uncontrollable blood glucose level might play a key role in causing diabetic neuropathy. Some times the diabetic neuropathy progresses to an extent

that it causes the irreversible damage that may proceed to axonal neuropathy and demyelination that in turns affect the nerve conduction velocity of nerve as they become decreased. The myelinated nerve axon conducts impulses in a saltatory fashion i.e. depolarization occurs at the nodes (Tasaki *et al*., 1942). The currents are prevented from penetrating the membrane between the nodes in the normal nerve due to an isolating myelin sheath. This means that the impulse propagation is much faster than if there was a continuous depolarization. The conduction velocity is also dependent on the axonal diameter and the properties of the membrane (Takeuchi, 1942). A normal axon conducts with a speed of 35-60 m/sec (Rosenfalck & Rosenfalck, 1975). The velocity is reduced if the myelin is defect due to pathological changes, if the Ion-channels at the nodal areas are block or if the axon diameter is smaller than normal (Lambert, 1962). It is also dependent on temperature. Disorders of myelin sheath slow the motor and sensory NCVS. Unraveling or fragmentation of the myelin reduces the impedance between spaces inside and outside the axons. This interferes with the electronic depolarization between nodes that is essential for salutatory conduction (Hodes *et al*., 1948). Demyelinated axons do not have the capacity to conduct in the same way as unmyelinated fibers. Therefore, if severe enough demyelinating disorder can result in failure of transmission of impulses down the nerve. Nerve conduction velocities are typically normal or near normal in disorders of neuronal and axonal degeneration because surviving axons conduct action potentials at a normal velocity (Lambert, 1962). However the amplitude of the compound action potential is often reduced, because the numbers of functioning axons is reduced. Disorders of muscle have normal NCS. If either motor or sensory conduction velocity is slower than three standards deviations below the mean, the study is interpreted as abnormal. This indicates an abnormality in the myelin component of the nerve. Axonal neuropathy may cause mild slowing of nerve conduction, usually not more than 5m/s below the lower limit of normal. Slowing of NCV parallels the degree of demyelination because the NCV is proportional to the outer fiber diameter of myelinated fibers, it is not difficult to understand that the loss of large-diameter fibers is responsible for the slow nerve conduction, however total loss of large-diameter fibers slows the NCV usually not more than 20% below the normal mean (Behse & Buchthal, 1978). This may be the pathological basis of the minimal slowing seen in axonal neuropathy. Slowing of conduction is the typical electrophysiological manifestation with mild segmental demyelination but in more serious demyelination (Simpson, 1964). Some demyelinated fibers fail to conduct the nerve impulse, producing a conduction block which is manifested in the reduction of the amplitudes of the CMAP and CNAP across the site of the block, as in the case of entrapment neuropathy (Gilliatt *et al*., 1960).

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