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F WAVE OF NERVE CONDUCTION STUDY IN PATIENTS OF TYPE 2 DIABETES MELLITUS

Physiology

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ABSTRACT

Diabetes mellitus is a syndrome of impaired carbohydrate, fat and protein metabolism caused by either lack of insulin secretion or decreased sensitivity of the tissues to insulin. Chronically elevated blood glucose level lead to metabolic derangement and as a result microvascular complication may occur as diabetic neuropathy.

Nerve conduction study (NCS) is considered to be sensitive, reliable and objective means of investigating neuropathy. Among the various parameters used in nerve conduction study, F wave is the parameter known to be one of the late responses. It is used to know the status of proximal segment of nerve.

In our study 100 subjects were included, 50 diagnosed cases of type 2 diabetes mellitus and 50 age and sex matched healthy subjects as control. We recorded F wave of nerve conduction study and then F minimum latencies (in milliseconds) were noted for both the diabetic and control group and compare it within these two groups.

It is observed that F minimum latencies were prolonged in bilateral median, ulnar, peroneal and tibial nerves in type 2 diabetic patients compared to controls and differences were statistically significant($p<0.05$). Prolonged F wave minimal latency in the tested nerves of upper and lower extremity bilaterally in diabetic group were suggestive of some sort of impairment in proximal segment of these nerve in diabetic group as F wave assess predominantly proximal segment of the nerve.

KEYWORDS

Nerve conduction study, F wave, F minimum latency, Diabetes Mellitus.

INTRODUCTION:

Diabetes mellitus (DM) is a syndrome of impaired carbohydrate, fat and protein metabolism caused by either lack of insulin secretion or decreased sensitivity of the tissues to insulin.[1] Over the past decade the prevalence of DM has risen dramatically in the worldwide.[2,3] There are many symptoms and signs that one may have to indicate the presence of type 2 diabetes which are depicted below- increased thirst, polyurea, polyphagia, nocturia, fatigue, recent change in weight, blurring of vision, irritability etc.[4,3] Chronically elevated blood glucose level lead to metabolic derangement and as a result nonvascular and vascular complications may observed. Non vascular complications include gastroparesis, diarrhoea, uropathy or sexual dysfunction, skin changes, infections, cataracts, glaucoma and hearing loss. The vascular complications of diabetes mellitus further subdivided into microvascular (neuropathy, retinopathy and nephropathy) and macrovascular (coronary heart disease, cerebrovascular disease and peripheral arterial disease) complications.[3,5] Among these one of the microvascular complication may be the diabetic neuropathy.[6,7]

Nerve conduction studies (NCS) are considered to be the sensitive, reliable and objective means of investigating neuropathy.[8] This techniques allow stimulation and recording of electrical activity from individual peripheral nerves along its course. Nerve conduction study includes motor nerve conduction studies , sensory nerve conduction studies and late responses (late response includes F wave and H reflex study). NCS provides information to locate lesions in the length of a nerve, and information about pathophysiology of nerve.[9,10] Peripheral nerve pathology primarily affects axons or myelin .These abnormality often coexist. In generalised processes it is important to determine whether a peripheral neuropathy is demyelinating or axonal. Further NCS can help to locate lesion in the length of nerve.[9,11,12] NCS is important as this helps in patient management and treatment.

Among the various parameters used in nerve conduction study, F wave is the parameter known to be one of the late responses. It is used to know whether there is proximal portion of nerve is affected. .Patients of diabetes may have some degree of neuropathy. It may involve either sensory , motor and autonomic nerves[13,14] It may involve distal or proximal portion of the nerve. Impairment of proximal portion of nerve may be detected by studying F wave in NCS Hence the present study was conducted to study the status of F wave of nerve conduction study in patients of type 2 diabetes mellitus as compared to healthy subjects.

MATERIAL AND METHODS:

The present study was designed as case control study, carried out in the Department of Physiology at MGIMS, Sewagram, Wardha, Maharashtra. It was approved from institutional ethics committee. In our study 100 subjects were included, 50 diagnosed cases of type 2 diabetes mellitus and 50 age and sex matched healthy subjects as control. Detail history of the patient was extracted which includes, demographic variables, socioeconomic variables and personal habits. Patients were enrolled from department of Medicine after being diagnosed as diabetics. Diabetes Mellitus was diagnosed on the basis of Fasting Blood Sugar (FBS) $\geq$126 mg/dl [6] with appropriate signs and symptoms of type 2 diabetes mellitus.[15] Mean duration of diabetes was about 5 years. Written Informed consent was obtained from all study participants. The exclusion criteria for this study were thyroid disorders, alcoholism, kidney diseases and those subjects who did not give consent.

The nerve conduction study was performed by instrument by RMS EMG EP MARK II, Chandigarh, available in clinical neurophysiological unit, Department of Physiology, MGIMS, Sevagram. F wave of diabetic and control subjects were studied from nerve conduction study.

F wave study

The F wave is late motor response characterised by low amplitude and ubiquitous inherently variable in amplitude, latency and configuration responses following supramaximal stimulation of peripheral nerve. F waves are recorded using surface electrodes over distal muscles with supramaximal nerve stimulation in the manner as motor nerve conduction studies. With external stimuli peripheral nerves evoke potentials that propagate both proximally and distally. With motor nerves, electrical activity moving distally (orthodromically) results in a direct motor response, the compound muscle action potential (CMAP), also known as the M response. Electrical activity propagating proximally (antidromically) activates a small percentage of motor neurons (they "backfire"), which then can generate another wave known as the F wave (also called the F response). The F wave is visible as a low amplitude late potential following the M response.[9,10]

F wave has the ability to assess the proximal part of the nerve and roots

which cannot be evaluated by conventional conduction studies. Most widely used parameter of F wave is the F minimal latency. The number of F waves used for analysis in clinical studies has varied because of inherent variability of F wave. 10-20 F waves is a reasonable balance feasibility and adequate data.

F wave response was obtained by supramaximal electrical stimulation of motor nerve which includes Median, Ulnar, Peroneal and Tibial nerves. For recording F min latencies surface disc electrodes were kept on abductor pollicis brevis for median nerve, abductor digiti minimi for ulnar nerve, extensor digitorum brevis for peroneal nerve and abductor halluces longus for tibial nerves. Ground electrode was placed between stimulating and recording electrodes.[16,17] Belly tendon montage was used with cathode and anode 3 cm apart. Electrical stimulation was given near the proximal end of the respective nerves. Minimum 10 stimuli were passed to obtain the F waves. For recording F wave duration was set up 100µs, sweep speed 10ms/D and filter was between 2 Hz to 10 kHz.[9,18]

F wave were recorded for 50 diabetic patients and 50 control subjects. From the F wave study, F minimum latencies (in milliseconds) were noted for both the diabetic and control group. F minimum latencies thus obtained were expressed as mean ± SD for diabetic and control group. It is then compared between these two groups.

Statistical analysis was done by using z-test for difference between two means. The p value of less than 0.05 ($p<0.05$) was considered statistically significant.

RESULTS:-

In our study 100 subjects were included , 50 diagnosed cases of type 2 diabetes mellitus (Male = 31, Female=19) and 50 age and sex matched healthy subjects as controls (Male = 33, Female=17).

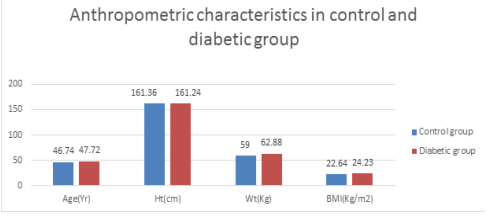
Observation of anthropometric variables and F wave of nerve conduction study in diabetic and control group are depicted below

Table 1: Anthropometric characteristics in control and diabetic group

Variables	Control Group		Diabetic Group		z-value	p-value
	Mean	SD	Mean	SD		
Age(Yr)	46.74	5.13	47.72	8.42	0.702	0.484NS,p>0.05
Ht(cm)	161.36	4.41	161.24	4.69	0.13	0.89 NS,p>0.05
Wt(Kg)	59	8.04	62.88	12.14	1.88	0.06 NS,p>0.05
BMI (Kg/m2)	22.64	2.83	24.23	4.77	2.03	0.045*S,p<0.05

*indicate statistically signicant difference
NS-Not significant, S-significant

Graph 1: Anthropometric characteristics in control and diabetic groups



Anthropometric parameters such as age, height and weight were matched as differences were statistically non significant in control and diabetic group.. But the BMI was found to be slightly more in diabetic group compared to control and difference was statistically significant.

F minimum latencies in type 2 Diabetes Mellitus and Controls are shown below:-

Table 2: Comparison of F wave study of nerves in diabetic patients and controls group.
(F-Minimum Latency : Right Side)

Variables	Control Group		Diabetic Group		z-value	p-value
	Mean	SD	Mean	SD		
Median(ms)	26.43	1.82	27.72	3.04	2.55	0.012*S,p<0.05
Ulnar(ms)	27.30	1.92	29.26	3.16	3.73	0.0001*S,p<0.05
Peroneal(ms)	43.64	3.88	47.60	6.54	3.57	0.001*S,p<0.05
Tibial(ms)	44.75	3.28	49.45	6.17	4.74	0.0001*S,p<0.05

*indicate significant difference
*indicate statistically signicant difference
S-significant

Graph 2: Comparison of F wave study of nerves in diabetic patients and controls groups.
(F-Minimum Latency : Right Side)

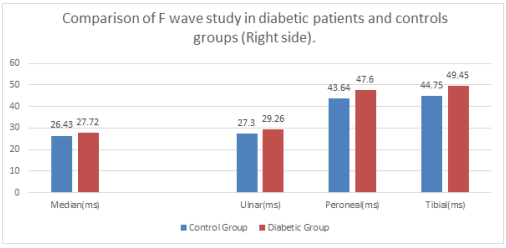
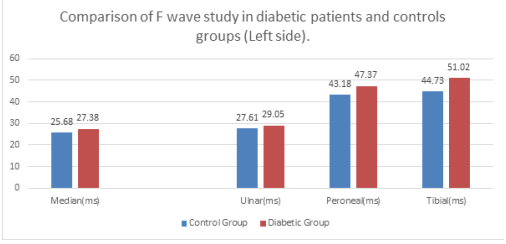


Table 3: Comparison of F wave study of nerves in diabetic patients and controls group.
(F-Minimum Latency : Left Side)

Variables	Control Group		Diabetic Group		z-value	p-value
	Mean	SD	Mean	SD		
Median(ms)	25.68	2.71	27.38	3.50	2.70	0.008*S,p<0.05
Ulnar(ms)	27.61	2.47	29.05	2.81	2.69	0.008*S,p<0.05
Peroneal(ms)	43.18	3.70	47.37	7.45	3.53	0.001*S,p<0.05
Tibial(ms)	44.73	3.66	51.02	5.55	6.64	0.0001*S,p<0.05

*indicate statistically signicant difference
S-significant

Graph 3: Comparison of F wave study of nerves in diabetic patients and controls group.
(F-Minimum Latency: Left Side)



As shown in table 2 &3 and graph 2&3, In Median nerve on right and left side, F minimum latencies were prolonged in cases (diabetic group) when compared with that of controls and differences were statistically significant ($p<0.05$) In Ulnar nerve on right and left side, F minimum latencies were prolonged in cases (diabetic group) when compared with that of controls and differences were statistically significant ($p<0.05$) In Peroneal nerve on right and left side, F minimum latencies were prolonged in case group (diabetic group) when compared to controls and differences were statistically significant ($p<0.05$) In Tibial nerve on right and left side, F minimum latencies were prolonged in cases (diabetic group) when compared with that of controls and differences were statistically significant ($p<0.05$)

Following observations are acquired from the analysis of the results-

- BMI was higher in type 2 diabetic patients compared to controls and difference was statistically significant ($p<0.05$).
- F minimum latencies were prolonged in bilateral median, ulnar, peroneal and tibial nerves in type 2 diabetic patients compared to controls and differences were statistically significant($p<0.05$).

DISCUSSION:

Diabetes mellitus is a syndrome of impaired carbohydrate, fat and protein metabolism. Nerve conduction studies (NCS)are considered to be the sensitive, reliable and objective means of investigating neuropathy. F wave is the parameter of NCS and has the ability to assess the proximal part of the nerve and roots which cannot be evaluated by conventional nerve conduction studies.

We studied the F wave in 50 diagnosed diabetic patients and 50 healthy control subjects.

In this study we found that BMI was higher in type 2 diabetic patients compared to controls and difference was statistically significant ($p<0.05$). This is because diabetes mellitus often closely associated with obesity thus in our study probably higher body mass was observed in diabetic than controls[3]

In this study we found that F minimum latencies were prolonged in bilateral Median, Ulnar, Peroneal and Tibial nerves in diabetic patients compared to controls and differences were statistically significant.

Our findings were supported by Ahmed TS *et al* (2001) [19]who reported significantly prolonged F wave minimal latency in peroneal and tibial nerves of diabetic patients. They also observed significant increase in F wave average duration in peroneal and tibial nerves. Similar findings were observed by Al Sadik FNA (2012)[20] who reported significantly prolonged F wave latencies in median, ulnar and tibial nerves in diabetic patients. Our observations were also supported by Gargate AR *et al* (2014)[21] who reported significant increased F wave minimum latency in median, ulnar, peroneal and tibial nerves of diabetic patients. Similar findings were also observed by Mankar K *et al* (2016)[22] who found significant increase in F minimum latencies in right median and bilateral ulnar nerves of type 2 diabetic patients.

In our study, we observed prolonged F wave minimal latency in the tested nerves of upper and lower extremity bilaterally which indicated some sort of impairment in proximal segment of these nerve in diabetic group as F wave assess proximal segment of the nerve. Although F responses are usually thought to assess the proximal nerve segments but in reality, they check the entire course of the nerve. The latencies of F waves may be prolonged and abnormal even when peripheral motor conduction studies are normal. Thus any nerve with a prolonged distal motor latency on routine nerve conduction studies will also have prolonged F responses. If there is generalised slowing of nerve conduction velocity from a polyneuropathy, the F response will also be slowed, reflecting the slowed conduction velocity of the entire nerve.

From the above observation it was clear that there was an involvement of proximal segments of nerves in upper and lower extremities as indicated by prolonged F minimal latencies in diabetic patients.

This impairment or nerve damage in diabetic patients may be possible and it may be due to various mechanisms proposed by which nerve damage can occur are as follow.

- Increased level of glucose in diabetic patients may activates the enzyme aldose reductase. Increase level of enzyme aldose reductase activates the polyol pathway which leads to intracellular accumulation of sorbitol and fructose. Accumulation of these osmolytes intracellularly is associated with reciprocal reduction of myoinositol, which in turn reduces cellular Na+-K+-ATPase activity as a result there is acute slowing of nerve conduction velocity and defects in axonal transport.[4,23]
- Moreover activation of polyol pathway in the nerve through an enzyme aldose reductase may induce non enzymatic glycosylation of structural nerve proteins which result in reduction of axonal transport. It reduces nerve function and shows an abnormal morphometry which leads to severe morbidity
- Elevated intracellular glucose as a result of hyperglycemia may lead to cellular toxicity in the endothelial cells of the vasa nervosum. These intracellular glucose can also be converted to the so called Amadori product and these in turn form Advanced Glycosylated End product (AGE), a crosslink matrix protein. These damages the blood vessels which results in ischaemia of the nerves and finally leads to neuropathy.[24]
- Further, elevated level of blood glucose may increase endothelial vascular resistance and reduces blood flow to the nerves resulting in endothelial hypoxia. These hypoxia leads to further damage of the capillary which in turn aggravates disturbance in axonal transport and impairment of nerve conduction. Hyperglycemia also induces oxidative stress and activation of protein kinase C has been linked to vascular damage in diabetic neuropathy.[14]

Thus it is observed that prolonged F minimum latencies were found in patients of type 2diabetes mellitus patients as compared to their healthy counterpart which indicates impairment of proximal segment of nerve.

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