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NERVE CONDUCTION STUDIES IN ASYMPTOMATIC HIV POSITIVE PERSONS

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ABSTRACT

Background: Nerve Conduction Studies were performed in asymptomatic HIV positive persons and corresponding controls to detect subclinical peripheral nervous system involvement in early stage of HIV.

Aims & Objective: To perform Nerve Conduction Studies in asymptomatic HIV positive persons and corresponding controls.

Material and Methods: In this study, 100 participants in the age group 25-45 years were selected. In study group, 50 participants who were HIV positive and asymptomatic (CD4 count > 350 cells/mm^3) and were not on Anti Retro Viral Treatment (ART), were included. In control group 50 healthy age matched HIV negative participants were included. We performed Nerve Conduction Studies in these participants. For motor nerves, Distal Latency (DL), Motor Nerve Conduction Velocity (MNCV), Compound Muscle Action Potential (CMAP) amplitude were measured and for sensory nerves Onset Latency (OL), Sensory Nerve Conduction Velocity (SNCV) and Sensory Nerve Action Potential (SNAP) amplitude were measured.

Results: Nerve Conduction Studies in asymptomatic HIV revealed that, MNCV was significantly decreased for median motor nerve and tibial motor nerve in study group compared to control group, SNAP was significantly reduced for median sensory nerve in study group compared to control group, OL was significantly prolonged for sural nerve in study group than control group and SNCV was significantly decreased for sural nerve in study group than control group.

Conclusion: Nerve Conduction Studies in asymptomatic HIV positive persons suggests subclinical peripheral nervous system involvement in early stages of HIV. Hence Nerve Conduction Studies can be important to detect subclinical peripheral nervous system involvement in the early stages of HIV.

INTRODUCTION:

The Acquired Immunodeficiency Syndrome (AIDS) is caused by the Human Immunodeficiency Virus (HIV). Acquired Immunodeficiency Syndrome (AIDS) is a condition characterized by immunosuppression which results in opportunistic infections, secondary neoplasms, and neurologic manifestations. The three major routes of transmission of HIV are, sexual contact, parenteral inoculation & passage of the virus from infected mothers to their newborns. HIV is a retrovirus which belongs to the family of lentiviruses.[1]

HIV is a major global public health issue, and it has claimed 36.3 million lives so far. There were an estimated 37.7 million people living with HIV at the end of 2020. [2] Most common neurologic complication associated with HIV infection is peripheral neuropathy. [3] Mild and slowly progressive peripheral neuropathy of the axonal type in addition to a more severe progressive myelopathy or myeloradiculopathy occur along with early HIV infection, which might be the result of a direct neurotropic action of HIV. [4] Peripheral Neuropathy occur at all stages of HIV and take a variety of forms. Initially in the course of HIV infection, an acute inflammatory demyelinating polyneuropathy might occur. Peripheral nerve biopsy in HIV shows a perivascular infiltrate. [5] At autopsy in HIV, one half of the cases have shown evidence of peripheral neuropathy. Virological and clinical evidence has shown that the HIV is both lymphotropic and neurotropic. Peripheral neuropathy is the most frequent complication of HIV infection. [6] Nerve Conduction Studies in HIV patients of CDC group IV has shown reduction in the motor conduction velocity of the deep peroneal nerve and the median nerve, and a similar reduction of the sensory conduction velocity of the sural nerve. [7] Nerve Conduction Studies in asymptomatic HIV-1 seropositive individuals have shown increased latencies and decreased velocities of conduction [8] Demyelinating polyneuropathy has been reported in 30 to 33% of HIV seropositive patients. Commonest neurological complication that occurs with HIV is Distal symmetrical polyneuropathy. Reduced peroneal and sural nerve action potentials were seen in AIDS patients without any sign of peripheral neuropathy and sural nerve biopsy in AIDS might show to up to 30% loss of myelinated fibers. [9]

In Nerve Conduction Studies nerves are stimulated with small electrical impulses over several points, usually limbs and resultant responses are measured. Nerve Conduction Studies are used to monitor nerve function over time to determine progression of disease. [10] So, Nerve Conduction Studies are useful in examination of peripheral nervous system and HIV affects peripheral nervous system. Hence, we did Nerve Conduction Studies to detect early involvement of peripheral nervous system in HIV infected asymptomatic persons of Central India.

MATERIAL & METHODS:

The study was carried out in the Department of Physiology, Indira Gandhi Government medical College, Nagpur, India. Study was approved by the Institutional Ethics Committee. This was a cross sectional study and it was conducted over a period of 2 years. Sample size of 100 participants was selected, participants of age group 25 - 45 years were selected. Selected participants were divided into study group and control group. Study group contained 50 HIV positive persons, which were detected from Anti-Retroviral Therapy Centre of the institute. Participants who were Elisa test positive for HIV, had CD4 count > 350 cells/mm^3 and were not on Anti- Retroviral Treatment (ART) were included in study group. In control group 50 healthy age matched individuals from same population who were HIV negative were included. Participants with history of alcoholism, smoking, drug abuse, diabetes mellitus, hypertension, auditory abnormality, Central Nervous System (CNS) impairment due to any other disease, tuberculosis, autoimmune disease, immunos uppressant drug treatment were excluded from the study. Participants were given detail information about the procedure prior to study and written informed consent was obtained from every participant.

Nerve Conduction Studies were done using standard RMS

EMG EP machine (Recorders and Medicare System Pvt. Ltd.). Recordings were done using standard procedure such as temperature control (32°-34° C) and careful distance measurements for recording of well-defined and artifact free responses. Prior to the test participants were properly instructed and motivated to provide full cooperation and they were fully relaxed. The room where study was conducted was quiet and comfortable. Before starting the test, skin overlying the nerve was cleaned with the spirit at the proximal and distal end and electrodes were fixed on the skin overlying the muscle supplied by the nerve. Electrodes were connected to the oscilloscope through the preamplifier and speed was kept at 5 ms/cm. With the help of stimulating electrodes, the stimulation was given first at distal end (S1) of the nerve and the stimulus potential was recorded on the oscilloscope. The stimulus artifact, which was due to current leak, appeared at the beginning of the sweep. This was useful for noting the point of stimulus. The latent period was measured as the interval between the beginning of the stimulus artifact and the first deflection of the muscle potential. Then, stimulation was given at the proximal end (S2) of the nerve and action potential was recorded and latent period was noted. The difference between two latent periods, gives the time taken by the impulse to travel from the proximal point to distal point. Distance between the points of stimulation was measured. Conduction velocity was calculated in m/s by the formula: distance/difference in latent periods.

For median motor, ulnar motor, tibial motor & sural nerves surface electrodes were used. Ring electrodes were used for median sensory and ulnar sensory nerves. For sensory nerves (median, ulnar and sural) antidromic surface stimulation was performed. The Distal Latency (DL), motor nerve conduction velocity (MNCV) of the tested segment and compound muscle action potential (CMAP) amplitudes were measured for median motor, ulnar motor and tibial motor nerve. For median sensory nerve, ulnar sensory nerve and sural nerve, Onset Latency (OL), Sensory Nerve Conduction Velocity (SNCV) of the tested segment and Sensory Nerve Action Potential (SNAP) amplitudes were measured. Values of Nerve Conduction Studies were recorded for both right and left side and mean value of both sides was taken for analysis. For statistical analysis the values Nerve Conduction Study were expressed as mean with standard deviation. Values of each parameter in the study group and the control group were compared and analysed by using unpaired student's t- Test. p value less than 0.05 was considered as an indicator of statistically significant difference between the compared values.

RESULTS:

Table 1: Comparison and analysis of various anthropometric parameters of control and study groups

parameter	control Group (n=50) Mean ± SD	study Group (n=50) Mean ± SD	p value
Age (years)	33.34 ± 5.64	32.34 ± 5.52	0.373
Height (cm)	166.82 ± 3.76	166.90 ± 3.56	0.913
Weight (kg)	59.58 ± 2.20	58.94 ± 2.68	0.195
BMI (kg/m^2)	21.42 ± 0.71	21.16 ± 0.84	0.106

BMI: Body Mass Index

Comparison of anthropometric parameters of the control and study group was done. There was no significant difference in age, height, weight and BMI of the control and study group ($P > 0.05$). (Table 1)

Table 2: Comparison and analysis between control and study groups for various motor conduction parameters of motor nerves

motor nerve	DL (ms)			CMAP Amplitude (mV)			MNCV (m/s)		
	control n = 50 Mean ± SD	study n = 50 Mean ± SD	p value	control n = 50 Mean ± SD	study n = 50 Mean ± SD	p value	control n = 50 Mean ± SD	study n = 50 Mean ± SD	p value
median	3.83 ± 0.04	3.85 ± 0.05	0.074	8.13 ± 0.03	8.13 ± 0.04	0.762	55.17 ± 0.62	54.40 ± 1.44	0.001
ulnar	2.90 ± 0.04	2.92 ± 0.06	0.068	5.57 ± 0.23	5.58 ± 0.21	0.787	61.56 ± 0.93	61.21 ± 0.95	0.072
tibial	5.28 ± 0.15	5.33 ± 0.13	0.070	4.67 ± 0.62	4.67 ± 0.66	0.975	52.77 ± 1.23	52.20 ± 1.49	0.039

DL: Distal Latency, CMAP: Compound Muscle Action potential, MNCV: Motor Nerve Conduction Velocity

It was observed that the mean values of MNCV in median motor nerve were decreased in study group compared to control group significantly. No significant difference was observed between study and control group for CMAP amplitude and DL for median motor nerve. No significant difference is observed between study and control group for DL, CMAP amplitude and MNCV of ulnar motor nerve. For tibial motor nerve, no significant difference was observed between study and control group for DL, CMAP amplitude but significant difference was observed between MNCV of tibial nerve of control and study group. MNCV was decreased significantly in study group than control group for tibial motor nerve. (Table 2)

Table 3: Comparison and analysis between control and study groups for various sensory conduction parameters of sensory nerves

sensory nerve	OL (ms)			SNAP Amplitude (μV)			SNCV (m/s)		
	control n = 50 Mean ± SD	study n = 50 Mean ± SD	p value	control n = 50 Mean ± SD	study n = 50 Mean ± SD	p value	control n = 50 Mean ± SD	study n = 50 Mean ± SD	p value
Median	3.01 ± 0.09	3.04 ± 0.09	0.125	9.14 ± 0.53	8.90 ± 0.63	0.046	50.13 ± 1.88	49.47 ± 1.51	0.054
Ulnar	3.24 ± 0.12	3.28 ± 0.11	0.065	6.07 ± 0.33	6.09 ± 0.34	0.743	56.79 ± 1.13	56.50 ± 1.29	0.245
Sural	4.19 ± 0.14	4.30 ± 0.23	0.003	10.72 ± 0.51	10.65 ± 0.48	0.496	50.82 ± 0.87	50.31 ± 1.11	0.012

OL: Onset latency, SNAP: Sensory nerve action potential, SNCV: Sensory nerve conduction velocity

Mean values of OL and SNCV were not significantly different between control and study groups for median sensory nerve. Whereas mean value of SNAP for median sensory nerve was significantly decreased in study group as compared to control group. No significant difference was observed between control and study groups for ulnar sensory nerves for OL, SNAP and SNCV. For sural nerve, OL was significantly prolonged in study group than control group. SNCV of sural nerve was significantly decreased in study group than control group. No significant difference was seen between control group and study group for SNAP of sural nerve. (Table 3)

DISCUSSION:

According to our findings, MNCV was significantly decreased in the study group than the control group for median motor nerve & tibial motor nerve, SNAP was significantly decreased in study group as compared to control group for median sensory nerve, OL was significantly prolonged in the study group compared to the control group for sural nerve & SNCV was significantly decreased in the study group than the

control group for sural nerve. We also observed that, nerves in lower limb were affected more than upper limb.

CMAP and DL of the median motor nerve showed no significant difference between the control and the study group. No significant difference was seen for the OL and SNCV of the median sensory nerve between the control and the study group. CMAP, DL and MNCV of the ulnar motor nerve showed no significant difference between the control and the study group. For ulnar sensory nerve as well, OL, SNAP amplitude and SNCV showed no significant difference the control and the study group. No significant difference was seen for DL, CMAP amplitude of the tibial nerve between the control and the study group. There was no significant difference for the SNAP amplitude of the sural nerve between the control and the study group.

Above results are in accordance with Sinha S, Satishchandra P, who did Nerve Conduction Studies in asymptomatic HIV positive individuals and found significantly reduced conduction velocities in median motor, median sensory and sural nerves and reduced SNAP amplitude of the sural nerve in the study group as compared to the controls. Nerve conduction velocities were reduced more often in the lower limb nerves when compared to the upper limb nerves. [11] Kakkad A performed Nerve Conduction Studies in neurologically asymptomatic HIV individuals and they also found demyelinating neuropathy in median motor nerve and axonal neuropathy peroneal and sural nerves which was suggestive of presence of subclinical peripheral nerve involvement in asymptomatic Human Immunodeficiency Virus seropositive patients. [12] Narisetty V, Pokalkar D performed Nerve Conduction Studies and found subclinical neuropathy in almost 69% of patients. [13] Malessa R et al studied neurologically asymptomatic HIV-seropositive homosexual men and they also found that, patients with normal CD4 cell counts had significantly lower mean sural nerve conduction velocities and higher tibial distal motor latencies compared to controls. [14] Tagliati M. et al found electrophysiological abnormalities indicating distal sensory and motor axonal neuropathy in 28% subjects without clinical evidence of Distal Symmetrical Polyneuropathy. [15] Gastaut JL et al did nerve conduction studies in HIV and found moderate sensory polyneuropathy, more often at the subclinical than at the clinical level and it concerned asymptomatic carriers as well along with symptomatic HIV. [16] Aznar-Bueno C. et al did motor and sensory nerve conduction study in HIV seropositive individuals of stage A of CDC – 93 classification. Alteration of sural nerve conduction velocity was found. [17] Jakobsen J. et al did electrophysiological study in HIV positive homosexual men. They found increased spinal latencies, increased conduction time from gluteal crease to T12 and also in median and tibial nerve. Conduction velocity of large myelinated fibers of the median nerve was reduced. Their results showed a silent peripheral neuropathy concomitant with the HIV infection. They suggested that after early attack at T12 a progressive lumbar spinal cord disorder develops during latent HIV infection and eventually leads to paresis and ataxia of legs. [5]

Whereas McAllister R. et al studied HIV seropositive men for Nerve Conduction Studies, no significant difference was found between HIV seropositive and seronegative group. [18] Rhonchi O. et al also didn't find any alterations in the asymptomatic stages of infection CDC group II and III in nerve conduction studies, while subclinical peripheral nervous system (PNS) impairment was detected in symptomatic HIV-1 stages CDC group IV. [7] Fuller G et al did electrophysiological study in HIV infected patients and found that sensory nerve action potential was reduced more in legs than arms. They did not find any significant difference between motor action potentials of the ulnar nerve and ulnar nerve distal motor latency. [19] In HIV the pattern of sensory loss begins in the feet and later the hands. By the time sensory changes occur in the hands, the ankle jerk reflex is almost always abolished. [20]

Strength of our study was that we performed Nerve Conduction Studies in asymptomatic HIV which was useful in the early detection of peripheral nervous system involvement in HIV. However, we did not perform Nerve Conduction Studies in symptomatic HIV, which would have been useful in comparing the extent of involvement of the peripheral nervous system of asymptomatic and symptomatic individuals which was the limitation of our study.

In demyelination there is loss of myelin resulting in slowed conduction which manifests as significant reduction in conduction velocities and temporal dispersion (increase in the duration). Therefore, prolonged distal latencies and reduced conduction velocities are observed along with normal sensory or motor amplitude in demyelinating disorders. However, in case of axonal degeneration reduced sensory or motor amplitudes are seen but distal latencies and conduction velocities may remain normal. [10] Therefore, in our study, decreased MNCV in median nerve and tibial nerve suggest demyelination. Reduced SNAP amplitude in median nerve suggests axonal degeneration. Increased OL and decreased SNCV in sural nerve suggests demyelination. Our study also suggests lower limbs were affected more than upper limbs.

CONCLUSION:

Nerve Conduction Studies in asymptomatic HIV positive persons suggests subclinical peripheral nervous system involvement in early stages of HIV as evidenced by decreased MNCV in median motor nerve and tibial motor nerve, reduced SNAP in median sensory nerve & prolonged OL and decreased SNCV in sural nerve. It also revealed that in HIV, subclinical peripheral nerve system involvement was more in the lower limbs than in the upper limbs. Hence, Nerve Conduction Studies can be important to detect subclinical peripheral nervous system involvement in the early stages of HIV.

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