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Original Research Article

A comparative study of the conduction velocity of motor and sensory fibres of ulnar and median nerves among leprosy patients and normal subjects

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ABSTRACT

Background: Leprosy and the associated scourge have affected humanity for thousands of years. One of the most debilitating consequences of leprosy is peripheral neuropathy. Nerve Conduction Velocity study provides us with a non-invasive modality to assess peripheral nerve involvement in leprosy.
Methods: With this in mind, a cross-sectional observational study was conducted including 30 leprosy patients as "Cases" and 30 age-matched healthy subjects, not suffering from any kind of neurological disorders, as "Controls". Using a digital electromyography machine, the Latency, Amplitude and Conduction Velocities of Motor and Sensory fibres of Ulnar and Median nerves were recorded. The results were compared among controls and cases using suitable statistical tests (descriptive statistics and significance testing using unpaired t-test).
Results: In this study, with regard to Sensory Nerve conduction Velocity (SNCV), statistically very significant difference was noted in case of right (p 0.0011) and left (p 0.0037) ulnar nerves among controls and cases. The difference in the amplitude of Motor Action potential (MAP) with regard to right median nerve, among cases and controls, was also statistically significant (p 0.0127). Further the amplitude of Sensory Nerve Action Potential (SNAP) values were higher among cases compared to controls.
Conclusions: As such, the findings of this study (and which is also corroborated by many previous studies) lead us to the conclusion that NCV studies can detect lepromatous neuropathy much before the emergence of frank clinical signs and this type of neuropathy is predominantly demyelinating in nature with occasional axonal loss.

Keywords: Leprosy, Latency 1, Latency 2, Nerve Conduction Velocity, Neuropathy, Sensory nerve conduction velocity

INTRODUCTION

Leprosy and the associated scourge have affected humanity for thousands of years.[1-4] Leprosy, primarily found in tropical and subtropical countries, is a chronic granulomatous infection caused by slowly multiplying acid-fast bacilli, *Mycobacterium leprae* and *Mycobacterium lepromatosis.*[5] Worldwide, two to three million people are estimated to be permanently disabled because of leprosy.[6,7] Although the number of cases worldwide continues to fall, pockets of high prevalence continue in certain areas such as Brazil, South Asia and some parts of Africa.[8] India has the greatest number of cases and it reports over 50% of world's total leprosy cases.

One of the most debilitating consequences of leprosy is peripheral neuropathy. The nerve lesions may be insidious and without any clinical manifestation.[9,10] Further, nerve involvement may be present much before

the patient manifests clinical symptoms.[11] So, diagnosis of neuropathy in leprosy becomes pretty crucial. Nerve Conduction Velocity (NCV) study provides us with a non-invasive modality, to assess the peripheral nerve involvement in leprosy.[12-14]

The NCV study also helps in evaluating patients with peripheral neuropathy as also assessing the disease progression.[7,15] So, introduction of NCV studies as routine screening tool can help in early diagnosis of suspected cases and thus enable timely treatment.[16-17]

Various studies conducted in different parts of the globe, have found the occurrence of reduced nerve conduction velocity in leprosy induced peripheral neuropathy.

However, researchers have stressed the need for undertaking more such studies to further substantiate these findings. It is with this view that authors undertook the present study aimed at comparing different parameters of nerve conduction study (NCS) of motor and sensory fibres of Ulnar and Median nerves among leprosy patients of Medical College and Hospital, Kolkata and age-matched normal subjects.

METHODS

This cross-sectional observational study was carried over a period of 18 months (January, 2016- June, 2017) in the Department of Physiology, Medical College and hospital, Kolkata.

The 'study' population comprised of outpatients (aged 14-60 years), attending the Leprosy Clinic of Medical College and Hospital, Kolkata, who were newly diagnosed to be suffering from leprosy and were registered for the first time requiring a full course of Multi Drug Therapy (MDT).

Inclusion and exclusion criteria

- Known, cases of peripheral neuropathy (Diabetes, chemotherapy, radiotherapy, drug, ischemia and vitamin B complex deficiency induced), cervical radiculopathy, collagen diseases, HIV infection, chronic toxicities (Acrylamide, Arsenic, Lead etc.) and users of drugs such as amiodarone, disulfiram, isoniazid, metronidazole etc. were excluded from the study population.[9,10] Age-matched normal subjects who were not suffering from any major metabolic, neurologic and connective tissue disorder or from any chronic illness for which they were compelled to consume the aforementioned drugs on a regular basis, were included in the study as 'control' population. The control group was also chosen from Medical College and Hospital, Kolkata. Vulnerable population such as pregnant women, children, mentally incapacitated, elderly persons, sexual minorities and addicts were not included in this study population.

Sample size was determined as follows

Based on the previous data obtained from a study conducted by Ehler et al, in February 2013 and the Indian Dermatology Online Journal (December, 2014. S71- S75) respectively, the mean of Compound Muscle Action Potential of ulnar nerve at wrist of normal healthy individual was found to be 9.6±2.3 mV and the same in leprosy patients was found to be 5.3±2.74 mV.[18,19] Keeping the significance level (α) at 0.05 and power (1-β) at 0.80, the required minimum sample size was calculated to be 8 in each group. However, authors proposed to study at least 30 individuals in each group.

Data collection comprised of history taking using 'Case Report Form'. Questionnaires were filled up through interview of subjects (both cases and controls) to obtain necessary information. General examination and neurological assessments were done on both controls and cases.

The nerve conduction study parameters of the study population were recorded using a digital electromyography machine (RMS EMG. EP Mark II (version I)), keeping the room temperature between 26-30 degree Celsius. Filters were set at 2-5 Hz and sweep speed was 5m/s per division for motor study and the corresponding settings for sensory study were 2-3KHz and 2m/s respectively. During recording, it was also ensured (through prior instructions), that the subject remained relaxed, following a good night's sleep and proper breakfast and without undertaking any hard work or exercise in the morning.

The quantitative data, so generated, have been analyzed using statistical software such as Microsoft Excel and Graphpad Instat. Unpaired Student t-test was carried out to analyze significance of difference of means between the two groups i.e., controls and cases.

RESULTS

In the present study aimed at comparing the parameters of Nerve Conduction velocity (NCV) study among leprosy patients and normal healthy individuals, 30 leprosy patients and 30 control subjects were included.

Highest percentage of leprosy patients (43.33%) were found in the age group of 31-40 years as well as highest percentage of control subjects were also from the same age group. This was probably due to the increased awareness of men and women in this age group. Sex-wise distribution of controls and cases were also fairly comparable.

The different study variables, that were recorded for each control subject as well as case subjects, cover both motor and sensory nerve conduction study parameters. The nerves that have been chosen are Median and Ulnar nerves of right and left sides. The variables are-

conduction velocities, amplitude of action potential and latency 1 and 2 of action potential, measured in each subject.

Table 1: Distribution of amplitude of compound motor action potential (CMAP) of right median nerve among controls and cases.

NCV Parameter	Controls (n=30) Mean±SD	Cases (n=30) Mean±SD	p-Value
Amplitude of MAP (mV)	9.36±4.13	7.04±2.71	0.0127 (significant)

The amplitude of compound motor action potential for right Median nerve is quite higher in control subjects as compared to leprosy patients. The difference in the amplitude of Compound Motor Action potential (CMAP) with regard to right median nerve among cases and controls, was statistically significant (p 0.0127) (Table 1).

The compound motor action potential of right median nerve was found to be significantly reduced along with severe reduction of force of muscle contraction in cases of leprosy as compared to healthy controls (Table 1).

During examination of nervous system of these patients, there was presence of varying degree of hypotonia as well as reduction of muscle power relative to age, sex and built matched controls. Similar findings were seen in other motor nerves that were tested, but they failed short to be statistically significant.

Table 2: Distribution of right ulnar nerve sensory conduction velocities among controls and cases.

NCV Parameter	Controls (n=3) Mean±SD	Cases (n=30) Mean±SD	p-Value
SNCV (m/s)	54.01±8.08	39.86±20.99	0.0011 (very significant)

It is seen that the sensory conduction velocities of right Ulnar nerves are reduced in leprosy patients as compared to normal subjects. The difference is statistically very significant (Table 2).

Table 3: Distribution of left ulnar nerve sensory conduction velocities among controls and cases.

NCV Parameter	Controls (n=30) Mean±SD	Cases (n=30) Mean±SD	p-Value
SNCV(m/s)	50±6.03	37.59±21.67	0.0037 (very significant)

The table shows that the sensory conduction velocity of leprosy affected left Ulnar nerves are reduced than the healthy nerves. The p-value is very significant once again (Table 3). The above nerve conduction study findings were significantly associated with hypaesthesia, anaesthesia (Table 2 and 3). Sometimes the patients also presented with loss of toes and chronic ulcers due complete lack of pain, temperature and touch sensations.

Table 4: Distribution of left ulnar nerve motor conduction velocities among controls and cases.

NCV Parameter	Controls (n=30) Mean±SD	Cases (n=30) Mean±SD	p-Value
MNCV(m/s)	56.03±9.41	50.34±21.83	0.196

The table shows that the motor conduction velocity of leprosy affected left Ulnar nerves are reduced than the healthy nerves. Conduction velocities are clearly higher in control subjects (Table 4).

In this study, the mean values of Motor Nerve Conduction Velocity (MNCV) of all the four nerves were more in healthy controls than in case of leprosy patients although the p value of this difference was not significant (Table 4). Out of 30 patients, no conduction velocity could be recorded in case of four (4) Right Ulnar Nerves, three (3) Left Ulnar Nerves and two Left Median Nerves. These patients were suffering either from LL Hansen or from BT Hansen and in each case, the duration of the disease was more than six months. And in all cases clinical nerve thickening was present in one or more peripheral nerves

Table 5: Distribution of latency 1 of motor action potential of right median nerve among controls and cases.

NCV parameter	Controls (n=30) Mean±SD	Cases (n=30) Mean±SD	p-Value
Latency 1 (MS)	3.14±0.64	3.49±0.85	0.075

It is seen that the onset latency of motor action potential of right median nerve is higher in case of leprosy patients in comparison with control subjects (Table 5).

Table 6: Distribution of latency 1 of motor action potential of right ulnar nerve among controls and cases.

NCV parameter	Controls (n=30) Mean±SD	Cases (n=30) Mean±SD	p-Value
Latency 1 (ms)	2.23±0.31	2.55±1.48	0.24

The onset latency of motor action potential of right Ulnar nerve shows that it is lower in case of healthy individuals

and increased in leprosy patients (Table 6). The onset latencies of right ulnar nerve and right median nerve are seen to be reduced in leprosy patients as compared to normal healthy subjects although they fail short to be statistically significant (Tables 5 and 6). The observations clearly indicate that in leprous neuropathy the time taken for the stimulus to initiate an evoked potential and the time taken by the impulse to travel along the fastest fibres are more than the healthy controls.

Table 7: Distribution of latency 1 of sensory action potential of left ulnar nerve among controls and cases.

NCV Parameter	Controls (n=30) Mean±SD	Cases (n=30) Mean±SD	p-Value
Latency 1 (ms)	23±0.24	10.77±1.01	0.0181 (significant)

In case of left Ulnar nerve the latency 1 of sensory action potential is higher in control subjects as compared to leprosy patients. In this case, the p value is seen to be significant (Table 7).

Table 8: Distribution of amplitude of sensory action potential of right ulnar nerve among controls and cases.

NCV Parameter	Controls (n=30) Mean±SD	Cases (n=30) Mean±SD	p-Value
Amplitude (mV)	0.006±0.003	0.04±0.03	0.0047 (very significant)

For right Ulnar nerve, the amplitude of sensory action potential is higher in leprosy affected nerves than in healthy nerves. The p value seems to be very significant in this case (Table 8).

The observations, amplitude of sensory action potential as well as the latency 1 of the sensory nerves, did not turn out to be as expected (Table 7 and 8). In both the instances the observed values were more in leprosy patients as compared to healthy controls where as it should have been just the reverse.

Lastly, latency 2 in case of MAP was found to be more among cases than controls (except for left median nerve), although the difference stopped short of being statistically significant.

Latency 2, in case of SNAP did not corroborate with the expected outcome. With regard to the measurement of SNAP peak latency (Latency 2), it is observed that peak latency is increased in leprosy affected Right and Left Median nerves.

Whereas, in case of affected Left and Right Ulnar Nerves, the mean values of peak latencies are more in control subjects (Figure 1 and 2).

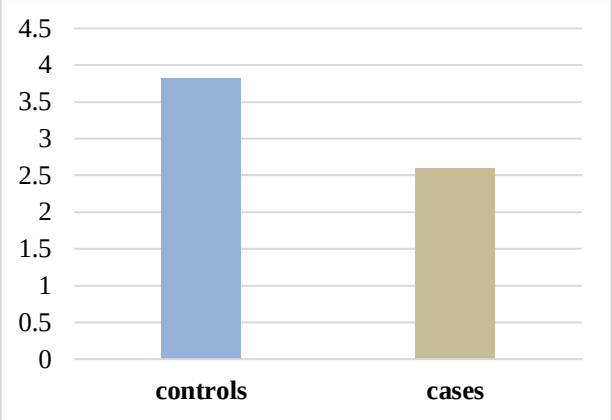

Figure 1: Distribution of latency 2 of sensory action potential of right ulnar nerve among controls and cases.

Latency 2 is more in control subjects than in cases. p value is very significant here.

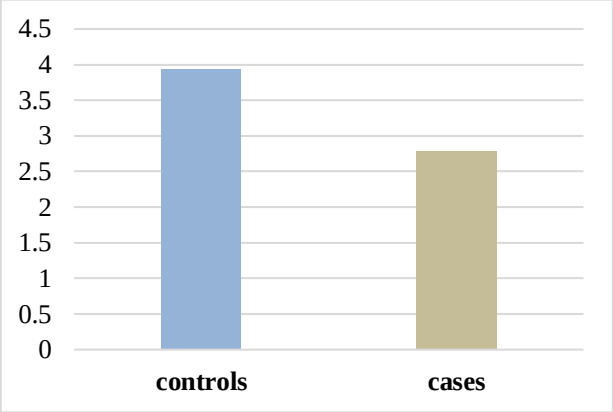

Figure 2: Distribution of latency 2 of sensory action potential of left ulnar nerve among controls and cases.

Latency 2 is more in control subjects than in cases. The p value is very significant.

DISCUSSION

In this study, the mean values of Motor Nerve Conduction Velocity (MNCV) of all the four nerves were more in healthy controls than in case of leprosy patients although the p value of this difference was not significant. Out of 30 patients, no conduction velocity could be recorded in case of four (4) Right Ulnar Nerves, three (3) Left Ulnar Nerves and two Left median Nerves. These patients were suffering either from LL Hansen or from BT Hansen and in each case, the duration of the disease was more than six months. And in all cases clinical nerve thickening was present in one or more peripheral nerves. Among all the 30 patients, seven (7) patients did not have any nerve thickening. So, when clinical examination was done the subjects seemed to be completely normal, although the signs of sensory loss,

like- hypo-aesthesia, anaesthesia, reduced temperature sensation etc. were always present in each case.

Comparable findings were reported by various other researchers. Husain and Malaviya, found reduced nerve Conduction Velocities (NCVs) in leprosy.[20] According to their study, the sensory domain of conduction velocity showed more changes in leprosy affected nerves. Cabalar et.al., in their study found that Ulnar nerve was the most commonly affected nerve in their study and abnormalities were frequent even on non-enlarged nerves.[21-25] Granger et.al., in their study, reported bilateral abnormal conduction velocity in right Median and Ulnar nerves (non-responsive).[26] Anita et.al., also found decreased elbow-wrist MNCV in Ulnar nerves they tested during their study.[27,28] Hackett et.al., found that leprosy patients with normal neurological evaluation of the peripheral nerve might have abnormally slow conduction velocity at elbow.[29]

With regard to Sensory Nerve Conduction Velocity (SNCV), statistically very significant difference was noted in case of right (p 0.0011) and left (p 0.0037) ulnar nerves among controls and cases. It implies a strong positive correlation between the leprosy induced neuropathy and marked reduction in conduction velocity of sensory fibres of Ulnar nerves. The difference in mean values of SNCV with regard to median nerves did not turn out to be statistically significant although the mean values per se were lower among cases compared to controls. Among 30 nerves tested, no sensory conduction velocity could be tested in six Right Ulnar Nerves, seven Left ulnar Nerves, three Right Median Nerves and in three Left Median Nerves and in all cases, the duration of the disease was more than six months.

Most of such studies, conducted worldwide, have found that changes in the different attributes of NCV study were more pronounced in the sensory domain than in their motor counterpart. Sensory Nerve Conduction study was also found to be the earliest affected test in leprosy induced peripheral neuropathy. These observations also keep parity with the findings of this study.

The difference in the amplitude of Motor Action potential (MAP) with regard to right median nerve among cases and controls, was statistically significant (p 0.0127) which demonstrates statistically significant correlation between lepromatous neuropathy and amplitude of MAP. The same was however, not the case with the other nerves (left median, right and left ulnar) although the mean values of amplitude were less among cases compared to controls (except for right ulnar nerve).

Interestingly, the amplitude of Sensory Nerve Action Potential (SNAP) values were higher among cases compared to controls. However, this finding of this study contradicts with the other studies. Rosenberg et al, in their study conducted in 1968, found that SNAP was of reduced amplitude in both right and left Ulnar nerves.[30,31] Kar et al, in their study, found changes in leprosy afflicted nerve fibres. Out of 10 cases in their study, amplitude of SNAP and MAP were found to be reduced in all 10 cases.[32,33] In another study, Brakel et al, found that SNAP amplitudes were the most frequently affected parameter in NCV study of leprosy.[16,34] This paradoxical finding can possibly be attributed to some technical factors and electrical noise which assume importance in sensory recordings as most of the sensory responses are very small and as such get easily affected by technical errors.

So, in short, it might be said that, low conduction velocity was often encountered in association with reduced amplitude and reduced latency 2 of action potential in case of the present study.

CONCLUSION

Based on relevant literature and the findings of this study, authors can conclude that in all types of leprosy, the parameters of sensory nerve conduction study are more extensively affected as evidenced by the derangement of conduction velocity, amplitude and the peak latency from their optimum values. The conduction velocity and the amplitude of MAP are also significantly affected in peripheral neuropathy of leprosy. In leprosy, the neuropathic lesion is predominantly demyelinating in nature as reflected by significant reduction in conduction velocities in both sensory and motor conduction studies. When conduction velocity is near a borderline value with a normal amplitude and normal latency 2, it usually represents demyelination. Whereas a borderline velocity with a markedly reduced amplitude and normal latency 2, most often, implies axonal loss. So, this study establishes the fact that leprosy is always associated with severe demyelination of peripheral nerves with occasional axonal damage. Peripheral neuropathy in leprosy might be present even before the clinical manifestation of the disease. If not interrupted by treatment, the neuropathy leads to progressive nerve degeneration, paralysis and permanent damage to different body parts. Multi Drug Therapy and Prednisolone can halt the progression of neuropathy. But the damage that has already occurred cannot be reverted in most of the cases. Yet Physiotherapy and rehabilitation can improve the standard of living if it is not too late. Sometimes regeneration of myelin sheath around the nerve fibres may also provide relief from the sensory symptoms.

As such, the present study, underscores the fact that Nerve Conduction study is of considerable significance for early diagnosis of peripheral neuropathy in leprosy and it might be resorted to as a screening tool for early detection of leprous neuropathy. However, there is still need for undertaking more such studies to further substantiate these findings.

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