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Original Article

Electrophysiological Study of Nerve Involvement in Rheumatoid Arthritis

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ABSTRACT

Background and Aim: Rheumatoid arthritis is a chronic systemic inflammatory disease of undetermined etiology. Rheumatoid arthritis is primarily considered a disease of joint but abnormal systemic immune response produce a variety of extra-articular manifestation. Rheumatoid Arthritis (RA) is associated with various neurological manifestations including nerve compression by synovial proliferation, sensory or sensorimotor neuropathies causing neurologic symptom. This study aims to assess peripheral nerve involvement on conduction in rheumatoid arthritis. **Methods:** 100 patients and healthy controls were included in this study. Rheumatoid arthritis patients diagnosed at the Department of Medicine in VIMSAR during the time period of November 2016-May 2017 were included in the study. Nerve conduction of median, ulnar (motor), posterior tibial and common personal nerves and surely nerves were studied for all healthy controls and patients. **Results:** In this study, peripheral neuropathy was detected in 54 patients; Mononeuritis simplex was the commonest lesion and detected in 36 out of the 54 patients. Mon neuritis multiplex was detected in 11 and symmetrical polyneuropathy found in 7 patients. The entrapment neuropathy was found in 25 patients, affecting the median in 13, posterior tibial 8 and ulnar 4. So, the axonopathy (mainly due to vasculitis) and local demyelination (mainly due to entrapment) were the common types of nerve injury seen in rheumatoid arthritis. **Conclusion:** Neurogenic lesions were detected in patients with rheumatoid arthritis without neurological symptoms. So, nerve conduction study are recommended in routine examination to diagnose early neuropathy in RA patients.

Key words: Nerve conduction study, Rheumatoid arthritis, SNCV, MNCV, CAMP, SNAP, SDL, DML, Electromyography.

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INTRODUCTION

Rheumatoid Arthritis (RA) is associated with various neurological extra-articular manifestations including nerve compression by synovial proliferation, sensory or sensorimotor neuropathies.[1] And on the Central Nervous System (CNS) causing neurologic symptoms.[2] Carpal tunnel syndrome is the most common compressive neuropathy in RA, Less common are tarsal tunnel syndrome and ulnar nerve entrapment.[3] Mononeuritis multiplex is a form of combined sensorimotor neuropathy caused by vasculitis of epineural and perineural arteries and can present as acute foot or wrist drop, such patients usually have severe longstanding RA with other extra-articular features.[4] Myopathy in RA is usually due to disuse atrophy, corticosteroid therapy, or both. Clinically significant disease-related myositis is very rare.[5] Denervation atrophy from peripheral neuropathy is another cause of muscle weakness.[6]

Nerve Conduction Studies (NCS) typically comprise the electrodiagnostic evaluation of function of motor neurons, nerve roots, peripheral nerves, neuro-muscular junction.[7] NCS are considered medically necessary for diagnosing the following conditions: Unexplained peripheral neuropathy with pain of a neuropathic pattern, demonstrated sensory or motor loss on physical examination, neuropathy suspected to be due to trauma, Carpal tunnel syndrome, ulnar neuropathy at the elbow or wrist, tarsal tunnel syndrome, peroneal palsy with foot drop, cervical and lumbar radiculopathy.

NCS provide information regarding the presence, severity and location of a lesion, symmetric/asymmetric neuropathy, mononeuropathy or disorders affecting the neuromuscular junctions. Also, the functional modality most involved (sensory or motor) and the predominant pattern of pathology (e.g., axonal, demyelinating, or both.[8,9] In NCS surface electrodes are usually used for both stimulation and recording of the electrical responses. However; needle electrodes are sometimes needed to evaluate a deep nerve, such as the sciatic or the femoral nerve.[8,9]

The aim is to study the nerve conduction in normal subjects and to evaluate the nerve involvement in rheumatoid arthritis patients.

METHODS

The study had been conducted at the Physiology Department, in VIMSAR, Burla, from November

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2016 - May 2017. The study was approved by the institutional ethical committee VIMSAR, Burla and informed consent was obtained from both the study and control group. 100 patients fulfilling American Revised Criteria (ARC) 1987.[10] were included in the study. 100 healthy volunteers of similar age and sex, were compared to rheumatoid arthritis patients, and were examined for nerve conduction. NCS for median, ulnar (motor), posterior tibial and common peroneal nerves and sural nerve were done for each patient and normal subject to study the distal motor and sensory latency (DML, DSL), compound motor and sensory action potentials (CMAP, SNAP) and motor and sensory nerve conduction velocities (MNCV, SNCV) by using the system 98- MyoQuik (micromed) EMG machine. Data were analysed by (SPSS) software; unpaired t-test was used to compare between the studied parameters. *P*-value equal to or less than 0.05 is considered to be significant.

RESULTS

Characteristics of the study populations with and without diabetes are given in Table 1.

It shows motor nerve conduction study in ulnar, median, posterior tibial and common peroneal nerve. There was prolonged distal latency for rheumatoid arthritis patients than that of normal subjects with significant difference between them (P =0.01). There was a decrease of the Compound Motor Action Potentials (CMAP) for rheumatoid arthritis patients compared to normal subjects with significant difference between them ($P \leq 0.05$). The Motor Nerve Conduction Velocities (MNCV) for patients were less than that of normal subjects with significant difference between them ($P < 0.01$).

It shows prolongation of Sensory Distal Latency (SDL) for rheumatoid arthritis patients compared to normal subjects with significant difference between them ($P = 0.01$). The Sensory Nerve Action Potential (SNAP) was less in rheumatoid arthritis patients than in normal subjects with significant difference between them ($P < 0.01$). The Sensory Nerve Conduction Velocities (SNCV) were less for rheumatoid arthritis patients than normal subjects with significant difference between them ($P < 0.05$).

Table 2 shows the type of peripheral neuropathy in RA patients, there are mononeuritis simplex detected in 35 patients (66.6%); mononeuritis multiplex detected in 12 patients (20.3%) and symmetrical polyneuropathy detected in seven patients (12.9%).

It shows nerve entrapment, which was detected in 25 patients (46.28%) (Out of 35 patients who developed mononeuritis simplex) affecting mainly the median (24%), ulnar (7.4%) and posterior tibial (14.8%) nerve.

Table 1: Demographic features of case and control group.

	RA	CONTROL	*P* Value
Age (yrs)	43.92 ± 8.55	39.85 ± 6.10	0.92 (NS)
Sex (male)	47	53	
BMI (Kg/m^2)	31.43 ± 3.21	25.63 ± 4.27	0.63 (NS)

RA: Rheumatoid arthritis; SD: standard deviation. $p < 0.05$ is significant.

DISCUSSION

This study demonstrates the involvement of peripheral nerves in rheumatoid arthritis patients, which is a complication of the disease. Nerve conduction study parameters like distal latency, compound motor action potential and nerve conduction study were significantly high in rheumatoid arthritis patients. The explanation for the differences in rheumatoid arthritis is that nerve compression (nerve entrapment) causes mechanical (direct) pressure that affects mainly the myelin sheath of these nerves, to prolong MDL and SDL and a decrease in MNCV and SNCV, with normal or slight decreases of CMAP and SNAP, which were detected by nerve conduction study. Later on, if this pressure persists, it will affect the axon leading to the decrease of the CMAP and SNAP. These findings may represent the preliminary picture of any peripheral neuropathy pattern.[11,12] Other causes are vasculitic lesions in rheumatoid arthritis which cause ischemic changes that affect the axon mainly and lead to axonopathy that causes the decrease of the CMAP and SNAP; and

Table 2: Nerve conduction study in sensory nerves.

Nerve	SNCV in RA (m/sec)		*P* value	SNAP IN RA (mv)		*P* value	SDL IN RA (m sec)		*P* value
	RA	Control		RA	Control		RA	Control	
MEDIAN N	60.91 ± 4.94	50.27 ± 7.86	0.01**	32.77 ± 7.49	23.22 ± 9.64	0.01**	3.39 ± 1.04	2.36 ± 0.21	0.01**
ULNAR N	60.57 ± 5.22	54.18 ± 5.56	0.04*	32.51 ± 6.81	27.09 ± 8.13	0.01**	2.93 ± 0.50	2.07 ± 0.15	0.01**

SNCV=sensory nerve conduction velocity, SNAP=sensory nerve action potential, SDL=sensory distal latency. **P<0.01, *P<0.05

Nerve conduction study in motor nerves.

Nerve	MNCV in (m/sec)		*P* value	CMAP IN (mv)		*P* value	DML IN (m sec)		*P* value
	RA	Control		RA	Control		RA	Control	
Median nerve	39.92 ± 8.55	60.93 ± 3.89	0.01**	10.53± 3.63	16.37± 2.72	0.02 *	3.920 ± 0.742	3.04 ± 0.31	0.01**
Ulnar nerve	44.11 ± 4.84	62.60 ± 5.13	0.01**	11.84 ± 3.58	15.76 ± 3.20	0.04 *	2.68 ± 0.52	2.24 ± 0.36	0.01**
Posterior tibial nerve	34.07 ± 6.38	51.55 ± 3.37	0.01**	8.59 ± 2.72	12.29± 2.36	0.04 *	5.04 ± 0.98	3.69 ± 0.24	0.01**
Common peroneal nerve	36.94 ± 4.13	52.09 ± 2.70	0.01**	8.36± 2.16	11.92± 2.88	0.05 *	4.53 ± 0.64	3.85 ± 0.22	0.01**

MNCV=motor nerve conduction velocity, CAMP=compound motor action potential, DML=distal motor latency. **P<0.01, *P<0.05

Types of pheripheral neuropathy.

Type	Positive peripheral neuropathy
Mononeuritis simplex	35(66.6%)
Mononeuritis multiplex	12(20.3%)
Symmetrical polyneuropathy	7(12.9%)

Types of nerve entrapment.

Nerve Involved in Entrapment	
Median N	13(24%)
Ulnar Nerve	4(7.4%)
Posterior Tibial Nerve	8(14.8%)

hence it was detected by nerve conduction study[13,14] In the present study, the peripheral neuropathy findings in RA patients were detected in 54 patients (54%) and these findings are in agreement with other studies.[15,16] This may be due to geographical similarity. Another cause is vasculopathy; vascular injury is considered as a key finding in the pathogenesis of rheumatoid arthritis. It is responsible for the different patterns of non-compressive peripheral neuropathy in RA including mononeuritis multiplex and distal symmetrical sensory or sensorimotor neuropathy.[17,18] In this study, mononeuritis simplex was detected in 35 patients (66.6%) out of 54 patients who developed peripheral neuropathy and this is in agreement with another study.[19] Entrapment neuropathy was found in 25 patients (46.28%) (Out of the 35 patients with mononeuritis simplex). The entrapment neuropathy affects mainly the median, ulnar and posterior tibial nerve. The carpal tunnel syndrome (CTS) of median nerve at the wrist is the most common form of median nerve entrapment and is the prototypical injury.[20] In present study CTS was detected in 12 patients (24.07%) and this was similar to other studies.[21,19] Carpal tunnel syndrome was detected in 13 patients (24.07%). The second common type of nerve entrapment in our study was tarsal tunnel syndrome of posterior tibial nerve, which was detected in 8 patients (14.81%) and this is nearly in agreement with another study.[22,23] The third common nerve entrapment in rheumatoid arthritis patients in this study was ulnar nerve entrapment which was detected in 4 patients (7.40%) and this was nearly similar to findings of another study;[15] the ulnar nerve entrapment at the cubital area was detected in 2 patients (3.70%) and at the Guyon canal by 2 patients (3.70%) also. Mononeuritis multiplex was detected in 11 patients (20.37%) and this is nearly in agreement with the findings in another study.[24,25] Symmetrical polyneuropathy was seen in 7 patients (12.9%) and this finding was similar to the findings of another study.[26,15]

CONCLUSION

Peripheral nerve involvement was common, in patients with rheumatoid arthritis. This study demonstrates the involvement of peripheral nerves in rheumatoid arthritis patients, which remain subclinical. As NCS is a non-invasive techniques should be recommended in patients of Rheumatoid arthritis as a routine for early detection of peripheral neuropathy.

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CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest.

Ethical Approval

Approved by IEC VIMSAR, Burla.

Informed Consent

Consent was taken from all the subjects of study group.

ABBREVIATIONS

RA: Rheumatoid Arthritis; **CNS:** Central Nervous System; **NCS:** Nerve Conduction Studies; **ARC:** American Revised Criteria; **SDL:** Sensory Distal Latency; **MDL:** Motor Distal Latency; **SNAP:** Sensory Nerve Action Potential; **SNCV:** Sensory Nerve Conduction Velocities; **CTS:** Carpal Tunnel Syndrome.

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