

RESEARCH PAPER

Comparison of Median and Ulnar Nerve Conduction Parameters in Patients with Neuralgic Upper Limb Pain Treated with Pregabalin and Gabapentin

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ABSTRACT

Background: The neuralgic pain of the upper limb is correlated with pain, functional disability and nerve conduction parameters changes. Gabapentin and pregabalin are used frequently in the treatment of neuropathic pain. In the present study we compared the clinical and electrophysiological results of these two treatments.

Methods: In this study, 60 patients with neuralgic upper limb pain were studied comparably, divided into Pregabalin (n=30) and Gabapentin (n=30) groups. Nerve conduction studies were performed on the bilateral median and ulnar nerves at baseline, 2 weeks and 6 weeks. Motor and sensory parameters were evaluated and compared between the two groups such as amplitude, latency and conduction velocity.

Results: The demographic characteristics of the two groups were comparable. The mean NRS score decreased from 7.16 ± 0.69 to 2.26 ± 1.01 in the Pregabalin group and from 6.83 ± 0.75 to 1.76 ± 0.62 in the Gabapentin group at 6 weeks. The reduction in NRS was statistically significant within both groups ($p < 0.001$). PDQ scores also decreased from 11.96 ± 2.55 to 3.73 ± 2.04 in the Pregabalin group and from 14.90 ± 3.06 to 3.20 ± 1.71 in the Gabapentin group ($p < 0.001$).

Conclusion: Both Pregabalin and Gabapentin were associated with improvement in pain and functional disability over the 6 week follow-up period. Nerve conduction parameters in median and ulnar nerves were similar in both treatment groups. Overall, the clinical and electrophysiological results were comparable in both groups.

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INTRODUCTION

Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage. Pain is often classified as acute or chronic. Acute pain subsides as healing takes place. Chronic pain is persistent.¹ Pain can be allodynia (pain due to stimulus that does not normally provoke pain), neuralgia and neuropathic. Neuralgic pain refers to pain in the distribution of nerve or nerves. Causes of neuralgic upper limb pain are broadly divided into spinal (radiculopathy or

myeloradiculopathy) and neural (involving peripheral nerve). Among the spinal causes, cervical radiculopathy is a common disorder affecting people most often in the fourth and fifth decades of life. Causes of cervical radiculopathy include osteoarthritis, osteophytes, herniated discs and ligamentum flavum hypertrophy. Patients commonly present with vertigo, neck stiffness, unilateral or bilateral aching pain in neck and shoulder. Patients may also present with pain, numbness and tingling sensation in the upper limb.² Among the neural

causes, carpal tunnel syndrome (CTS) is the most common cause of neuralgic upper limb pain. Carpal tunnel syndrome occurs due to entrapment of the median nerve at the wrist and is characterized by numbness or tingling in the sensory distribution of the nerve in the hand.³ Other neural causes of neuralgic upper limb pain are entrapment neuropathies involving median, ulnar and radial nerves. Ulnar neuropathy at the elbow (UNE) is a common peripheral neuropathy, second only to carpal tunnel syndrome in incidence and is characterized by numbness, tingling, and pain in the fourth and fifth fingers with hand weakness and can be due to compression injury of the ulnar nerve.⁴ Radial neuropathy is another cause for neuralgic upper limb pain. Radial nerve is more vulnerable to injury because of its long and winding course.⁵ The neuropathy can be caused by trauma and very rare to be caused by entrapment. Patient commonly presents with localized tenderness over the lateral part of the proximal forearm, an area distal to the lateral epicondyle.

Nerve conduction study (NCS) is a test of the speed of signals through a nerve. There are essentially no risks involved. A NCS test shows the condition of the best surviving nerve fibres and may remain normal in some cases. A normal NCS test result can occur in some persons with significant nerve disease.⁶ Nerve conduction studies (NCS) enable the clinician to detect signs that cannot be confirmed by neurological examination alone and can guide in diagnosis and treatment. Nerve conduction studies are also used to monitor nerve function over time to determine disease progression, to assess the complications of treatment, as well as identifying the disease course (acute/subacute/chronic).⁷ Pregabalin and gabapentin are the first line drugs for the management of neuralgic pain. Pregabalin (S-3-aminomethyl-5-methylhexanoic acid) is a structural derivative of the inhibitory neurotransmitter γ -aminobutyric acid (GABA). Pregabalin is generally well tolerated with no contraindications. Pregabalin undergoes negligible metabolism in humans and is eliminated from systemic circulation primarily by renal excretion as unchanged drug.^{8,9} The most common adverse effects of pregabalin are dizziness and drowsiness. Arezzo et al evaluated the effect of pregabalin on pain and nerve conduction velocity in patients of painful diabetic peripheral neuropathy (DPN) and there was a significant improvement in pain but no significant effect on nerve conduction velocity in patients with painful DPN.¹⁰ Siddall et al investigated the effect of pregabalin in central neuropathic pain due to spinal cord injury and observed a significant improvement in pain

score from baseline.¹¹ Gabapentin, (1-aminomethyl cyclohexane acetic acid), was originally synthesized as a cyclic analogue of gamma aminobutyric acid (GABA). Gabapentin appears to be an effective treatment for neuropathic pain, acting centrally to reduce hyperalgesia and allodynia. Rosenberg et al concluded that gabapentin may be a useful adjunct for treating neuropathic pain with a minimum of side effects, particularly in patients with postherpetic neuralgia and direct peripheral nerve injuries.¹⁴ The most common side effects of gabapentin in adult patients include dizziness, fatigue, drowsiness, weight gain, and peripheral edema.¹² Michael et al evaluated the clinical effectiveness of gabapentin in the treatment of neuropathic pain and found significant reduction in neuropathic pain.¹³ Thus, this study is planned to compare and correlate nerve conduction velocity and clinical parameters in patients with neuralgic pain of upper limb treated with pregabalin or gabapentin.

MATERIALS AND METHODS

The present prospective, randomized study was conducted in the Department of Physiology in collaboration with Department of Anaesthesiology & Critical Care, Pt. B.D. Sharma PGIMS, Rohtak. Sixty patients of either sex, in the age group of 18-60 years, attending pain clinic were enrolled in the study.

The patients were randomly divided in two groups of 30 each by a computer-generated randomization number table.

Group-I (n=30): Pregabalin was given in doses of 75mg at bed time for three days and then twice daily for six weeks.

Group-II (n=30): Gabapentin was given in doses of 300mg at bed time for three days and then twice daily for six weeks.

Evaluation of Nerve Conduction Study Parameters

Nerve conduction study was done in Department of Physiology using an Aleron 401 model electromyography machine. Two small button type silver electrodes were used as reference and recording electrodes for nerve conduction studies. Ground electrode was used for earthing. The following electro physiological tests were performed after explaining the procedure to patient in his/her own language, to allay the apprehension.

The basal recording of nerve conduction velocity (both sensory and motor) for radial, median and ulnar nerves was done. Amplitude (μ V), latency (ms) and conduction velocity (m/s) were recorded automatically by the machine and

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a printout was obtained. Patients were followed up at two and six weeks. On both the follow up visits, all patients underwent repeat nerve conduction velocity.

Motor Nerve Conduction Study

- Median nerve (right and left)
- Ulnar nerve (right and left)

Sensory Nerve Conduction Study

- Median nerve (right and left)
- Ulnar nerve (right and left)

RESULT

The present, prospective, randomized study was conducted in the Department of Physiology and Department of Anesthesiology & Critical Care,

Pt. B.D. Sharma PGIMS, Rohtak. Sixty patients of either sex, in the age group of 18-60 years attending Pain Clinic were enrolled in the study. The patients were randomly divided into two groups of 30 each by a computer-generated randomization number table.

Group-1(n=30): Pregabalin was given in doses of 75mg at bed time for three days and then twice daily for six weeks.

Group-2(n=30): Gabapentin was given in doses of 300mg at bed time for three days and then twice daily for six weeks.

All patients were subjected to detailed clinical history and physical examination in the Pain Clinic. Evaluation of Nerve Conduction Velocity (NCV) was done in department of Physiology using an Aleron 401 model electromyography machine.

Table 1. Bilateral median nerve motor conduction parameters

Side	Parameter	Time	Pregabalin	Gabapentin	p
Right	Amplitude (mV)	Baseline	8.74±4.98	9.46±3.69	0.983
Right	Amplitude (mV)	2 weeks	8.41±4.92	9.83±3.78	0.243
Right	Amplitude (mV)	6 weeks	8.27±4.91	9.75±3.66	0.221
Right	Latency (ms)	Baseline	4.49±1.13	4.30±0.64	0.226
Right	Latency (ms)	2 weeks	4.35±1.08	4.17±0.56	0.587
Right	Latency (ms)	6 weeks	3.96±0.43	4.05±0.64	0.314
Right	Conduction velocity (m/s)	Baseline	50.34±6.38	49.64±6.73	0.624
Right	Conduction velocity (m/s)	2 weeks	50.92±6.25	49.44±10.81	0.136
Right	Conduction velocity (m/s)	6 weeks	53.70±4.44	52.87±6.86	0.871
Left	Amplitude (mV)	Baseline	8.44±4.73	10.31±4.53	0.078
Left	Amplitude (mV)	2 weeks	9.98±4.83	10.62±4.30	0.754
Left	Amplitude (mV)	6 weeks	9.67±4.80	10.63±4.21	0.375
Left	Latency (ms)	Baseline	4.38±0.88	4.11±0.56	0.172
Left	Latency (ms)	2 weeks	4.24±0.77	3.95±0.46	0.386
Left	Latency (ms)	6 weeks	3.89±0.39	3.94±0.65	0.259
Left	Conduction velocity (m/s)	Baseline	50.08±5.73	51.64±6.76	0.162
Left	Conduction velocity (m/s)	2 weeks	52.63±5.69	53.85±5.94	0.098
Left	Conduction velocity (m/s)	6 weeks	54.67±4.46	54.41±6.49	0.750

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Table 2. Bilateral median nerve sensory conduction parameters

Side	Parameter	Time	Pregabalin	Gabapentin	p
Right	Amplitude (μV)	Baseline	51.59±28.25	55.19±17.85	0.605
Right	Amplitude (μV)	2 weeks	53.19±24.23	55.37±20.33	0.645
Right	Amplitude (μV)	6 weeks	57.28±36.85	56.08±24.37	0.237
Right	Latency (ms)	Baseline	2.75±0.57	2.63±0.61	0.260
Right	Latency (ms)	2 weeks	2.65±0.53	2.51±0.57	0.730
Right	Latency (ms)	6 weeks	3.17±0.51	2.47±0.55	0.400
Right	Conduction velocity (m/s)	Baseline	43.83±8.57	45.33±8.60	0.070
Right	Conduction velocity (m/s)	2 weeks	45.43±8.36	47.19±8.91	0.880
Right	Conduction velocity (m/s)	6 weeks	45.18±8.67	47.59±8.85	0.830
Left	Amplitude (μV)	Baseline	64.89±23.64	62.52±18.60	0.364
Left	Amplitude (μV)	2 weeks	66.91±25.31	62.78±29.37	0.531
Left	Amplitude (μV)	6 weeks	68.80±24.63	64.03±24.20	0.315
Left	Latency (ms)	Baseline	2.73±1.02	2.58±0.55	0.784
Left	Latency (ms)	2 weeks	2.60±0.65	2.46±0.49	0.691
Left	Latency (ms)	6 weeks	2.52±0.59	2.42±0.50	0.361
Left	Conduction velocity (m/s)	Baseline	45.32±9.37	45.87±8.10	0.941
Left	Conduction velocity (m/s)	2 weeks	46.68±9.41	47.49±7.57	0.890
Left	Conduction velocity (m/s)	6 weeks	48.19±9.39	48.59±7.84	0.805

Table 3. Bilateral ulnar nerve motor conduction parameters

Side	Parameter	Time	Pregabalin	Gabapentin	p
Right	Amplitude (mV)	Baseline	10.15±2.80	10.76±2.96	0.151
Right	Amplitude (mV)	2 weeks	10.68±2.70	11.21±2.95	0.072
Right	Amplitude (mV)	6 weeks	10.53±2.87	10.73±2.28	0.058
Right	Latency (ms)	Baseline	4.48±0.58	4.45±0.55	0.609
Right	Latency (ms)	2 weeks	4.38±0.54	4.25±0.53	0.893
Right	Latency (ms)	6 weeks	4.17±0.43	4.13±0.44	0.951
Right	Conduction velocity (m/s)	Baseline	55.49±4.15	55.12±5.38	0.812
Right	Conduction velocity (m/s)	2 weeks	56.43±3.37	57.55±6.09	0.768
Right	Conduction velocity (m/s)	6 weeks	57.59±4.07	57.63±10.37	0.399
Left	Amplitude (mV)	Baseline	9.02±2.17	9.58±3.04	0.271
Left	Amplitude	2 weeks	9.21±2.28	9.01±4.07	0.073

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	(mV)				
Left	Amplitude (mV)	6 weeks	9.19±3.15	9.16±3.54	0.082
Left	Latency (ms)	Baseline	4.45±0.58	4.47±0.58	0.966
Left	Latency (ms)	2 weeks	4.42±0.63	4.29±0.53	0.148
Left	Latency (ms)	6 weeks	4.35±0.58	4.17±0.55	0.753
Left	Conduction velocity (m/s)	Baseline	59.76±13.27	59.94±16.08	0.722
Left	Conduction velocity (m/s)	2 weeks	61.20±14.85	62.09±15.57	0.862
Left	Conduction velocity (m/s)	6 weeks	61.63±15.29	63.60±15.89	0.361

Table 4. Bilateral ulnar nerve sensory conduction parameters

Side	Parameter	Time	Pregabalin	Gabapentin	p
Right	Amplitude (μV)	Baseline	19.01±9.56	18.26±11.81	0.230
Right	Amplitude (μV)	2 weeks	20.63±6.42	19.25±17.41	0.892
Right	Amplitude (μV)	6 weeks	21.75±12.57	22.06±13.95	0.629
Right	Latency (ms)	Baseline	2.05±0.28	2.17±0.41	0.053
Right	Latency (ms)	2 weeks	2.06±0.28	1.99±0.29	0.792
Right	Latency (ms)	6 weeks	2.01±0.30	1.94±0.26	0.404
Right	Conduction velocity (m/s)	Baseline	47.14±4.98	48.32±6.81	0.255
Right	Conduction velocity (m/s)	2 weeks	47.01±6.07	49.31±6.11	0.570
Right	Conduction velocity (m/s)	6 weeks	48.26±6.97	49.70±12.08	0.395
Left	Amplitude (μV)	Baseline	15.62±5.37	14.48±9.69	0.301
Left	Amplitude (μV)	2 weeks	16.36±6.84	16.08±8.54	0.869
Left	Amplitude (μV)	6 weeks	18.11±6.29	18.89±6.52	0.854
Left	Latency (ms)	Baseline	1.92±0.34	2.06±0.35	0.871
Left	Latency (ms)	2 weeks	1.93±0.30	1.98±0.33	0.523
Left	Latency (ms)	6 weeks	1.83±0.32	1.95±0.32	0.839
Left	Conduction velocity (m/s)	Baseline	47.73±5.40	44.09±6.08	0.208
Left	Conduction velocity (m/s)	2 weeks	47.75±6.09	45.75±6.52	0.877
Left	Conduction velocity (m/s)	6 weeks	49.79±6.48	46.25±6.15	0.381

Pregabalin and Gabapentin groups had similar median and ulnar nerve conduction parameters at baseline, 2 weeks and 6 weeks. There were no significant differences between groups for motor or sensory parameters of the median and ulnar nerves ($p>0.05$). During follow-up the conduction velocity showed an increasing trend in both groups. Electrophysiological findings were similar in the two treatment groups overall.

DISCUSSION

Neuralgic upper limb pain is an important clinical, social, economic and public health problem widely affecting the Indian population. Neuralgic pain refers to pain in the distribution of nerve or nerves. Causes of neuralgic upper limb pain are broadly divided into spinal (radiculopathy or myeloradiculopathy) and neural (involving peripheral nerve). Among the spinal causes, cervical radiculopathy is a common disorder, affecting people most often in the fourth and fifth decades of life. Among the neural causes, carpal tunnel syndrome (CTS) is

the most common cause of neuralgic upper limb pain. Other neural causes of neuralgic upper limb pain are entrapment neuropathies involving median, ulnar and radial nerves.

Pregabalin and gabapentin are the first line drugs for the management of neuralgic pain. Pregabalin (S-3-aminomethyl-5-methylhexanoic acid) is a structural derivative of the inhibitory neurotransmitter γ -aminobutyric acid (GABA). Pregabalin is generally well tolerated with no contraindications. Pregabalin undergoes negligible metabolism in humans and is eliminated from systemic circulation primarily by renal excretion as unchanged drug. The most common adverse effects of pregabalin are dizziness and drowsiness. Gabapentin, (1-aminomethyl cyclohexane acetic acid), was originally synthesized as a cyclic analogue of gamma aminobutyric acid (GABA). The most common side effects of gabapentin in adult patients include dizziness, fatigue, drowsiness, weight gain and peripheral edema. Pregabalin and gabapentin appear to be an effective treatment for neuropathic pain, acting centrally to reduce hyperalgesia and allodynia.

Numeric rating scale (NRS) and pain detect questionnaire (PDQ) are important tools for the screening and quantification of neuralgic pain. Both NRS and PDQ have been widely used to assess the response of interventions on progression of pain.

In our study, both groups were comparable regarding baseline patient profile (Table 1). All of our patients were in the age group of 18-60 years and 75% of them were females. This could be attributed to the social milieu of our region. The females are regularly engaged in lifting heavy weights as a part of their daily routine; like domestic work, agriculture work, animal husbandry, labor activities, etc.

In our study, there was an improvement in nerve conduction velocity and latency in most of the nerves over six weeks of treatment with pregabalin i.e. in group I. However, this improvement was not statistically significant. The changes in amplitude were inconsistent. Arezzo et al evaluated the effect of pregabalin on pain and nerve conduction velocity in eighty-two patients of painful diabetic peripheral neuropathy (DPN). They concluded that there was no statistically significant effect on nerve conduction velocity parameters in patients with painful DPN.¹⁰ Similarly, Patel et al evaluated the efficacy and safety of carbamazepine, pregabalin and alpha-lipoic acid in 101 patients of diabetic neuropathy. Nerve conduction

velocity (NCV) was measured at baseline and then at the end of 3 and 6 months. They concluded that the relief from diabetic neuropathy (as per DNE score) is superior with pregabalin administration as compared with carbamazepine and alpha lipoic acid. However, no improvement in NCV was evident with 6 months of the treatment with pregabalin.¹⁴ Dizaye et al evaluated the effects of pregabalin and vitamin-B complex on nerve conduction velocity parameters in 45 patients with diabetic peripheral neuropathy (DPN). They concluded that vitamin B-group was more efficacious than pregabalin in improving latency and also found that no significant differences were observed between pregabalin, vitamin B-group and their combination in improving the conduction velocity in patients with DPN.¹⁵ Our findings of the effects of pregabalin on nerve conduction study parameters were similar to other previous studies.

In group II, there was an improvement in nerve conduction velocity and latency in some of the nerves over six weeks of treatment with gabapentin. This improvement was also not statistically significant. The changes in amplitude were also inconsistent in group II (Table 2 to 8). Pan et al investigated the effects of intravenous gabapentin, in a dose of 30 to 90 mg/kg in neuropathic rats. They concluded that conduction velocity and responses of 12 normal afferent fibers to mechanical stimulation were not affected by gabapentin.¹⁶ Our findings of the effects of gabapentin on nerve conduction study parameters were similar to other previous study.

In our study, there was no significant difference observed in the nerve conduction study parameters between two groups. Thus, our study demonstrated that there was no significant improvement in conduction velocity, latency and amplitude with the 6 weeks of treatment with either pregabalin or gabapentin in the patients of neuralgic upper limb pain.

CONCLUSION

The study demonstrated similar median and ulnar nerve conduction parameters between the Pregabalin and Gabapentin groups. There were no statistically significant differences in motor and sensory nerve conduction parameters between the two treatment groups. During the follow-up period, conduction velocity showed an increasing trend in both groups. To summarize, the electrophysiological results were similar between the two treatment groups. These findings may be validated with larger studies and increased sample sizes.

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