Original Research Article

Clinical and Electrophysiological Profile of Chronic Kidney Disease Patients Undergoing Peritoneal Dialysis at a Tertiary Care Centre of Bihar

Mritunjay Kumar Azad[1], Abha Prasad[2*], Malti Kumari[3]

[1]Assistant Professor, Department of Physiology, J.N.K.T. Medical College, Madhepura, Bihar, India
[2]Tutor, Department of Physiology, J.N.K.T. Medical College, Madhepura, Bihar, India
[3]Professor, Department of Physiology, J.N.K.T. Medical College, Madhepura, Bihar, India

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Abstract

Chronic kidney disease (CKD) is a progressive decline in renal function, which is responsible for significant morbidity and mortality. The present study was carried out to assess prevalence of peripheral neuropathy in CKD patients on PD patients with special emphasis on electrophysiological parameters and severity of peripheral neuropathy and its relation with diabetes mellitus. **Methodology:** During the period from November 2020 to April 2020, 50 consecutive patients diagnosed to have CKD and are on OPD at J.N.K.T. Medical College, Madhepura, Bihar, India were included in the present study. Patients with pre-existing peripheral neuropathy prior to the diagnosis of CKD were excluded from the present study. The study was approved by the Institutional Ethics Committee and written informed consent was obtained from the patients for their participation in the study. The patients were divided into two equal groups, randomly: Group 1 included 25 diabetic patients Group 2 included 25 nondiabetic patients. All cases were subjected to nerve conduction studies (NCS) using Medelec synergy and Natus machines. NCS procedure was done for both motor conductions and sensory conductions. Median nerve, ulnar nerve, common peroneal nerve, and posterior tibial nerve were assessed for motor conductions. Median nerve, ulnar nerve, and sural nerve were assessed for sensory conductions. **Results:** The prevalence of peripheral neuropathy among the study participants was 62% (31 out of 50) based on clinical symptoms and 80% (40 out of 50) based on electrophysiological parameters. Based on electrophysiological data, prevalence of peripheral neuropathy in CKD patients on PD with DM and without DM was 100% and 60%, respectively. **Conclusion:** Rationale management of diabetes in CKD patients on PD probably lowers the prevalence and severity of peripheral neuropathy.

Key Words: Clinical and Electrophysiological Profile, Chronic Kidney Disease, Peritoneal Dialysis.

Introduction

Chronic kidney disease (CKD) is a progressive decline in renal function, which is responsible for significant morbidity and mortality. Due to decline in renal function, there will be accumulation of toxins resulting in multiple systemic complications. Uremia leads to several neurological complications which include uremic encephalopathy, atherosclerosis, neuropathy, and myopathy. Electrophysiological studies in adults revealed that almost 80% of CKD patients had electrophysiological evidence of impaired nerve function, although only one-half of these patients were symptomatic. [1, 2, 3] Kussmaul was the first to report this neurological complication. [4] The uremic neuropathy was suspected by Charcot in 1880. [5] and then by Osler in 1892. In 1962, the detailed explanation regarding the pathologic and clinical features was given by Asbury et al. [6] Males have more predilection to develop uremic neuropathy than females. The female-to-male ratio is 49:60 in 109 patients as observed by Nielsen. [7] The present concept of uremic neuropathy was established by Dyck et al, in 1971. [8]

Neuropathy in CKD patients is often multifactorial. Uremic toxins, [9] middle molecules, [10] and vitamin deficiency [11] are various factors which were proposed in the pathogenesis of uremic neuropathy. Studies revealed that patients treated with peritoneal dialysis (PD) had lower rates of uremic neuropathy which may suggest that the neuropathy-caused toxin more efficiently cleared by the peritoneum than by the membranes used in hemodialysis (HD).

Correspondence
Dr. Abha Prasad
Tutor, Department of Physiology, J.N.K.T. Medical College, Madhepura, Bihar, India.
E-mail: prasad4abha@gmail.com

The data about electrophysiological features and patterns of uremic neuropathy among patients undergoing peritoneal dialysis is very sparse in Indian literature. The present study was carried out to assess prevalence of peripheral neuropathy in CKD patients on PD patients with special emphasis on electrophysiological parameters and severity of peripheral neuropathy and its relation with diabetes mellitus.

Methodology

During the period from November 2020 to April 2020, 50 consecutive patients diagnosed to have CKD and are on PD at J.N.K.T. Medical College, Madhepura, Bihar, India were included in the present study. Patients with pre-existing peripheral neuropathy prior to the diagnosis of CKD were excluded from the present study. The study was approved by the Institutional Ethics Committee and written informed consent was obtained from the patients for their participation in the study. The patients were divided into two equal groups, randomly: Group 1 included 25 diabetic patients Group 2 included 25 nondiabetic patients. Detailed history was elicited pertaining to symptoms of peripheral neuropathy and diabetes mellitus (DM). Detailed general physical examination and neurological examination were done and documented. Duration of PD was noted in all the patients. Biochemical investigations included blood urea, serum creatinine, and blood sugars.

All cases were subjected to nerve conduction studies (NCS) using Medelec synergy and Natus machines. NCS procedure was done for both motor conductions and sensory conductions. Median nerve, ulnar nerve, common peroneal nerve, and posterior tibial nerve were assessed for motor conductions. Median nerve, ulnar nerve, and sural nerve were assessed for sensory conductions. In motor conductions, distal latency, conduction velocity, amplitude, and F wave were assessed. In sensory conductions, distal latency, conduction velocity,

and amplitude were assessed. Only right upper limb parameters were used as many dialysis patients who participated in the study had an arteriovenous fistula on their left upper limb. In lower limbs, sensory and motor conductions were done in both the lower limbs.The gain was normally set at 2–5 mV per division for the motor conduction studies. The recording electrodes were placed on the muscle being studied. The belly-tendon montage was used commonly. The center of the muscle belly (over the motor endplate) was used for placing the active recording electrode (also known as G1) and the reference electrode (also known as G2) was placed distally, over the tendon of the muscle. The nerve that supplies the muscle was used for placing the stimulator, where the cathode was placed close to the recording electrode. The duration of the electrical pulse was generally set to 200 ms for the motor NCS. To achieve supramaximal stimulation, current in the range of 20 to 50 mA was used. The underlying nerve fibers were brought to action potential as the current was steadily increased from a baseline, usually by 5-10 mA. The summation of all the underlying individual muscle fiber action potentials was represented by the compound muscle action potential (CMAP). When all the nerve fibers have been excited and the supra-maximal stimulation has been achieved then the CMAP shall no longer increase in size. For median nerve motor conduction studies, the recording electrode was placed over the motor point of the abductor pollicis brevis muscle, at the midpoint of a line drawn from the first metacarpophalangeal joint to the insertion of the tendon of the flexor carpi radialis muscle, and the reference electrode was placed over the distal interphalangeal joint. Mid arm, antecubital fossa, and wrist were sites of stimulation for median nerve motor conduction studies. For ulnar nerve motor conduction studies, the recording electrode was placed over the motor point of the abductor digiti minimi muscle, at the midpoint of a line between the 5th metacarpopha-langeal joint and the pisiform bone, with the reference electrode over the middle phalanx of digit V. Axilla, above elbow, ulnar groove, and medial wrist were sites of stimulation for ulnar nerve motor conduction studies. For the posterior tibial nerve, the CMAP was recorded by placing the active electrode over the middle of the adductor hallucis muscle, and the reference electrode over the proximal phalanx of digit I. The posterior tibial nerve was stimulated below the medial malleolus and in the popliteal fossa. For common peroneal nerve motor conduction studies, the recording electrode was placed in the middle of the extensor digitorum brevis muscle. The common peroneal nerve was stimulated at the ankle, 80 mm proximal to the recording electrode, lateral to the tendon of tibialis anterior muscle, and below the knee 20–50 mm distal to the proximal part of the caput fibula.Latency was described as the time from the stimulus to the initial CMAP deflection from the baseline. The CMAP amplitude was measured from the baseline to the negative peak. Conduction velocity was calculated using the formula - Distance between the proximal and distal stimulation sites/proximal latency- distal latency. The standardized normal adult values of motor NCS in both upper and lower extremities were taken as per the electrophysiological references. [12]The F response also known as the late motor response occurs after the CMAP. [13] Normal minimal F latency was 25–30 ms in median and ulnar nerves, whereas it was 45–59 ms in common peroneal and posterior tibial nerves. Median and ulnar sensory nerve action potentials (SNAPs) were obtained orthodromically, stimulating from the index finger (median nerve) or the little finger (ulnar nerve) and recording at the wrist. Sural SNAPs were obtained antidromically, recording behind the lateral malleolus and stimulating on the dorsal aspect of the calf, 140 mm proximal to the recording site. The responses were averaged at least 10 times. The standardized normal adult values of sensory NCS in both upper and lower extremities were used. [14]Based on electrophysiological parameters, peripheral neuropathy patterns were sub classified into axonal neuropathy, demyelinating neuropathy, and mixed neuropathy. In axonal neuropathy, CMAP's decrease, conduction velocities are normal or slightly decreased but never <75% of the lower limit of normal, distal latencies are normal or slightly prolonged but never >130% of the upper limit of normal. In demyelinating neuropathy, CMAP's are usually normal with marked slowing of conduction velocity (slower than 75% of the lower limit of normal) and/or marked prolongation of distal latency (longer than 130% of the upper limit of normal). It was classified as mixed neuropathy if it has features of both axonal neuropathy and demyelinating neuropathy. Degree of severity of peripheral neuropathy was divided into three groups as follows: normal, early damage and definite damage, according to the number of peripheral nerves involved. Normal or no peripheral damage was defined if NCS were normal or only one peripheral nerve was involved. Early damage, if two or three peripheral nerves were involved and definite damage, if more than three peripheral nerves were involved.The data were tabulated and analyzed using Statistical Package for Social Sciences (SPSS) version 20.0 (SPSS Inc. Chicago, IL, USA). All the continuous variables were expressed as mean ± standard deviation or median with interquartile range as appropriate. All categorical variables were expressed as frequencies (percentage). Independent *t*-test and ANOVA test were applied to compare nominal data between the groups and $P < 0.05$ was considered statistically significant.

Results

The prevalence of peripheral neuropathy among the study participants was 62% (31 out of 50) based on clinical symptoms and 80% (40 out of 50) based on electrophysiological parameters. Based on electrophysiological data, prevalence of peripheral neuropathy in CKD patients on PD with DM and without DM was 100% and 60%, respectively. The mean age was 57.9 ± 11.2 years with a male dominance. The mean age of patients in Group 1 and 2 was 58.9 ± 9.5 years and 54.7 ± 12.1 years. The mean serum creatinine of CKD patients on PD, with and without DM was 7.9 ± 4.8 mg/dL and 6.2 ± 3.5 mg/dL, respectively. The mean blood urea of CKD patients on PD, with and without DM was 100.2 ± 32.5 mg/dL and 91.9 ± 35.2 mg/dL, respectively. The mean duration of DM was 9.2 ± 2.8 years. The mean duration of patients on PD was 5.4 ± 2.1 years.Comparison of symptoms and signs of CKD patients on PD who participated in the study is shown in Table 1. On comparing symptoms and signs of peripheral neuropathy in CKD patients on PD, patients with DM showed statistical significance in the presence of negative symptoms.Comparison of electrophysiological parameters of 100 CKD patients on PD who participated in the study is shown in table 3. On comparing electrophysiological data; patients with DM showed statistically significant prolonged median nerve motor distal latency, low median nerve motor amplitude, prolonged median nerve F wave, prolonged ulnar nerve motor distal latency , low ulnar nerve motor conduction velocity, prolonged ulnar nerve F wave, low common peroneal nerve motor conduction velocity, low common peroneal nerve motor amplitude, absent common peroneal F wave, low posterior tibial nerve motor conduction velocity, low posterior tibial nerve motor amplitude, absent posterior tibial nerve F wave, low median nerve sensory conduction velocity, low median nerve (sensory amplitude, low ulnar nerve sensory conduction velocity, low ulnar nerve sensory amplitude, low sural nerve sensory conduction velocity, and low sural nerve sensory amplitude. CKD patients on PD and without DM showed statistical significance in the presence of prolonged common peroneal nerve motor distal latency, prolonged ulnar nerve sensory distal latency and prolonged sural nerve sensory distal latency.

Table 1: Comparison of symptoms and signs of CKD patients of both the groups

Signs and symptoms	Group 1 patients (N = 25)	Group 2 patients (N = 25)
Motor weakness	6	2
Positive sensory symptoms	20	12
Negative sensory symptoms	22	8
Autonomic symptoms	7	3
Wasting of limbs	0	0
Absent ankle jerk	25	21
Impaired pain and temperature sensation	14	10
Impaired vibration and joint position sense	22	15

Table 2: Comparison of Electrophysiological parameters

Electrophysiological parameters	Group 1 patients	Group 2 patients
A. **Median nerve**		
dL (ms)	4.2 ± 1.1	3.1 ± 0.6
CV (m/s)	44.5 ± 6.5	44.4 ± 15.2
Amplitude (millivolts)	4.1 ± 2.1	7.3 ± 1.9
F wave		
Normal	4	15
Prolonged	18	10
Absent	3	0
B. **Ulnar nerve**		
dL (ms)	3.1 ± 0.8	2.5 ± 0.2
CV (m/s)	44.6 ± 6.9	55.4 ± 4.9
Amplitude (millivolts)	5.5 ± 4.1	6.9 ± 1.1
F wave		
Normal	3	13
Prolonged	19	12
Absent	3	0
C. **Common Peroneal nerve**		
dL (ms)	2.2 ± 2.1	3.2 ± 0.6
CV (m/s)	19.4 ± 17.9	41. 3± 6.5
Amplitude (millivolts)	0.4 ± 1.1	3.2 ± 2.1
F wave		
Normal	1	17
Prolonged	1	0
Absent	23	8
D. **Posterior tibial nerve**		
dL (ms)	4.1 ± 2.1	2.6 ± 1.1
CV (m/s)	21.7 ± 16.2	36.9 ± 15.8
Amplitude (millivolts)	1.1 ± 1.7	5.3 ± 2.9
F wave		
Normal	3	20
Prolonged	4	0
Absent	18	5
E. **Median nerve sensory**		
dL (ms)	2.4 ± 1.9	2.2 ± 1.4
CV (m/s)	31.9 ± 21.2	44.7 ± 16.9
Amplitude (millivolts)	4.4 ± 5.2	20.6 ± 12.2
F. **Ulnar nerve sensory**		
dL (ms)	1.1 ± 1.2	2.6 ± 0.3
CV (m/s)	22.5 ± 24.6	50.4 ± 3.9
Amplitude (millivolts)	3.0 ± 1.9	11.4 ± 5.1
G. **Sural nerve**		
dL (ms)	0.4 ± 1.1	2.5 ± 0.6
CV (m/s)	7.1 ± 16.8	45.7 ± 18.2
Amplitude (millivolts)	0.5 ± 1.1	9.8 ± 7.1

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Discussion

Peripheral neuropathy is a common neurological complication seen in CKD patients, prevalence of which increases in end-stage renal disease patients. Patients who are on maintenance dialysis have more prevalence of peripheral neuropathy when compared to predialysis patients. Patients on PD have relatively less severe peripheral neuropathy when compared to patients on maintenance HD. NCS are the most commonly used diagnostic procedure used for establishing the presence and type of peripheral neuropathy. Indian literature regarding prevalence, electrophysiological parameters, and severity of peripheral neuropathy in CKD patients on PD is sparse. Hence, the present study was undertaken to study the prevalence, clinical features, electrophysiological features, and severity of peripheral neuropathy in CKD patients on PD in the South Indian population and to study the effect of the presence of DM on peripheral neuropathy. The present study showed a high prevalence of uremic neuropathy;

About 62% based on clinical symptoms and 80% according to electrophysiological studies. About 77.4% of CKD patients on PD showed evidence of peripheral neuropathy according to Janda et al.[15] Comparable prevalence rates of peripheral neuropathy were documented in other published international studies.[17],[18]The mean age of patients who participated in the study was almost similar to other published studies.[16],[17],[18] Kim et al, studied 29 CKD on PD, while Kayalar et al, and Tilki et al, studied 16 patients and 12 patients, respectively.

Sixty-two percent patients on PD were symptomatic for peripheral neuropathy in the present study in the form of both positive and negative symptoms. However, around 90% of patients had absent ankle jerk, all of whom had electrophysiological evidence of peripheral neuropathy. Hence, good clinical examination and meticulous history elicitation regarding peripheral neuropathy will help in judicious use of NCS. The mean serum creatinine and urea of patients were almost similar to study by Kayalar et al,[17] on 16 CKD patients on PD, in which mean serum creatinine and blood urea were 9.1 ± 1.8 mg/dL and 100.0 ± 43.8 mg/dL, respectively.

On comparing electrophysiological parameters of CKD patients on PD with other published studies, motor amplitude and motor conduction velocity were higher in our study. Eighty percent patients had significant peripheral neuropathy. Most common nerves involved in the present study were median motor nerve, sural nerve, ulnar sensory nerve, common peroneal nerve, posterior tibial nerve followed by median the sensory nerve in the present study. Lower limbs were most commonly affected than upper limbs, which indicate a length dependent pattern. Sensory nerves were commonly affected than motor nerves in the present study.

Diabetic patients on PD showed higher prevalence and severity of peripheral neuropathy when compared to nondiabetic CKD patients. In addition to factors responsible for uremic neuropathy, probably the presence of DM might contribute to higher prevalence and severity of peripheral neuropathy in diabetic CKD patients. Statistically most significant electrophysiological parameters differentiating diabetic CKD patients on PD and nondiabetic CKD patients on PD were median nerve motor distal latency, ulnar nerve motor conduction velocity, common peroneal nerve motor conduction velocity, common peroneal nerve motor amplitude, common peroneal F wave, posterior tibial nerve motor amplitude, posterior tibial nerve F wave, median nerve sensory amplitude, ulnar nerve sensory conduction velocity, ulnar nerve sensory amplitude, sural nerve sensory conduction velocity and sural nerve sensory amplitude.

In developing countries like India, financial constraints become a major issue for periodic NCS. However to diagnose peripheral neuropathy early to minimize discomfort to the patient, meticulous history, and neurological examination with judicious use of NCS is required. Moreover most of our population belong to rural areas, who consult medical care very late, which might be responsible for higher prevalence and severity of uremic neuropathy. However, newer treatment modalities are required to manage uremic neuropathy better.

Conclusion

Peripheral neuropathy is common in CKD patients on PD, with higher prevalence and severity in elderly females. CKD patients with DM on PD showed higher prevalence and more severe peripheral neuropathy when compared to nondiabetic patients. Rationale management of diabetes in CKD patients on PD probably lowers the prevalence and severity of peripheral neuropathy.

Conflict of Interest: Nil Source of support: Nil

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