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Original Research Article

Assessment of Visual Evoked Potentials in Patients with Chronic Kidney Disease: A Study in an Urban Tertiary Care Centre in Chennai, Tamil Nadu

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Abstract:

Chronic kidney disease (CKD) is linked to functional alterations in the central nervous system (CNS), which may not display clinical symptoms in its early stages. Early CNS involvement can be detected through the evaluation of electrocortical activity. Visual evoked potentials (VEP) represent valuable diagnostic tools for early identification of CNS participation in CKD, exhibiting greater sensitivity when compared to electroencephalography. The study encompassed 20 adult patients with chronic kidney disease (CKD) and an equal number of control participants. Comprehensive evaluations of clinical and biochemical parameters were conducted for both patient groups and controls, followed by visual evoked potential (VEP) assessments for all individuals. The Serum urea (66.10±5.22 Vs 27.00±0.776) and Serum creatinine (5.22±1.64 Vs 0.776±0.13) of the study groups were compared with control group with significant P value <0.01. The analysis of VEP revealed extended latencies for all three peaks (N75, P100, and N145) when compared to the control group. Central nervous system (CNS) dysfunction is a prevalent occurrence in individuals with chronic kidney disease (CKD). Utilizing electrophysiological VEP tests can aid in the early detection of these disorders, even during subclinical stages, thereby enabling more effective management.

Keywords: Visual Evoked Potential, chronic kidney disease, Serum urea, Serum creatinine, central nervous system.

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Introduction

Chronic kidney disease (CKD) is a medical condition defined by the accumulation of uremic toxins resulting from the irreversible decline in kidney function. Chronic kidney disease (CKD) encompasses a spectrum of different pathophysiologic processes associated with abnormal kidney function and a progressive decline in glomerular filtration rate[1]. Chronic kidney disease (CKD) is defined as kidney damage or an estimated glomerular filtration rate (eGFR) below 60 ml/min/1.73 m² persisting for 3 months or more irrespective of the cause[2].

These uremic toxins are recognized to exert harmful effects on various body tissues, including the brain. As a consequence, CRF frequently presents with complications such as peripheral neuropathy and disturbances in the central nervous system (CNS)[3-7]. While the precise factors responsible for central nervous system (CNS) dysfunction in individuals with chronic kidney disease (CKD) remain unclear, it has been postulated that the accumulation of various organic and inorganic substances, such as urea, guanidine compounds, uric acid, hippurate, polyamines, indolic acid, acetone, glucuronate, carnitine, myoinositol, sulfate, and phosphate, can adversely affect the entire neurological system. Additionally, some authors have suggested the presence of unidentified neurotoxins in uremic patients, which may harm both axonal membranes and synaptic mechanisms (8-10). Furthermore, there is evidence indicating that elevated levels of parathyroid hormone (PTH) in individuals with CRF may contribute to CNS dysfunction (11-13). Reports have documented CNS complications in patients with CKD as well (14).

Patients with uremia frequently encounter physical symptoms resulting from central nervous system

(CNS) dysfunction. Among the initial signs of progressive chronic uremia, fatigue and cognitive decline are commonly observed (14). It is often advisable to initiate advanced treatment methods such as dialysis before complications become apparent. Modern diagnostic techniques are valuable for early detection of CNS issues in individuals with uremia. Research has demonstrated that the metabolic changes in chronic kidney disease (CKD) lead to abnormalities in visual evoked potentials (VEPs), which have already proven to offer objective insights into the functional state of CNS structures (8, 10, 15-18). However, there is still limited available data concerning VEPs in CKD patients.

Aim of the Study

The aim and objective of the study is

1. To evaluate the subclinical neuropathy in chronic kidney disease patients
2. To compare the visual evoked potential in normal subject with chronic kidney disease patients.

Materials and Methods

Patients were recruited and laboratory measurements were conducted as part of a routine visit to the outpatient transplant clinic at the Department of Nephrology, Transplantation, and Internal Medicine located at Government Kilpauk Medical College in Chennai. The study employs a comparative cross-sectional design with a total sample size of 40 (15 females, 25 males) participants, divided into two groups. Group 1 comprises 20 healthy volunteers selected based on age and gender matching and serves as the control group. Group 2 consists of 20 individuals with Chronic Kidney Disease (CKD) who have a Glomerular Filtration Rate (GFR) between 15-30 ml/min and a duration of more than 3 months.

Height, weight, BMI, Serum urea, Serum creatinine, and Blood pressure and VEP parameters were measured. Statistical analysis was done to compare the findings between the controls and the study groups and also within the study groups. ANOVA and Post Hoctest LSD – Least Significant Difference were used for Multiple Comparisons between controls and study groups and also within the study groups. The mean difference is significant at the 0.05 level. This study was done in accordance with the Declaration of Helsinki and approved by Institutional Ethics Committee, Government Kilpauk Medical College in Chennai (Protocol ID No10/2017 Dated: 08-06-2017).

Inclusion Criteria

The inclusion criteria for this study are as follows:

1. Patients must have been diagnosed with Chronic Kidney Disease (CKD) in the Department of Nephrology and have a Glomerular Filtration Rate (GFR) between 15 and 30 ml/min.
2. The duration of CKD should be greater than 3 months.
3. Male and female individuals between the ages of 20 and 35 are eligible.
4. Patients must express a willingness to participate in the study.

Exclusion Criteria

The exclusion criteria for this study are as follows: Presence of cataract, Diagnosis of glaucoma, Presence of optic atrophy, Any underlying neurological disorder, Visual acuity less than 6/18, History of traumatic neuropathy, Use of nephrotoxic drugs. These criteria specify the conditions or factors that would disqualify individuals from participating in the study.

Patients who qualify for the study will be enrolled and undergo the following assessments:Blood pressure, Height, Weight, Visual acuity using Snellen's chart, Fundus examination to rule out retinal pathology, Brief history to rule out drug intake, hypertension, and diabetes mellitus and General clinical examination.

Procedure of VEP

The patient is put at ease and made to sit comfortably in a relaxed state. Thorough cleaning of the electrode recording sites on the scalp. Electrode paste is applied on the recording surface of disk electrodes. Then electrodes are affixed at predetermined positions on the scalp according to 10/20 international system of electrode placement. The patient is asked to fix the gaze at the centre of the checker board screen. Each eye is checked separately. Prerequisites: i. Hairspray or oil after hair wash is advised not to use. ii. Spectacles should be put on during the test. iii. Visual acuity is done before the test. iv. Miotic or Mydriatic drugs 12 hours before the test is avoided. Equipment set up for VEP: Suggested Montage: i. Recording electrode is placed at Oz. ii. Reference electrode is placed at Fpz or 12cm above the nasion. iii. Ground electrode is placed at the wrist. Recording conditions: i Filter: low filter cut at 1-3 Hz, high filter cut at 100-300 Hz. ii. Amplification between 20, 00 and 1, 00,000. iii. Sweep duration between 250 and 500 msec. iv. Number of epochs: At least 100 are averaged. v. Electrode impedence kept below 5 kilo-ohms. Stimulation options: i. Black and white checker board or vertical grating. ii. Distance between subject and screen 70-100cm. iii. Contrast between 50-80%. iv. Fixation point for full field size > 8º. v. Size of pattern element 14 X 16 minute. vi. Stimulation rate for transient VEP 1 Hz and for steady state VEP 4-8 Hz. vii. Central luminance 50cd/m2 and background luminance 20-40 cd/m2. The signals picked up by the electrodes

are filtered, amplified, averaged and displayed on the screen of MEDICAID, Computerised Physiolab, Neuro perfect plus, and recorded. The normal VEP recording consists of N75, P100, N145 waves. Normal Value Any deviations from these normal values, Latency 100 ± 3.2msec, Amplitude 10± 4.2µV and Duration 60 ± 7.7sec are considered abnormal. Any deviations from these normal values are considered abnormal. The visual Evoked Potentials of patients with chronic kidney disease will be analysed and compared with age and gender matched controls.

Data Analysis

The statistical analysis for the required sample size per group was carried out using Statistica version 9 (StatSoft, Inc, 1984-2009, USA). All other statistical analyses were performed using the Statistical Package for Social Sciences for Windows 8.0 software. The results are presented as means with their respective standard deviations. To make comparisons, analysis of variance (ANOVA) was employed, followed by Tukey's post hoc test for multiple comparisons and the independent samples Student's t-test. Pearson correlation analysis was used to calculate correlations between variables. The results were evaluated within a 95% confidence interval, and significance was determined with a probability level of less than 0.05.

Results

The mean ± SD of the Height and Weight of the study groups were compared with the P value of 0.902 and 0.142 respectively which is insignificant. The mean ±SD of the BMI of the study groups were compared with the P value of 0.076 which is insignificant.

As table 1 shows The S.urea and Serum Creatinine of the study groups were compared with control group with significant P value <0.01.

Table 1: Comparison of S. Urea and Serum Creatinine between Controls and CKD

	Controls N = 20	CKD N = 20	P Value
S. Urea	27 ± 0.776	66.1± 5.22	< 0.01
S. Creatinine	0.776 ± 0.13	5.22 ± 1.64	< 0.01

Table 2 The study groups are compared with control groups with a F value195.849 (systolic BP) and 80.981(Diastolic BP) and highly significant P value0.000.

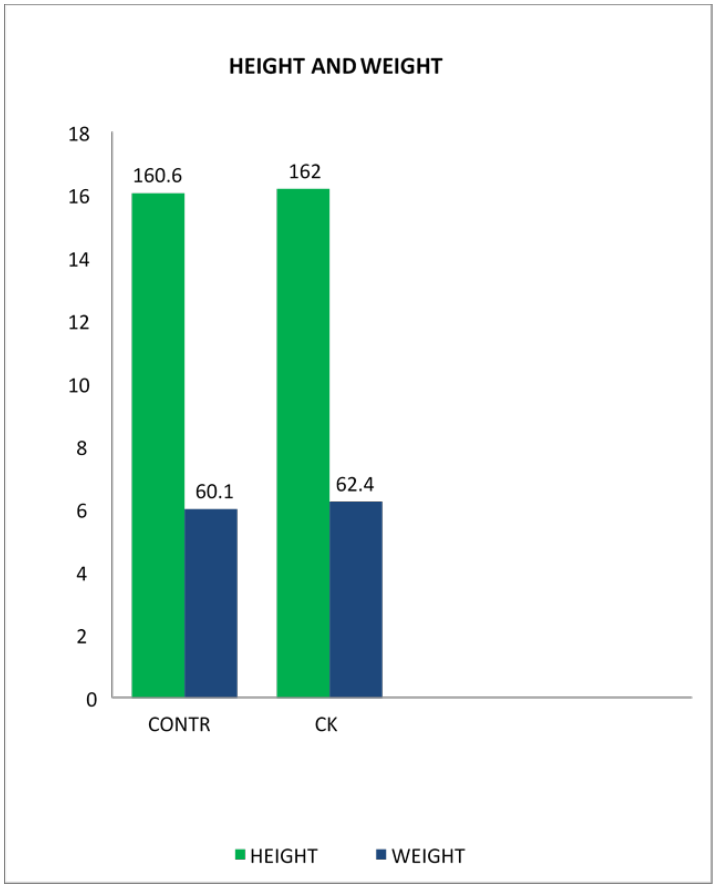

Figure 1: Comparison of Anthropometry of Subjects between Controls and CKD

Table 2: Comparison of Systolic and Diastolic Bp between controls and CKD

Variables	Controls N = 20	CKD N = 20	P Value
Systolic Bp	109.8 ± 7.13	144.9± 7.26	< 0.01
Diastolic Bp	79.7± 6.23	95.8 ± 3.88	< 0.01

Table 3: Comparison of Latency N 75, N 100, N 145 and Amplitude in Right & Left Eye Between controls and CKD

	Controls N = 20		CKD N = 20		P Value
	Right Eye	Left Eye	Right Eye	Left Eye	
Latency N 75	74.97 ± 0.549	75.17 ± 0.74	81.82 ± 0.59	81.82 ± 0.92	< 0.01
Latency P 100	100.10 ± 0.44	100.25 ± 0.573	108.17 ± 0.67	108.17 ± 0.94	< 0.01
Latency N 145	144.95 ± 0.605	145.05 ± 0.759	148.55 ± 0.605	148.35 ± 0.860	< 0.01
Amplitude	8.03 ± 0.418	8.124 ± 0.523	5.14 ± 0.543	5.092 ± 0.694	< 0.01

Table 3 presents a comparison between the study groups and control groups. For the right eye, the F value is notably high at 1390.209, with a highly significant p-value of less than 0.01. Specifically, the P100 latency is found to be significantly higher than the N75 and N145 latencies, with a right eye F value of 1805.100 and an extremely significant p-value of 0.000. Furthermore, when comparing the N145 latency of the right eye with the control group, a significant difference is observed, with a right eye F value of 346.18 and a significant p-value of less than 0.01. It is worth noting that as the latency of VEP prolongs, the amplitude (measured in μV) decreases. This decrease in amplitude is evident in the study group when compared to the control group. In terms of amplitude (μV), the right eye shows a substantial F value of 485.066 and an exceptionally significant p-value of 0.000.

Discussion

It is established that the uremic condition has detrimental impacts on various bodily tissues, including the brain [16, 19-25]. Furthermore, it is widely recognized that neurological, behavioral, cognitive, and emotional irregularities frequently correspond to the duration of chronic kidney disease (CKD) and have been observed to be linked with imbalances in electrolytes, elevated blood urea levels, increased serum creatinine, elevated non-protein nitrogen levels, and increased parathyroid hormone (PTH) levels over time [18,26].

Extensive research has been conducted to develop diagnostic approaches for the early detection of subclinical central nervous system (CNS) involvement in individuals with uremia. Among these methods, visual evoked potentials (VEPs) have emerged as a valuable non-invasive and easily applicable electrophysiological technique for assessing CNS function.

The primary outcome of our study indicates significant differences in VEPs between both hemodialysis (HD) and continuous ambulatory peritoneal dialysis (CAPD) patients when compared to healthy controls. Furthermore, it has been proposed that VEPs offer quantitative insights into the extent of renal insufficiency, illustrating variations in VEP parameters among uremic patients compared to established norms and showcasing alterations related to different clinical conditions [8, 27]. Previous research has also documented increased amplitudes and extended latencies in VEP recordings among HD patients [13, 28].

Lewis et al. studied Flash-VEP and demonstrated that the latencies were prolonged and bigger amplitudes in controls when compared to cases i.e.,8 patients on hemodialysis were taken.They stated that there is no association between VEP results and blood biochemical parameters'7. The results of the above study were consistent with this study that P100 and N140 latencies in patients under hemodialysis were longer than those of controls[29].

Lowitzsch et al. studied VEP findings in 2 CKD patients 3 times before and after hemodialysis Latencies and amplitudes were finally demonstrated to be normal in both patients [8]. In contrast to this study, our findings showed a significant difference in latencies of waves in CKD patients, CKD under hemodialysis, CKD patients who underwent Renal Transplantation, compared to the control group; however, there were significant differences in amplitudes also[30].

Conclusion

Central nervous system (CNS) dysfunction is a prevalent occurrence in individuals with chronic kidney disease (CKD). Utilizing electrophysiological VEP tests can aid in the early detection of these disorders, even during subclinical stages, thereby enabling more effective management. The Chronic Kidney Disease (CKD) cases we examined displayed comparable impacts on Visual Evoked Potentials (VEPs). As CKD advances, we observed a decline in VEPs, indicating damage to the visual neuronal system. This suggests that VEPs can be utilized for diagnosing CNS dysfunctions and potentially

guiding additional therapeutic strategies in the management of CKD.

Limitations

As this was a single center study with a comparatively short sample size, results of this study cannot be generalized. Generalization requires the support of results from similar large studies

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Ethical Statement

Institutional ethical committee accepted this study. The study was approved by the institutional human ethics committee, Government Kilpauk Medical College in Chennai (Protocol ID No10/2017 Dated: 08-06-2017). Informed written consent was obtained from all the study participants and only those participants willing to sign the informed consent were included in the study. The risks and benefits involved in the study and the voluntary nature of participation were explained to the participants before obtaining consent. The confidentiality of the study participants was maintained.

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Author's Contributions

Dr Suganya Gunasekaran- conceptualization, data curation, investigation, methodology, project administration, visualization, writing—original draft, writing—review and editing; Dr Dhivya Krishnamoorthy-conceptualization, methodology, writing—original draft, writing—review and editing; Dr Mathumithaa Subburayalu - conceptualization, visualization, supervision, writing—original draft; Dr Ramya selvaraj - methodology, writing—original draft, writing, review and editing. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work. All authors have read and agreed to the published version of the manuscript.

Data Availability

All datasets generated or analyzed during this study are included in the manuscript.

Informed Consent

Written informed consent was obtained from the participants before enrolling in the study

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