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Original Article

Internal Medicine Section

Dynamics of Electroencephalogram (EEG) in Different Stages of Chronic Kidney Disease

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ABSTRACT

Aim: To study Electroencephalogram (EEG) in different stages of chronic kidney disease (CKD).

Materials and Methods: This observational study was carried out in the Department of Medicine, Jawaharlal Nehru Medical College, Sawangi (Meghe), Wardha conducted over a period of 24 months, spanning from August 2011 to August 2013. Eighty three cases of CKD at different stages were studied. EEG was done in all the subjects and the various EEG dynamics like morphometric waveform patterns, symmetricity, amplitude were recorded and compared with the different stages of CKD.

Results: We found that characteristic changes were observed with increasing severity of CKD. Slow delta wave patterns were more prominent in stage 5 ($p<0.0001$), asymmetric discharges, dysthymia, sharp wave transients and low amplitude wave forms were more prominent beyond Stage 4 ($p<0.0001$).

Conclusion: EEG can be used as an effective tool for detection of subclinical or latent uremic encephalopathy. EEG findings which are characteristics of uremic encephalopathy can be present in CKD patients without overt signs of encephalopathy. So, EEG can be used as a prognostic indicator of response to clinical therapy of CKD.

Keywords: Dysthymia, Encephalopathy, Uremia

INTRODUCTION

Chronic kidney disease (CKD) is a worldwide public health problem. It is recognised as a common condition that is associated with an increased risk of multiple organ dysfunction. Treatment of earlier stages of CKD is effective in slowing the progression towards kidney failure [1].

K/DOQI 2002, classification is based on estimated GFR, and recognises five stages of chronic kidney disease [2]. The overall magnitude and pattern of CKD in India has been studied sporadically [3-7]. Uremic symptoms vividly occur in late stages of CKD. Encephalopathy is a global cerebral dysfunction, often in the absence of primary structural brain disease, which can also cause permanent brain injury. The symptoms begin insidiously and are often not noticed by the patients but by their family members or caregivers. Most encephalopathies are reversible, making prompt recognition and treatment important [8].

The symptoms which characterize the clinical uremic encephalopathy due to renal failure include mental sluggishness, diminished mental acuity and vigilance, drowsiness, stupor, coma, irritability, restlessness, myoclonus, seizures, anorexia, nausea, vomiting, itching, and hypothermia [9].

EEG is useful in assessing patients in uremic encephalopathy and in monitoring their progress. Electroencephalographic (EEG) findings correlate with clinical symptoms and, therefore, may be of diagnostic value. In addition, it can be useful to exclude other causes of confusion such as infection or structural abnormalities [8]. The EEG in uremic encephalopathy is generally abnormal, showing generalized slowing that becomes more severe as the condition worsens. EEG in CKD usually shows irregular low voltage with slowing of the posterior dominant alpha rhythm and occasional theta bursts. Prolonged bursts of bilateral, synchronous slow and sharp waves or spike and waves are characteristic. These changes stabilize with dialysis. EEG abnormalities in uremic encephalopathy is reflected through appearance of theta waves, disappearance of normal basic rhythms and diminished reactivity of EEG to afferent stimulation and domination by generalised delta activity. All these changes are mostly appreciated in the frontal leads [10,11].

A lot of studies have been done about uremic encephalopathy in acute renal failure patients. Very few data are available regarding EEG changes in CKD. This study evaluates the EEG findings in different stages of CKD.

AIMS AND OBJECTIVES

To Study EEG in different stages of chronic kidney disease.

MATERIALS AND METHODS

The present cross-sectional study was carried out in the Department of Medicine, Jawaharlal Nehru Medical College, Sawangi (Meghe), Wardha, India, an advanced tertiary centre with facilities for dialysis and renal transplant in central India over a period of 24 months, spanning from August 2011 to August 2013. Institutional ethical committee clearance was taken. Out of 134 cases of CKD attended to the hospital 83 cases of CKD aged more than 17 y at different stages of CKD were selected for study. The remaining cases were excluded who fitted in one of the exclusion criterias like age more than 80 y, patients with history of stroke, epilepsy, dementia, metabolic abnormalities, chronic liver diseases, COAD.

Screening of prospective cases: One hundred and thirty four cases attending the study centre with diagnosis of CKD were screened on the basis of pre-defined inclusion and exclusion criteria, out of which 83 were selected as stated vide supra. After routine screening, all patients of CKD were counselled regarding the objectives and methodology of the study and those who consented in writing were enrolled.

Base-line data collection: A pre-designed Semi-structured case-record form was used to collect detailed demographic and clinical history of each enrolled cases, numbered consecutively. Apart from routine investigations (Serum creatinine, Serum urea, 24 h urine albumin, spot urine protein/creatinine ratio, urine routine and microscopy), each enrolled case was evaluated in detail with following base-line investigations.

GFR was calculated by MDRD formula [12] MDRD – GFR (ml/min/1,73 m^2) = 170 x $(PCr)^{-0.999}$ x $(age)^{-0.176}$ x (0.762 if patient is female) x (1.180 if patient is female) x (1.180 if patient is black) x $(SUN)^{-0.170}$ x $(Alb)^{+0.318}$

Where PCr = serum creatinine concentration (mg/dl) (alkaline picrate method); SUN = serum urea nitrogen concentration (mg/dl) (urease method); Albumin = serum albumin concentration (g/dl) (bromocresol green method) USG was done for renal size [13].

EEG was recorded from 23 surface electrodes according to international 10/20 system with a separate reference electrode.

Classification of disease severity: All cases were classified as per the 'The Kidney Disease Outcomes Quality Initiative' (K/DOQI) of the National Kidney Foundation (NKF) classification of 2002 [1]. Accordingly, all cases were classified on initial evaluation as – a) Stage I, b) Stage II, c) Stage III, d) Stage IV and e) Stage V.

Classification of Chronic Kidney Disease (CKD)

Stage	GFR, mL/min per 1.73 m²
1	90
2	60–89
3	30–59
4	15–29
5	<15

STATISTICAL ANALYSIS

Individual case data from study subjects of CKD was obtained. Statistical analysis was done by using descriptive and inferential statistics using chi-square test. The software used in analysis was SPSS 17.0 version and Graphpad Prism 5.0 version and $p < 0.05$ was considered as significant.

RESULTS

[Table/Fig-1,2,3, and 5].

Wave forms	Stage I	Stage II	Stage III	Stage IV	Stage V
Alpha	12(100%)	11(68.75%)	9(56.25%)	4(28.57%)	10(38.46%)
Alpha + Beta			1(6.25%)	1(7.14%)	
Beta		4(25%)	2(12.50%)	3(21.43%)	4(15.38%)
Alpha + Theta					2(7.69%)
Theta					
Theta+Beta			1(6.25%)	2(14.29%)	4(15.38%)
Delta				2(14.29%)	3(11.54%)
Change of α on stimulation		1(6.25%)	2(12.50%)	2(14.29%)	3(11.54%)
Any other atypical wave					
Total	12(100%)	16(100%)	15(100%)	14(100%)	26(100%)
χ^2-value	213.2				
p-value	p < 0.0001, Significant				

[Table/Fig-1]: Stage wise distribution of morphometric pattern of wave forms of EEG in patients of CKD

Symmetry of waves	Stage I	Stage II	Stage III	Stage IV	Stage V
Symmetry	12(100%)	12(75%)	7(46.67%)	4(26.67%)	4(15.38%)
Asymmetry		2(12.50%)	3(20%)	4(26.67%)	13(50%)
Dysrhythmia		2(12.50%)	5(33.33%)	6(40%)	9(34.62%)
Total	12(100%)	16(100%)	15(100%)	14(100%)	26(100%)
χ^2-value	201.20				
p-value	p<0.0001, Significant				

[Table/Fig-2]: Stage wise distribution of symmetricity of waves of EEG in patients of CKD

DISCUSSION

In this prospective observational study, we enrolled 83 patients in different stages of CKD. The age ranged from 17 to 80 y. Of these, maximum patients were in age group 61-70 (24.1%). Mean age of the patients enrolled for EEG was 50.5 ± 15.5 y.

Amplitude of waves	Stage I	Stage II	Stage III	Stage IV	Stage V
Low Amplitude		2(12.5%)	5(33.33%)	8(57.14%)	15(57.69%)
Medium Amplitude	12(100%)	5(31.25%)	7(46.67%)	5(35.71%)	10(38.46%)
High Amplitude		9(56.25%)	3(20%)	1(7.14%)	1(3.85%)
Total	12(100%)	16(100%)	15(100%)	14(100%)	26(100%)
χ^2-value	267.1				
p-value	p<0.0001, Significant				

[Table/Fig-3]: Stage wise distribution of amplitude of waves of EEG in patients of CKD

Sharp Waves Tansients	Stage I	Stage II	Stage III	Stage IV	Stage V
Centrofrontal		1(50%)	1(33.33%)		
Centrotemporal			1(33.33%)		
Paritooccipital		1(50%)	1(33.33%)		
Occipital					1(14.29%)
Frontal				2(50%)	5(71.43%)
Temporo Frontal				2(50%)	1(14.29%)
Total		2(100%)	3100%)	4100%)	7(100%)
χ^2-value	553.7				
p-value	p<0.0001,S,p<0.05				

[Table/Fig-4]: Stagewise distribution of sharp wave transients in patients of CKD

Slow Waves	Stage I	Stage II	Stage III	Stage IV	Stage V
Unilateral		1(50%)	1(50%)		
Bilateral				4(50%)	6(60%)
Multifocal		1(50%)	1(50%)	1(12.5%)	
Generalized				2(25%)	3(30%)
Periodic				1(12.5%)	1(10%)
Total		2(100%)	2(100%)	8((100%)	10(100%)
χ^2-value	553.7				
p-value	p<0.0001,S,p<0.05				

[Table/Fig-5]: Stagewise distribution of slow waves in patients of CKD

Of these 83 patients one third patients were in stage V (31.3%), stage IV and stage III consists of (16.9%) and (18.1%) respectively. Less patients were seen in stage I (14.5%) suggesting there is a delayed diagnosis of CKD on onset.

We found that with increasing stages of CKD mean creatinine value increases and also severity of disease increases. Manoj K Bansal et al., [14] in their study found that the severity of the abnormal EEG changes correlated well with the severity of the clinical features and with the renal damage. Similarly other studies have also confirmed that generalized slow wave patterns in EEG proportionately correspond to the severity of renal failure [15-17].

[Table/Fig-1] illustrates distribution of morphometric EEG pattern with relation to different stages of CKD. Almost all patients were awake during the EEG recording and it is evident that alpha activity has remained predominantly in the entire stages of CKD. However, in addition to alpha pattern stage II, stage IV and stage V have shown a significant decrease in beta activity 25%, 21.43% and 15.38% respectively. It was also documented that 14.29% of stage IV and 15.38 % of patients of stage V have shown theta and beta records both. Usually, theta and beta records are reflection of excitatory post-synaptic cumulative neuronal transmission which suggests that firing rate in stage IV and stage V increases to certain extent. We also observed that there is progressive increase in the change of alpha wave on afferent stimulation as the CKD stages progress. Interestingly, 14.29%, 11.54% of stage 5 patients have demonstrated generalised delta activity and they were found to be significant (p<0.0001).

JE Röhl et al., [18] also found out that electrical power was most prominent in delta, theta and alpha frequencies in the temporal and

central brain areas. Similarly, Bourne JR et al., [16] also found EEG slowing is highly correlated with uremia associated variables.

Morphometric symmetry and rhythm pattern [Table/Fig-2] according to various stages of CKD confirmed that in Stage I patients have typically symmetric discharges. The evidence of asymmetry and dysrhythmia were noted from stage II onwards. As the stage of CKD progresses both asymmetricity and dysrhythmia tend to consolidate 12.5% to 50 % for asymmetricity and 12.5% to 34.62% for dysrhythmia and they were found to be significant (p<0.0001). Likewise, Neundorfer B et al., [19] in his study of 80 patients has found pathological EEG in the form of background slowing and general dysrhythmia and there was tendency to increase in pathological EEG findings in correlation with increase of retention values.

[Table/Fig-3] in our study shows distribution of amplitude of background EEG vis-a-vis various stages of CKD. Our study shows progressively disappearing high amplitude (>150 uV), whereas there is a sudden surge of low amplitude (<50 uV) in stage IV (57.14%) and stage V (57.69 %) respectively. There are equivocal reflections in medium amplitude, however, both low amplitude and high amplitude pattern of EEG have found to be significant (p< 0.0001) as the stage progresses. Abdulkadir Koçer et al., [20], also found out that in the early stages of uremia, EEG recordings were generally normal but as the disease progressed low amplitude waves predominates.

[Table/Fig-4] shows the pattern of dispersion of sharp waves transients in the various stages of CKD. We could notice a relative predominance of centro-frontal sharp wave transients in an awake recording in stage II (50%) and stage III (33.33%) and isolated centro-temporal sharp wave transients in stage III (33.33%) and parieto-occipital sharp wave transients simulated the centro frontal pattern in CKD. Interestingly, frontal and fronto – temporal sharp wave transients were noted as the stage progressed and were prominently present in stage IV and stage V, frontal sharp wave transients 50% in stage IV and 71.43% in stage V and temporo frontal sharp wave transients 50 % in stage IV and 14.29% in stage V. Abdulkadir et al., [20] also found sharp wave transients in the latter stages of CKD. Occipital sharp wave transients is noted in stage V and p-value is found to be significant in the distributional pattern at different progressive stages of CKD.

[Table/Fig-5] shows distribution of slow wave pattern in group of CKD in various stages .In stage I CKD we did not find any slow wave discharges while stage II patients have shown isolated presence of focal discharge in one patient and multifocal discharge in other patient. Stage III has also witnessed a pattern similar to stage II and there was no significant difference of observation between these two stages. However, there was prolific difference of appearance, morphometric pattern of slow waves ranging from bilateral 50% in stage IV and 60% in stage V, multifocal in 12.5% in stage IV, generalised 25% of stage IV and 30% in stage V and possible periodic slow waves are seen in equal distribution in only one patient in each group of stage IV and stage V. Statistically, the distribution of slow waves in various stages of CKD was found to be significant (p< 0.0001).

Abdulkadir Koçer et al., [20] found out that after termination of acute encephalopathy, slow waves persisted continuously. Bourne JR et al., [16] in his study found out that EEG slowing increased in later stages of CKD. Likewise Manoj K Bansal et al., [14] found out that with increasing severity there is increase in the slow wave activity. Ginn HE et al., [17] and Teschan et al., [15] also concluded that pathologic EEG changes correlates with creatinine levels.

CONCLUSION

Uremic encephalopathy is a known complication of CKD. EEG is an effective tool for diagnosis of uremic encephalopathy. Interestingly, EEG can be used as an effective tool for detection of subclinical or latent uremic encephalopathy, where patients do not show any overt clinical signs of uremic encephalopathy.

EEG findings which are characteristics of uremic encephalopathy can be present in CKD patients without frank signs of encephalopathy, suggesting that the neurologic electrophysiological abnormality persists whether or not the patients shows any overt signs of uremic encephalopathy. We recommend that EEG can be used to detect latent or subclinical encephalopathy, it will be helpful as a prognostic indicator of response to clinical therapy of CKD.

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