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Original Research Article

Evaluation of Brainstem Auditory Evoked Potentials in Chronic Kidney Disease Patients, Hemodialysis Patients and Renal Transplantation Patients

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Conflict of interest: Nil

Abstract:

Introduction and Background: Chronic kidney Disease (CKD) is defined as the presence of Kidney damage or a decreased level of kidney function for a period of 3 months or more. Auditory system abnormalities commonly occur in patients with Chronic Kidney Disease and End Stage Renal Disease patients undergoing hemodialysis. This Study was done to evaluate Brainstem Auditory Evoked Potentials in CKD patients, and patients undergoing hemodialysis and to document the reversibility of the BAEP changes after successful Renal Transplantation.

Aims: The aim of our study was to evaluate Brainstem Auditory Evoked potentials in chronic kidney disease patients and patients on hemodialysis and in those who have undergone Renal transplantation.

Methodology: The Experimental Group included 20 patients with CKD, 20 patients with CKD stage 5 undergoing hemodialysis and 20 Pateints who have undergone Renal Transplantation within one year of Diagnosis of CKD. Control Group Had 20 Healthy volunteers. Measurements included Absolute Peak Latencies I, II, III, IV & V and Inter peak Latencies I-III, III-V & I-V of the Auditory Brainstem Responses.

Results: Abnormal BAEP Recordings were seen in CKD patients and hemodialysis patients in the form of Prolonged Absolute Peak Latencies and Interpeak Latencies. There was a significant improvement in the BAEP Waveforms after Renal Transplantation. Hence this study showed that neural conduction along the Auditory Pathway is delayed in patients with CKD and CKD patients who were on hemodialysis. Renal transplantation significantly improves the auditory function.

Keywords: Chronic Kidney Disease, Brain stem Auditory Evoked Potentials, Hemodialysis, Renal transplantation.

Introduction

An Evoked potential is an electrical potential recorded from the nervous system of a human following a brief stimuli. Such potentials are useful for electro diagnosis and monitoring. Signals can be recorded from the cerebral cortex, brainstem & spinal cord on the peripheral nerves. Chronic renal failure (CRF) and end stage renal disease (ESRD) can cause malfunction of multiple organs, including auditory and vestibular systems. [1] Although the etiology of this malfunction is not definitely described, multiple factors have been proposed. Electrolyte disturbances, elevated serum urea level, episodes of hypotension, hypoxia, altered pharmacodynamics of ototoxic drugs, dysfunction or loss of hair cells, collapse of the endolymphatic space, edema and atrophy of specialized auditory cells, neuropathy, and in some patients, dialysis and its associated complications such as wide fluctuation in blood pressure during hemodialysis (HD) and accumulation of contaminants from dialysate water are some assumed ethiopathologies. [2-6] The auditory brainstem response (ABR) reflects neural function along the ascending auditory pathway, from the cochlea to the inferior colliculus. [7]A comparison of ABR recordings prior to and following

hemodialysis in the study done by Andreas K et al 1 showed a significant improvement in wave I and V latencies in the slow repetition rate and wave V latency in the fast repetition rate. [6]

The five distinct waves of a normal ABR waveform are mainly generated by successive nuclei in the ascending auditory pathway: waves I and II originate from the distal and proximal portions of the auditory nerve, respectively; wave III from the cochlear nucleus; wave IV from the superior olivary complex; and wave V from the lateral lemniscus/ inferior colliculus. Each higher level order wave receives contributions from lower levels of the pathway. [8] Cochlear dysfunction in kidney disease was first established as "Hereditary Familial Congenital Hemorrhagic Nephritis". [9] This syndrome is characterized by nephropathy, bilateral symmetric sensorineural hearing loss, ocular abnormalities and hereditary origin. The association of hereditary nephritis and deafness was established by examination of hearing with controlled audiometry and the structural abnormalities between glomerulus and stria vascularis showed that both the kidney and cochlea were concerned with electrolyte transport. [10,11] Changes in the outer hair cells and spiral ganglia do occur in CKD as witnessed in different temporal bone sections and audiovestibular changes result from the water and electrolyte imbalance accompanying CKD. [12] The function of both the kidney and the cochlea includes complex processes of water and ion regulation which are dependent on the functioning of different proton pump systems which maintain homeostasis of pH and ions. [13,14]

Materials and Methods

This study was conducted at the Department of Physiology in Kilpauk Medical College, Chennai.

Study Design: Observational study.

Subject Selection: Total sample size was 80 which included 20 controls, 20 CKD Patients, 20 patients on Hemodialysis and 20 patients who underwent Renal transplantation.

Inclusion Criteria

1. Patients diagnosed to have Chronic kidney disease in the department of Nephrology with eGFR <60 with duration more than 3 months.
2. Chronic Kidney disease patients undergoing hemodialysis for more than one month in the department of Nephrology, KMC.
3. Chronic Kidney disease patients who underwent Renal transplantation in the department of Nephrology, KMC.
4. Male &female < 18 years and >70 years old

Exclusion Criteria

1. Ischemic heart disease.
2. Cerebrovascular disease
3. Alcoholism.
4. Any neurological disease
5. Previous history of Hearing impairment
6. Alport syndrome

Controls

Healthy volunteers who were age and sex matched were chosen as controls.

Screening Procedures

Patients who qualified under the inclusion criteria were enrolled in the study. Blood pressure, Height and Weight were recorded. Brief history to rule out ischemic heart disease, diabetes, hearing impairment, alcoholism, drug intake was carried out. General clinical examination was done.

Consent

A written informed consent was obtained from patients & controls after explaining the procedure and its significance in their vernacular language.

Equipment Details

Brainstem auditory evoked potentials studies were carried out on a computerized Nerve conduction testing equipment: Medicaid, computerized physiolab, Neuroperfect plus**.**

Ethical Considerations

Institutional Ethical committee approval was obtained from Kilpauk medical college Chennai - 10.

The settings were as follows:

Stimulus Parameter

Click stimulus having intensity 70 db was presented to both ears monoaurally. During stimulation of one ear, the other ear was masked by 40 db sound. A total of 2000 stimulations generated by passing 0.1 millisecond square pulse through shielded headphones with alternating polarity were applied on both ears monoaurally. Stimulus were at the rate of 11.1/sec.

Filters

1. low: 100 Hz
2. high: 3 KHz

Stimulus polarity

- Two types of clicks were produced.
- One, moving the earphone diaphragm away from the eardrum (rarefaction click).
- The other moving it in the opposite direction (condensation or compression click).

In this study, stimulus with rarefaction click is given.

Recording electrodes

- The volume-conducted evoked responses are picked up from scalp by electrodes. Two electrodes were attached, one to right mastoid and other to left one as ground electrode to forehead, termed as F_z. All the electrodes were pluged to the junction box. Skin-to-electrode impedance was monitored and kept below 5 kΩ.
- Recommended montage for BAEP:
- CHANNEL 1: mastoid, designated as A_i and A_c respectively; one reference electrode on vertex , labeled as C_z; and $C_z - A_i$
- CHANNEL 2 : C_Z - A_c
- GROUND: F_Z

Prerequisites for the Study

A) The subjects were advised to clean and keep their head oil free.
B) The research lab was made quiet and sound proof to the patients.
C) Subjects were made to remove their ornaments.

Procedure

The BAEP Recording was done in the research laboratory, in the Department of physiology, Kilpauk medical college using Neuroperfect Plus-Medicaid Physiolab. In all the subjects, both right and left ears were tested separately.

Recording of BAEP-Instrument Setting

The requirements were

1. Recording electrodes
2. Amplifier and average
3. Electrode paste
4. Ear phone Equipment set up

Suggested Montage

1. Channel Ai-Cz-Active electrodes
2. Channel Ac –Cz –ipsilateral ear (Ai), contralateral ear (Ac) or mastoid process
3. Ground ;Fz-Reference electrode ;Cz, at vertex

Recording conditions

1. Filter, low filter cut at 10-100 Hz ,high at 3000 Hz
2. Amplification in the range of 2,00,000-5,00,000
3. Sweep speed at 1 msec/division
4. Electrode impedance kept below 5 kilo-ohms

Stimulation options

1. Sensitivity at 0.3uv/division
2. 60 db sensory level, the point at which the individual barely appreciates the stimulus.

Steps

1. The instrument is kept out of view of the subject.
2. The subject is allowed to sit comfortably on a chair.
3. Skin at the point where electrodes are placed is cleaned with spirit.
4. Using a conducting jelly or electrode paste the active recording electrodes are placed on both the ears ipsilateral ear (Ai) and contralateral ear (Ac) or mastoid process as per 10-20 international system of EEG electrode placement ;the reference electrode is placed at the vertex i.e at Cz..the ground electrode is placed at Fz
5. The electrodes are connected through the preamplifier to the cathode ray oscilloscope
6. A brief click stimulus which is a square wave pulse of 0.1 msec duration is given. A click rate of 11-31 Hz is used mostly in clinical practice.
7. The effects of click intensity is observed and the BAEP waveforms are compared with the normal.

Parameters Studied are the wave latencies I, II, III, IV & V and interpeak latency I-III, I-V, and III-V…Total duration of recording the waveforms is within 10 msec of stimulus. Thus brainstem auditory evoked potentials are recorded from the ear and scalp in response to a brief auditory stimuli. The evoked potentials that appear following transduction of acoustic stimulus by ear cells create an electric signal that is carried to the cerebral cortex via the auditory pathway.

Results

Control Group

There were 20 subjects in the control group with average of 31.60 $\pm$9.9 years, average weight 60.3 $\pm$11.8 and creatinine 0.712 ± 0.12

Chronic Kidney Disease Group

There were 20 CKD patients ranging from 18 to 60 years of age with an average weight of 58.65 $\pm$7.6 kg and creatinine 6.32 ± 1.36.

Hemodialysis Group

There were 20 patients who were on hemodialysis in the department of nephrology, KMC with an average weight of 50.05$\pm$4.3 kg and creatinine 6.2 ± 1.34.

Renal Transplantation Group

There were 20 patients who were treated with renal transplantation with an average weight of 60.20 $\pm$6.9 kg and creatinine 1.13 ± 0.48. CKD patients were graded on the basis of Creatinine and GFR and the average values of BAEP with Absolute and Inter peak latencies were recorded and given in table 5, 8, 11 & 14. The average value of Absolute peak latency and Inter peak latencies of

hemodialysis patients were recorded and are given in table 6, 9, 12 & 15.

The average value of Absolute peak latency and Inter peak latencies of RT patients were recorded and given in table 7, 10, 13 & 16.

In Chronic kidney disease group, there was a significant increase in the latencies of wave, III and inter peak latencies did not vary significantly in both ears.

In hemodialysis group there was a significant increase in the absolute peak latencies of I & III and inter peak latencies I-III, III-V in both the ears.

In renal transplantation group there was no significant change in either the absolute or the inter peak latencies in both the ears.

Table 1: Anthropometric Measurement of Cases (CKD) and Controls

Variables	Cases –CKD (20) Mean +SD	Controls N=20	P Value
Age (Yrs)	49+ 12.73	31.60+9.95	0.000
Weight (Kg)	58.65+ 7.6	63.37+11	0.242

Table 2: Anthropometric Measurement of Cases (on Hemodialysis- [HD]) with Controls

Variables	Case =HD (20) Mean +SD	Controls (N=20) Mean +_SD	P Value
Age (Yrs)	36.75+_ 15.3	31.60+ 9.9	0.502
Weight (Kg)	58.05+_4.3	63.37+_11.8	0.822

Table 3: Anthropometric Measurement of Cases (Renal Transplant) with Controls

Variables	Case =RT (20) Mean +SD	Controls (N=20) Mean +_SD	P Value
Age (Yrs)	45.15+ 13	31.60+ 9.9	0.002
Weight (Kg)	61.20+ 6.925	63.37+ 11.8	0.822

Table 4: Comparison of Serum Creatinine in Cases and Controls

Serum. Creatinine	Mean	SD	P Value
Controls	0.712	0.1228	<0.001
CKD	6.325	1.3692	<0.001
Dialysis	6.280	1.3621	<0.001
Renal Transplant	1.130	0.4842	0.418

'p' Value is significant for controls, CKD & HD patients.

Table 5: Comparison of Absolute Peak Latencies of Right Ear- Between Chronic Kidney Patients & Controls

Latencies	Case (CKD) Mean +_SD	Control Mean+-SD	P Value
I	1.82+-0.24	1.75+-0.07	0.771
II	2.87+ 0.14	2.83+ 0.15	0.889
III	4.21+ 0.31	3.98+ 0.06	0.044
IV	4.99+ 0.47	5.08+ 0.17	0.859
V	5.61+ 0.47	5.69+ 0.17	0.902

Absolute peak latency of III waveform is significantly prolonged with a 'p' value of 0.044.

Table 6: Comparison of Absolute Peak Latencies of Right Ear-Between Hemodialysis Patients & Controls

Latencies	Case (HD) Mean +_SD	Control Mean+-SD	P Value
I	1.98+ 0.48	1.75+ 0.07	0.013
II	2.79+ 0.22	2.83+-0.15	0.891
III	3.72+ 0.33	3.98+ 0.06	0.020
IV	5.02+ 0.15	5.08+ 0.17	0.961
V	5.78+ 0.29	5.69+ 0.17	0.851

Absolute peak latency of waves I & III are prolonged with a 'p' value of 0.013 & 0.020.

Table 7: Comparison of Absolute Peak Latencies of Right Ear -Between Renal Transplantation Patients & Controls

Latencies	Case (HD) Mean + SD	Control Mean+-SD	P Value
I	1.74+ 0.08	1.75+ 0.07	1.000
II	2.78+ 0.26	2.83+ 0.15	0.749
III	3.87+ 0.45	3.98+ 0.06	0.564
IV	4.90+ 0.64	5.08+ 0.17	0.424
V	5.61+ 0.63	5.69+ 0.17	0.898

There is no significant prolongation of absolute peak latency.

Table 8: Comparison of Inter Peak Latencies of Right Ear-Between Chronic Kidney Disease Patients & Controls

Latencies	CKD Patients	Control	P Value
I-Iii	2.39+ 0.49	2.23+ 0.10	0.604
Iii-V	1.50+ 0.35	1.70+-0.18	0.127
I-V	3.89+ 0.24	3.92+ 0.22	0.991

There is no significant prolongation of inter peak latencies.

Table 9: Comparison of Inter Peak Latencies of Right Ear- Between Hemodialysis Patients & Controls

Latencies	CKD Patients	Control	P Value
I-Iii	1.79+ 0.68	2.23+ 0.10	0.005
Iii-V	2.15+ 0.50	1.70+ 0.18	0.000
I-V	3.84+ 0.52	3.92+ 0.22	0.901

There is significant prolongation of I-III & I-V interpeak latencies with ‘p’ value of 0.005 & 0.000.

Table 10: Comparison of Inter Peak Latencies of Right Ear-Between Renal Transplantation Patients & Controls

Interpeak Latencies	RT Patents	Control	P Value
I-III	2.13+-0.43	2.23+ 0.10	0.604
III-V	1.71	1.70+-0.18	0.127
I-V	3.89+ 0.24	3.92+ 0.22	0.991

There is no significant prolongation of interpeak latencies.

Table 11: Comparison of Absolute Peak Latencies of Left Ear-Between Chronic Kidney Disease Patients & Controls

Latencies	Case (CKD) Mean + SD	Control Mean+-SD	P Value
I	1.79+ 0.06	1.74+ 0.11	0.764
II	2.96+-0.26	2.85+ 0.20	0.248
III	4.21+ 0.31	3.98+ 0.06	0.044
IV	4.96+ 0.28	4.99+ 0.52	0.994
V	5.79+ 0.24	5.67+ 0.58	0.717

The absolute peak latency of waveform III is prolonged with ‘p’ value 0.044.

Table 12: Comparison of Absolute Peak Latencies of Left Ear - Between Hemodialysis Patients & Controls

Latencies	Case (HD) Mean + SD	Control Mean+-SD	P Value
I	1.90+ 0.36	1.74+ 0.11	0.018
II	2.82+ 0.21	2.85+ 0.20	0.946
III	3.60+ 0.38	3.93+ 0.37	0.003
IV	4.91+ 0.35	4.99+ 0.52	0.898
V	5.80+ 0.26	5.67+ 0.58	0.661

There is significant prolongation of absolute peak latency of waveform I & III.

Table 13: Comparison of Absolute Peak Latencies of Left Ear-Between Renal Transplantation Patients & Controls

Latencies	Case (HD) Mean + _SD	Control Mean+-SD	P Value
I	1.74+ 0.07	1.74+ 0.11	1.000
II	2.87+ 0.07	2.85+ 0.20	0.974
III	3.92+ 0.23	3.93+ 0.37	1.000
IV	5.06 + 0.14	4.99+ 0.52	0.894
V	5.72+ 0.26	5.67+ 0.58	0.967

There is no significant prolongation of Absolute peak latencies

Table 14: Comparison of Inter Peak Latencies of Left Ear-Between Chronic Kidney Disease Patients & Controls

Interpeak Latencies	RT Patients	Control	P Value
I-III	2.24+-0.19	2.18+ 0.30	0.957
III-V	1.74+ 0.31	1.75+ 0.24	0.999
I-V	4.00+ 0.22	3.93+ 0.51	0.936

There is no significant prolongation of interpeak latencies.

Table 15: Comparison of Inter Peak Latencies of Left Ear- Between Hemodialysis Patients & Controls

Interpeak Latencies	RT Patients	Control	P Value
I-III	1.78+ 0.66	2.18+ 0.30	0.003
III-V	2.20+ 0.37	1.75+ 0.24	0.000
I-V	3.84+ 0.46	3.93+ 0.51	0.881

There is significant prolongation of interpeak latencies I-III & III-V with a 'p' value of 0.003 & 0.000

Table 16: Comparison of Inter Peak Latencies of Left Ear-Between Renal Transplantation Patients & Controls

Interpeak Latencies	RT Patients	Control	P Value
I-III	2.19+ 0.25	2.18+ 0.30	1.000
III-V	1.80+ 0.20	1.75+ 0.24	0.931
I-V	3.99+ 0.27	3.93+ 0.51	0..959

There is no significant prolongation of interpeak latencies.

Discussion

Quic CA, Fish A [15] studied the relationship between cochlea and kidney and concluded that cochlea and kidney have the same physiological process, Active transport of fluid & electrolytes accomplished by in cochlea and kidney by stria vascularis and glomerulus respectively. They also attributed the similar effect of certain medications (ototoxic medication) on these two organs. Alder et al. [16] in their study demonstrated the fact that there was a significant inhibition of Na+K+ATP ase in the inner ear of guinea pigs which had uraemia.

They also suggested an inverse correlation between serum creatinine levels and Na+K+ATP ase activity which is vital for maintaining the cationic gradients in the inner ear. Hence, inhibition of this enzyme contributed to inner ear abnormalities in uremic patients. In this study, there was prolongation of Absolute and Inter peak Latencies in both the ears of hemodialysis patients compared to Chronic Kidney Disease patients who were not started on hemodialysis. This finding correlates with that of the study done by Naderpour M, Mortazavi F et al. [17] in which abnormal ABR recordings were seen in patients with Chronic kidney disease who were on hemodialysis compared to chronic kidney disease patients who were yet to start on hemodialysis. The Present study showed prolongation of Absolute Peak Latencies I & III and Inter peak latencies I-III, III-V in patients undergoing hemodialysis which correlates with the study done by Aspris ak, Thodi CD et al. [6], who demonstrated the effects of chronic kidney disease on auditory function & changes in the auditory function following hemodialysis. It was seen that the absolute latency of wave III and inter peak latencies III-V & I-III were significantly prolonged in patients undergoing hemodialysis compared to Chronic Kidney disease patients not on hemodialysis .This may be due to marked biochemical changes seen in CKD as this reverses after successful transplantation.

Hoth S, Weber FN et al. [18] in their study pointed out that the small increase in the ABR recordings were due to the broadening of the excited area & its shifting towards a more apical position if the hair cell population in the basal turn is depleted..

In our study, there was a highly significant improvement in hearing and Absolute & Inter peak latencies after successful renal transplantation. This partially correlates with the study of Bains KS, Chopra H et al. [19] who documented Brainstem evoked response audiometry in Chronic kidney disease patients who underwent renal transplantation. Compared with the pre-transplant values, after transplantation, there was a significant improvement in the I, III V latencies and hence it was concluded that, there is a definite improvement in hearing and wave latencies after successful renal transplantation.

Conclusion

This study has documented BAEP Changes in CKD and HD patients. The changes in BAEP Waveforms are in both cochlear and retro cochlear components of Auditory pathway. The marked changes in BAEP Waveforms in patients undergoing hemodialysis may reflect the intensity and fluctuation in biochemical changes related to CKD. The reversal of BAEP changes after successful renal transplantation throws light on the rehabilitatory potential of renal transplantation on audiological dysfunction.

Limitations of the Study

The value of biochemical markers of CKD on the day of recording BAEP could have been recorded which would have helped in explaining the marked changes seen in patients under hemodialysis.

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