National Journal of Physiology, Pharmacy and Pharmacology

RESEARCH ARTICLE

Cochlear and brainstem auditory responses in patients with generalized epilepsy – A cross-sectional study

Rajeev Sharma[1], Smily Goyal[2], Ratul Dey[3], Ramandeep Singh Dang[4]

[1]Department of Physiology, Guru Gobind Singh Medical College, Faridkot, Punjab, India, [2]MBBS Student, Guru Gobind Singh Medical College, Faridkot, Punjab, India, [3]Department of Audiology, Guru Gobind Singh Medical College, Faridkot, Punjab, India, [4]Department of Neurosurgery, Guru Gobind Singh Medical College, Faridkot, Punjab, India

Correspondence to: Rajeev Sharma, E-mail: rajeevsharma.md@gmail.com

Received: February 02, 2020; **Accepted:** February 20, 2020

ABSTRACT

Background: Epilepsy being a neurological disorder is characterized by excessive abnormal discharge in neurons of brain. Such abnormal activity rapidly engages many cortical and subcortical structures. As a result, this could influence auditory information processing of neuronal pathways in brainstem. **Aims and Objectives:** The objectives of the study were (1) To assess the cochlear responses transient evoked otoacoustic emissions (TEOAEs) in newly diagnosed drug-naive patients of epilepsy and (2) To assess the brainstem auditory evoked responses (ABR) in newly diagnosed drug-naive patients of epilepsy. **Materials and Methods:** The study was done in the department of audiology in a tertiary care institute. Three audiological tests, i.e., pure tone audiometry (PTA), auditory brainstem evoked responses (ABR), and TEOAEs were recorded on 30 patients in the age group of 15–45 years diagnosed with epilepsy and 30 age- and gender-matched controls. **Results:** All the participants chosen for the study were having normal hearing thresholds bilaterally as confirmed by PTA (air conduction thresholds below 25 dB HL across the audiometric frequencies of 250 Hz–8000 Hz). The absolute latency values of ABR were prolonged in patients of epilepsy ($P < 0.05$). The difference in interpeak latencies was found to be statistically non-significant. The amplitude values for waves III and V of ABR were reduced in epileptics ($P < 0.05$). The TEOAEs recorded in these patients of epilepsy showed no significant change in amplitude, noise floor, and signal-to-noise ratio. **Conclusion:** The findings of this study suggest that the epileptic patients have delayed absolute peak latencies and decreased amplitudes of waves III and V, indicating the possible involvement of lower brainstem due to seizure activity. However, this study also suggests that epileptic seizure is less likely to result in any alteration at the level of outer hair cells.

KEY WORDS: Epilepsy; Auditory Brainstem Evoked Response; Hearing Threshold; Absolute Latency

INTRODUCTION

Epilepsy is a neurological disorder characterized predominantly by recurrent and unpredictable interruption of normal brain activity. Epileptic seizure is a transient occurrence of signs and/or symptoms due to abnormally excessive neuronal activity in brain.[1] Seizures are classified into generalized seizures, focal seizures, and seizures of unknown origin. Generalized epileptic seizures are known to originate at one point within brain and could rapidly involve whole neuronal networks in brain cortical and subcortical structures.[2] Audiological profile consists of various diagnostic tests to assess the integrity of the hearing mechanism. This includes subjective or behavioral as well as objective or physiological and electrophysiological auditory tests such as pure tone audiometry (PTA), auditory brainstem

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Website: www.njppp.com	Quick Response code
DOI: 10.5455/njppp.2020.10.02045202020022020	

evoked responses (ABR), and transient evoked otoacoustic emission (TEOAE) testing. PTA helps to determine the hearing sensitivity of an individual, both through air conduction and bone conduction. Auditory brainstem evoked response measures the potentials from cochlear nerve to midbrain in response to a click stimulus. For TEOAE, a click stimulus is given that causes the emission of several frequencies at the same time to measure the presence or absence of sound waves generated by the cochlear outer hair cells of inner ear.[3] Epilepsy and the auditory system are closely related since these attacks are associated with various cochlear and vestibular symptoms, particularly during aura of epilepsy.[4] Neurological disorders are among the risk factors for disruption in auditory information processing.[5] Various studies suggest that patients of different types of epilepsy exhibit altered brainstem responses in terms of absolute and interpeak latencies and amplitudes of ABR.[6,7] At the same time, few other studies have not been able to detect any significant alterations in ABR in patients of partial epilepsy.[8] Drug treatment with different anticonvulsants and duration of epilepsy has also shown to alter the auditory brainstem responses.[8,9] However, there are scarce studies to ascertain the effects on brainstem due to epilepsy or drug treatment. Similarly, cochlear assessment in terms of OAE in the patients of epilepsy on drug treatment has been reported but not on new patients of epilepsy. Therefore, the present study was planned with an objective of substantiating the neurological findings at cochlear and lower brainstem levels in newly diagnosed patients of generalized epilepsy previously untreated with anticonvulsant medication.

MATERIALS AND METHODS

This cross-sectional study was conducted in a tertiary care hospital, on 30 newly diagnosed patients of generalized epilepsy, previously untreated with anticonvulsants. The control group comprised 30 healthy subjects with normal hearing and matched age and gender distribution. The study was carried out after the approval of the Institutional Research and Ethics Committee. A written informed consent was obtained before starting the procedures. Hearing thresholds in all the participants of the study were determined by PTA. PTA was done inside a two-room acoustically treated set-up (ambient noise <35 dB A at 1 kHz) using ALPS AD2100 advance digital audiometer. TDH 39 supra-aural headphones and radio ear B-71 bone vibrator were used for testing through air conduction and bone conduction, respectively. Auditory thresholds were obtained through bracketing method of estimation at octave frequencies between 250 Hz and 8 kHz for air conduction and 250 Hz–4 kHz for bone conduction.

TEOAEs were recorded inside a double-walled acoustically treated room using Neurosoft Neuro-Audio (version 2010) device. The participants were instructed to sit quiet, breathe normally and not to cough or swallow during the whole test period. Stimulus was delivered through ER 10-D probe with a sensitivity of 25 μa/Pa. One thousand sweeps of click were presented at 75 dB SPL at the rate of 40 Hz. A 25 ms recording window was used for the recording. The amplitude of OAE, noise floor, and signal-to-noise ratio (SNR) were measured.

Auditory brainstem evoked responses (ABR) were measured using Neurosoft Neuro-Audio (version 2010) device. Participants were made to lie down in supine position, close their eyes and relax. Skin at the electrode sites was prepared by rubbing Nuprep abrasive gel. The evoked response was recorded using gold plated cup electrodes. Vertical recording montage (Cz-Fpz- A1/A2) was used for the recording. An impedance check was run before starting the procedure to ensure proper skin preparation and placement of the electrodes. Absolute as well as interelectrode impedance values were maintained below 0.3 kΩ. ER 3 A insert earphones (3M E-A-RTone gold) were used to deliver the signal. Alternating polarity clicks of 1 ms duration (1500 sweeps) at two stimulation rates, i.e., 30.1/s and 60.1/s were employed. Intensity level of the clicks was fixed for both the rates at 85 dB nHL. The high-pass and low-pass filters were set at 100 Hz and 3000 Hz, respectively. The response was recorded in a 10 ms time window. Ear specific absolute latencies of waves I, III, and V, interwave latency differences for waves I-III, III-V, and I-V, and ear specific absolute amplitude (measured from peak to trough) for waves I, III, and V were measured. At least two recordings were taken for each rate of stimulation to ensure the reproducibility of the waveforms. Ongoing EEG activities were simultaneously monitored to ensure a stable electrophysiological status and limited artifacts.

Statistical Analysis

The absolute peak latencies I, III, and V; interpeak latencies I-III, III-V, and I-V; and absolute amplitudes of waves I, III, and V were measured and compared in epileptic and normal participants using Student's *t*-test. Similarly, parameters of otoacoustic emission such as amplitude, noise floor, and SNR were measured at different frequencies and compared. $P < 0.05$ was considered to be statistically significant.

RESULTS

All the participants chosen for the study were having normal hearing thresholds bilaterally as confirmed by PTA (air conduction thresholds below 25 dB HL across the audiometric frequencies of 250 Hz–8000 Hz). Hearing threshold of cases (23.67 ± 6.32) was marginally higher than the control group (21.41 ± 6.95) but was statistically non-significant ($P = 0.066$). The audiological profile, including auditory brainstem response (ABR) and TEOAE, was assessed in 30 epileptic patients and 30 age- and sex-matched controls.

The values of ABR and OAE obtained were averaged out for the right and left ear (both in cases and controls) as the difference in readings between the right and left ears was non-significant. As a result, the comparison was made between 60 healthy ears and 60 ears of patients with epilepsy.

Table 1 shows absolute latency values of waves I, III, and V at two different rates, i.e., 30.1/s and 60.1/s for auditory brainstem response. The absolute latency for all the waves was found to be more in patients of epilepsy and the difference in absolute latency values between cases and controls for both the rates was statistically significant ($P < 0.05$).

The interwave latency values were marginally higher in epileptics. However, the difference of interwave latency values (I-III, III-V, and I-V) between cases and controls at the two rates was found non-significant statistically, as shown in Table 2.

Table 3 depicts the absolute amplitude of different waves of ABR at two rates, i.e., 30.1 and 60.1. The amplitude of waves I, III, and V at both the rates of stimulation was found to be lower in patients of epilepsy. It was also observed that the difference in amplitude between cases and controls for waves III and V at both the rates was significant. However, no significant difference was observed in amplitude for wave I.

Tables 4-6 show various attributes of TEOAE, i.e., amplitude, noise floor, and SNR, respectively. No statistically significant difference was found between the healthy and diseased groups in terms of values of amplitude, noise floor, as well as SNR.

Table 1: ABR – absolute latency values (ms)

Rate	Wave	Cases	Controls	*P*-value
30.1	I	1.57±0.26	1.43±0.10	0.007*
	III	3.66±0.34	3.52±0.16	0.044*
	V	5.59±0.32	5.35±0.23	0.002*
60.1	I	1.68±0.34	1.49±0.15	0.007*
	III	3.77±0.27	3.61±0.14	0.005*
	V	5.75±0.34	5.55±0.16	0.005*

*P<0.05 statistically significant

Table 2: ABR – interpeak latency difference values (ms)

Rate	Wave	Cases	Controls	*P*-value
30.1	I-III	2.09±0.25	2.06±0.19	0.581
	III-V	1.96±0.38	1.88±0.12	0.299
	I-V	3.99±0.99	3.91±0.36	0.477
60.1	I-III	2.14±0.25	2.10±0.25	0.934
	III-V	2.02±0.39	1.93±0.24	0.291
	I-V	4.07±0.78	4.01±0.45	0.859

*P<0.05 statistically significant

Table 3: ABR – absolute amplitude (μV)

Rate	Wave	Cases	Controls	*P*-value
30.1	I	0.19±0.13	0.27±0.91	0.267
	III	0.20±0.11	0.31±0.14	0.002*
	V	0.31±0.12	0.46±0.16	0.000*
60.1	I	0.16±0.10	0.19±0.07	0.208
	III	0.17±0.09	0.23±0.09	0.017*
	V	0.30±0.12	0.37±0.12	0.024*

*P<0.05 statistically significant

DISCUSSION

This study was carried out to assess the audiological profile in newly diagnosed drug-naive patients of generalized epilepsy. Auditory brainstem response (ABR) and TEOAE were recorded to find out the lower brainstem or cochlear involvement in such patients. The auditory brainstem response (ABR) was assessed for three attributes which were absolute latency, interpeak latency values, and amplitude of response. Absolute latency of all the ABR waves was prolonged in patients of epilepsy as compared to normal subjects and this difference in delay was statistically significant ($P < 0.05$). Interpeak latencies for all the waves were marginally higher in epileptics, but the difference in interpeak latencies was found to be non-significant. The amplitude values for waves III and V were reduced in epileptics as compared to normal

Table 4: Otoacoustic emissions – amplitude (dB)

Frequency	Cases	Controls	*P*-value
1 kHz	2.63±4.29	4.58±5.58	0.134
2 kHz	−0.28±7.78	2.85±6.09	0.087
3 kHz	−7.64±8.07	−4.47±6.11	0.092
4 kHz	−13.49±8.02	−11.06±6.25	0.194
5 kHz	−17.71±8.19	8.19±7.79	0.674

Table 5: Otoacoustic emissions – noise floor (dB)

Frequency	Cases	Controls	*P*-value
1 kHz	−4.45±5.64	−4.60±4.80	0.909
2 kHz	−8.17±5.66	−6.92±5.34	0.382
3 kHz	−10.70±5.16	−10.15±4.12	0.651
4 kHz	−14.60±4.76	−13.32±4.12	0.276
5 kHz	−19.07±5.29	−18.81±5.21	0.850

Table 6: Otoacoustic emissions – SNR

Frequency	Cases	Controls	*P*-value
1 kHz	5.96±5.63	8.51±5.58	0.084
2 kHz	7.39±7.01	8.79±5.28	0.387
3 kHz	3.76±3.11	4.98±3.92	0.189
4 kHz	−0.10±4.75	2.33±4.48	0.065
5 kHz	−2.74±4.92	−1.56±5.48	0.386

SNR: Signal-to-noise ratio

controls which were statistically significant ($P < 0.05$). The TEOAE values obtained in epileptics were non-significant when compared with controls.

Increased absolute latencies suggest a delay in brainstem auditory information processing in these patients.[10] Decreased amplitude of waves III and V indicates decreased summation of responses at the level of superior olivary nucleus and lateral lemniscus.[11] Elevated ABR thresholds have been reported by Soliman *et al*. in patients of generalized epilepsy when compared with temporal lobe epilepsy. They reported positive correlation of these elevated thresholds with chronicity of grand mal seizures.[12] We did not go for the ABR threshold measurement and studied the responses only at a fixed intensity level of 85 dB after ascertaining their normal hearing thresholds as we had selected only the fresh cases of epilepsy. Studies by Rodin *et al*. have shown significantly longer absolute and interpeak latencies and reduced amplitudes in the patients of epilepsy. They have attributed these changes to severity, extent of brain damage, and anticonvulsant medication also.[6] Phillips *et al*. have also found prolonged peak latencies of ABR waves III and V in patients of generalized epilepsy.[13] Therefore, the findings of our study are in consonance with the above findings. ABR wave complex is known to depict activity at the lower brainstem level.[7,14] Soliman *et al*.[12] have postulated that biochemical disturbances in the form of neurotransmitter imbalance extending down to subcortical levels or hypoxic damage to brain during epilepsy could lead to subsequent dysfunction of auditory brainstem pathways. The present findings in our study also suggest possible lower brainstem level involvement in the form of neurochemical disruption in brainstem auditory pathways in the patients of generalized epilepsy. Normal interpeak latencies and within range values of peak latencies could be attributed to the fact that the tests were performed immediately after the first reporting of seizure. These effects on latencies have also been attributed to the effects of antiepileptic drugs.[13] However, we were able to detect these changes in drug-naive patients also.

The TEOAE studies done in these subjects suggested no significant change in OAE amplitude, noise floor, and SNR in the patients of epilepsy. As otoacoustic emissions depict a cochlear response which reflects healthy outer hair cells, our study suggests that epileptic seizure is less likely to cause any alteration at the outer hair cells level.

Strength and Limitations

Therefore, this study has been able to provide some insight into possible involvement of lower brainstem without any cochlear involvement in drug-naive patients of generalized epilepsy even after the first seizure. However, extended study on higher number of patients, different variants of epilepsy, and follow-up studies for subsequent brainstem responses in such patients after drug therapy could be more conclusive.

CONCLUSION

This study suggests that the epileptic patients have altered brainstem evoked responses in the form of delayed absolute peak latencies and decreased amplitudes of waves III and V that indicate the possible involvement of lower brainstem due to seizure activity. However, this study also shows that epileptic seizure is less likely to result in any alteration at the level of outer hair cells.

ACKNOWLEDGMENT

We are highly thankful to ICMR, New Delhi, for granting this project as ICMR-STS to Smily Goyal, MBBS student. We also thank Mr. Baltej Singh, Assistant Prof. of Statistics for his help during data analysis of the study.

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How to cite this article: Sharma R, Goyal S, Dey R, Dang RS. Cochlear and brainstem auditory responses in patients with generalized epilepsy – A cross-sectional study. Natl J Physiol Pharm Pharmacol 2020;10(04):319-323.

Source of Support: Nil, **Conflicts of Interest:** None declared.