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Original Article

Auditory Evaluation of Three Most Commonly Used Anti-Seizure Medications Valproate (VPA), Carbamazepine (CBZ) and Levetiracetam (LEV) in School-Aged Children: A Single Center Prospective Study with Extensive Auditory Test Design in a Small Epileptic Cohort

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Keywords: Anti-seizure medications; auditory brainstem response; distortion-product otoacoustic emissions; ototoxicity; pediatric epilepsy; pure-tone audiometry.

ABSTRACT

Objective: This study aimed to assess the effects of commonly used anti-seizure medications (ASMs)—valproate (VPA), carbamazepine (CBZ), and levetiracetam (LEV)—on hearing function in school-aged children with newly diagnosed epilepsy.

Methods: A prospective study was conducted on 16 treatment-naive children (mean age 11.5±3.7 years) diagnosed with idiopathic generalized or self-limited focal epilepsy per 2017 ILAE criteria. Patients received VPA (n=12), CBZ (n=2), or LEV (n=2), titrated to therapeutic levels within one month. Audiological assessments—including pure-tone audiometry (0.25–8 kHz), tympanometry with acoustic reflexes, distortion-product otoacoustic emissions (DPOAE), and auditory brainstem response (ABR)—were performed before treatment and after a mean follow-up of 10 months. Paired t-tests compared baseline and follow-up results (significance set at $p<0.05$).

Results: All baseline hearing thresholds were ≤25 dB HL. Post-treatment thresholds were unchanged except for a slight increase at 4 kHz in the right ear (+3.8 dB HL, p=0.009). ABR latencies and inter-peak intervals remained stable. Tympanometry and acoustic reflexes were unchanged. DPOAE amplitudes declined at 2 kHz (−7.3 dB, p=0.001) and 6 kHz (−4.7 dB, p=0.006) in the right ear, while left-ear measures remained stable. No auditory symptoms or adverse events were reported.

Conclusion: Monotherapy with VPA, CBZ, or LEV over ~10 months did not result in clinically significant hearing impairment in children. However, minor frequency-specific reductions in cochlear emissions were noted. Further large-scale, drug-specific studies are needed to validate these preliminary findings.

INTRODUCTION

Epilepsy is one of the most common neurological diseases in childhood with an incidence rate of 0.5 to 8 per 1000 person-years.[1,2] Considering the chronic nature of the disease and the need for long-term treatment, the possible side effects of the drugs should be taken into consideration at the beginning of the treatment.[1] It is widely recognized that certain medications can have ototoxic (cochleotoxic or vestibulotoxic) effects, which may be either temporary or permanent.[3]

Anti-seizure medications (ASM) are the mainstay of epilepsy treatment.[4] Approximately 80% of children with epilepsy have seizure control with an appropriate medical treatment.[5,6] However, 20% of patients fail to respond to antiepileptic drugs and belong to the drug-resistant epilepsy group in which more than two antiepileptics are used. Side effects of the medications used are very important, especially in this particular epilepsy group.[7]

Generally known side effects of most commonly used antiepileptic drugs are headache, nausea, dizziness, a tendency to sleep, liver dysfunction, pancreatitis, kidney stones, visual disturbances, allergic reactions, hyperlipidemia, thyroid dysfunctions, cognitive dysfunction; and the patients are regularly monitored for these side effects by the clinician who initiates the treatment(3). Cognitive and language dysfunctions can be comorbid conditions related to the underlying etiology of epilepsy as well as complications of long-term antiepileptic drug use.[8,9]

Auditory symptoms like sound or voice hallucinations and tinnitus are known ictal manifestations of some epilepsy types (temporal, temporal-parietal-occipital epilepsies) and have been related to the underlying genetic etiology but could also be the result of ototoxic side effects of antiepileptic drugs used.[9,10]

Considering the fact that the highest incidence of childhood epilepsy is reported in the first year of life, possible deleterious side effects of antiepileptics on the auditory system need to be taken into special consideration and precautions and careful monitoring should be performed to prevent any long-term language and cognitive delay related with auditory dysfunction.[11,12] And also long-term use of antiepileptic drugs can affect central nervous system (CNS) functions even in the absence of clinical neurotoxicity symptoms.[3]

Tinnitus, disturbed pitch perception, reversible sensorineural hearing loss, and vestibular dysfunction are the auditory problems reported in the literature which have been attributed to side effects of some widely used anti-seizure medications like carbamazepine, oxcarbazepine, valproic acid, phenytoin, gabapentin and vigabatrin.[13,14] Pitch perception abnormalities have been reported by carbamezapine (CBZ) but not by valproic acid (VPA) or levetirasetam (LEV).[15] CBZ is also reported to inhibit the neural activity.[3]

There are proposed pathophysiological mechanisms for demonstrated auditory side effects associated with the main mechanisms of actions of the drugs in case series but still randomized controlled prospective studies are lacking in the literature.

CBZ, VPA, and LEV are the most commonly used and studied anti-seizure medications in childhood epilepsy, while the first two are old-generation drugs with well-documented side effects, LEV is among new-generation drugs with similar effects but with the least documented side effects related with auditory system.[5,16,17]

The aim of this prospective study was to detect any possible effects of the most commonly used antiepileptics carbamazepine, valproic acid, and levetirasetam on the auditory system by the extensive diagnostic evaluation.

MATERIALS AND METHODS

Participants and Treatment Protocol

This study included patients aged 6 to 18 years who were newly diagnosed with either focal or generalized seizures, in accordance with the 2017 International League Against Epilepsy (ILAE) classification system. Only individuals classified under idiopathic generalized epilepsy or self-limited focal epilepsy subgroups were considered for inclusion.[18] Eligible participants were those for whom initiation of monotherapy with valproic acid (VPA), carbamazepine (CBZ), or levetiracetam (LEV) was planned. None of the included patients had previously received any antiepileptic drug (AED) therapy.

Exclusion criteria comprised the presence of neurocognitive delay or autistic features that could impair the individual's ability to cooperate with audiological testing procedures.

Initial antiepileptic drug dosing was standardized as follows:

Valproic acid (VPA): 10 mg/kg/day divided into two doses

Carbamazepine (CBZ): 5 mg/kg/day divided into two doses

Levetiracetam (LEV): 10 mg/kg/day divided into two doses

Titration schedules were individualized, with the goal of achieving therapeutic target doses by the end of the first month. This approach was guided by established pediatric epilepsy management protocols.[19,20] At the time of the second audiological assessment, all participants were receiving effective therapeutic doses below the maximum allowable thresholds. No participants reported adverse effects attributable to the medications during the course of the study.

The maximum accepted daily doses were as follows:

VPA: up to 60 mg/kg/day, not exceeding 2.5 g/day
CBZ: up to 40 mg/kg/day, not exceeding 2 g/day
LEV: up to 60 mg/kg/day, not exceeding 3 g/day

Patients who were unable to tolerate the prescribed medication or who demonstrated poor adherence, resulting in failure to reach therapeutic levels, were excluded from final analysis.

Patients previously diagnosed with hearing loss attributable to other causes including craniofacial malformation, middle ear disease, craniofacial surgery, history of meningitidis, other ototoxic drug exposure and/or those using any other medication for any chronic disease were excluded. Patients with neuromotor retardation or who could not cooperate to hearing tests were also not included. This study included patients with normal hearing with pure tone audiometry thresholds better than 25 dB HL.

All the patients underwent a basal audiological evaluation before they started to use the prescribed medication and a second audiological evaluation including the same tests was performed to the patients after minimum 6 month of ongoing treatment with an average of 10 months.

Audiological evaluation

The hearing was evaluated by pure-tone audiometry, acoustic immitancemetry, otoacoustic emissions and auditory brainstem response (ABR).

All equipment used in the audiological evaluation was calibrated before the research according to the American National Standards Institute/Acoustical Society of America (ANSI/ASA S3.6-2010). Pure tone audiometry is a behavioral test that assesses air and bone conduction proccesses of the auditory system and detects the auditory thresholds.[21,22]

All participants were evaluated with an AC-40 clinical audiometer (Interacoustics A/S, Audiometer Alle 1 5500 Middelfart, Denmark) in a soundproof booth. All participants completed an audiological evaluation consisting of air and bone-conducted pure-tone thresholds (0.25 to 8 kilohertz -kHz- octave frequencies for air conduction; 0.5 to 4 kHz for bone conduction) for both ears, using the American Speech and Hearing Association (ASHA) guidelines.[23]

Acoustic immitancemetry assesses the integrity of the middle ear.[24] Acoustic immittance assessment was conducted using the AT 235(Middelfart, Denmark) model device. The tympanometric assessment was conducted using a 226 Hz probe tone. Acoustic reflexes were assessed ipsilaterally at 0.5 kHz, 1 kHz, and 2 kHz. Tympanometry measurement results were evaluated based on Jerger's tympanogram classification system, ensuring standardized interpretation of middle ear function.

Distortion product otoacoustic emission (DPOAE) is a diagnostic tool used to assess outer hair cell integrity and cochlear function.[25] When applied correctly in audiology settings, they provide a reliable diagnostic method for accurately detecting hearing loss.[26] The test also enables us to assess the extent to which cochlear function is affected by the ototoxicity.

Distortion product otoacoustic emission (DPOAE) was examined with the ILO292 USB-I Otoacoustic Emissions Instrument (Otodynamics Ltd., Beaconsfield Road Hatfield, AL10 8BB, U.K.). Simultaneous pure-tone signals were presented to each ear at 2 different frequencies (f1 and f2) at different intensities (l1 and l2; 65 and 55 dB sound pressure level-SPL), where f2>f1 with an f1:f2 ratio of 1.22 was used to measure DPOAE. The f1-f2 intermodulation distortion-product component was measured as a function of f2 frequency at 1/3-octave frequency intervals and was recorded in the form of DP grams. According to the characteristics of the device in the clinic participating in the study 1, 1.5, 2, 3, 4, 6, 8 and 10 kHz responses were obtained. DPOAE amplitudes were recorded at each frequency, DPOAE responses were considered valid when at least the lowest amplitude of 0 dB was reached and the signal/noise ratio (SNR) was >6 dB for 3 frequencies.[27]

The auditory brainstem response (ABR) is a neurophysiological signal generated by the brainstem following an auditory stimulus.[28] It reflects the synchronous electrical activity of neural structures along the auditory pathway. The ABR waveform typically consists of five to seven distinct peaks, labeled waves I through VII, each representing successive activation of specific, although sometimes overlapping, anatomical sites within the auditory system.[29]

ABR was recorded using the Interacoustics Eclipse EP 25 system (Middelfart, Denmark) for auditory evoked potentials. Diagnostic assessment was conducted at 70 dB nHL utilizing CE-Chirp® LS stimulus, delivered via insert earphones (3M EARTONE Insert Earphone 3A BR, Littleton, Colorado, USA), ensuring precise evaluation of auditory pathway integrity.

The recording electrodes were gold cup surface electrodes with impedance <5 kΩ. The active electrode was positioned centrally at Cz, following the 10–20 electrode system, while the reference and ground electrodes were placed at the ipsilateral and contralateral mastoid, respectively. The responses were band-pass filtered within a frequency range of 100-3000 Hz, spanning a 12 ms post-stimulus period.

Peak latencies for waves I, III, and V were identified, with their absolute and interpeak latencies subsequently analyzed for further response evaluation.

All these tests were performed on the patients for the purpose of comparison in case of abnormality to choose the optimal screening test with the highest diagnostic yield for audiological evaluation in patients using antiepileptic drugs.

The second hearing evaluation was performed before the first year of the treatment, on the patients who did not discontinue the antiepileptic drug for a minimum 6 months.

The patients were checked to use their medication in optimal treatment dose ranges appropriate for age and weight. Patients who were using the medications in dosages apart from recommended dose ranges or those with a history of ear infection after initiation of antiepileptic treatment were excluded. Patients whose antiepileptic dosages were changed frequently or a second antiepileptic drug was added to the treatment were excluded as well.

Local ethics committee approval was obtained for the study and it's been conducted according to the Helsinki Declaration.

Statistical analyses were performed using IBM SPSS software (version 22, USA), ensuring rigorous and standardized data processing. Statistical analysis student's t-paired test used for statistical analyses

RESULTS

Out of 30 patients whose initial audiological evaluation were performed 16 patients who fulfilled the inclusion criteria for the second audiological evaluation were included in the study (9 females, 56%) Used drug distribution was as follows: VPA (n=12), CBZ (n=2), LEV (n=2)

The mean patient age at the time of study was 11.5±3.7 (6-17) years. The mean time passed after initiation of treatment for the second evaluation was 10.1±1.2 (6-12) months.

Mean pure tone audiometry measurements of all patients were found to be within normal values and there was no statistically significant difference between the two measurement values of the patients, except for 4 kHz of the right ears. (Table 1a-1b).

Table 1a. Pure tone audiometry-right ear (pre/post treatment)

Side	Test time	Mean	SD	t	df	P*
Right ear						
SSO	Pre	7.87	3.519	1.047	15	0.311
	Post	6.81	3.936			
250 Hz	Pre	11.25	5.916	-0.187	15	0.855
	Post	11.56	6.511			
500 Hz	Pre	8.43	4.732	0.643	15	0.530
	Post	7.50	6.055			
1000 Hz	Pre	6.56	4.366	-0.222	15	0.827
	Post	6.87	6.551			
2000 Hz	Pre	6.87	4.366	1.159	15	0.264
	Post	5.31	6.551			
4000 Hz	Pre	3.43	3.520	-3.000	15	0.009*
	Post	7.18	5.764			
6000 Hz	Pre	10.00	8.56	1.065	15	0.304
	Post	8.12	7.719			
8000 Hz	Pre	7.50	9.309	-1.496	15	0.155
	Post	10.31	9.74			

*paired samples t-test.

Table 1b. Pure tone audiometry-left ear (pre/post treatment) (pre/post treatment)

Side	Test time	Mean	SD	t	df	P*
SSO	Pre	7.00	5.513	0.000	15	1.000
	Post	7.00	5.440			
250 Hz	Pre	9.66	8.653	-0.745	15	0.468
	Post	11.25	5.322			
500 Hz	Pre	7.66	6.289	-0.833	15	0.418
	Post	9.37	6.291			
1000 Hz	Pre	6.33	7.180	-0.421	15	0.680
	Post	6.87	6.551			
2000 Hz	Pre	7.33	5.120	1.585	15	0.134
	Post	5.31	5.617			
4000 Hz	Pre	4.66	5.617	-1.348	15	0.198
	Post	6.87	6.551			
6000 Hz	Pre	8.66	9.030	0.451	15	0.658
	Post	7.50	6.324			
8000 Hz	Pre	13.00	16.30	-0.805	15	0.4337
	Post	13.00	6.29			

*paired samples t-test.

Table 2a. ABR results-right ear (pre/post treatment)

Side	Component	Test time	Mean	SD	t	df	P*
Right ear	I. wave	Pre	1.58	0.269	-0.982	15	0.341
(70 dB nHL)		Post	2.36	3.109			
	III. wave	Pre	3.66	0.432	-0.200	15	0.844
		Post	3.69	0.634			
	V. wave	Pre	5.59	0.451	0.179	15	0.860
		Post	5.56	0.637			
	I-III	Pre	2.15	0.226	-1.305	15	0.211
		Post	2.43	0.752			
	III-V	Pre	1.97	0.637	0.893	15	0.386
		Post	1.84	0.169			
	I-V	Pre	3.88	0.686	-0.408	15	0.689
		Post	3.98	0.657			

*paired samples t-test.

Table 2b. ABR results-left ear (pre/post treatment)

Side	Component	Test time	Mean	SD	t	df	P*
Left ear	I.wave	Pre	1.53	0.139	-0.730	15	0.477
(70 dB nHL)		Post	1.57	0.141			
	III.wave	Pre	3.68	0.174	-0.435	15	0.670
		Post	3.71	0.253			
	V. wave	Pre	5.51	0.270	-0.250	15	0.860
		Post	5.53	0.280			
	I-III	Pre	2.17	0.227	-0.380	15	0.709
		Post	2.20	0.259			
	III-V	Pre	1.93	0.644	0.550	15	0.591
		Post	1.82	0.178			
	I-V	Pre	3.98	0.197	0.054	15	0.957
		Post	3.97	0.363			

*paired samples t-test.

Table 3a. Acoustic immitance testing-right ear (pre/post treatment)

Frequency		Test time	Mean	SD	t	df	P*
Right ear	500 Hz	Pre	89.64	5.35	-0.486	13	0.635
Acustic		Post	90.35	5.35			
immitence	1000 Hz	Pre	93.00	6.21	-0.435	14	0.670
threshold		Post	93.66	6.11			
(ipsilateral)	2000 Hz	Pre	94.28	7.031	-1.058	14	0.869
		Post	94.36	5.061			

*paired samples t-test.

ABR absolute peak latencies and interpeak latencies results of all patients were found to be in within normal ranges and no statistical difference was found between the mean values of the the basal and control measures($p>0.05$) (Table 2a-2b).

Acoustic immittance testing values of all of the patients were found in normal limits and control values also were not statistically different compared to the basal values. Type A tympanograms were obtained in all subjects (Table 3a-3b)

Table 3b. Acoustic immitance testing-left ear (pre/post treatment)

Frequency		Test time	Mean	SD	t	df	p
Left ear	500 Hz	Pre	91.42	6.629	-0.862	13	0.404
Acustic		Post	93.21	7.992			
immitence	1000 Hz	Pre	93.92	5.941	-0.168	13	0.869
threshold		Post	94.28	7.032			
(ipsilateral)	2000 Hz	Pre	94.28	7.032	-1.047	13	0.314
		Post	96.78	5.041			

*paired samples t-test.

Table 4a. Distortion product otoacoustic emission (DPOAE)-right ear (pre/post- treatment)

Side		Test time	Mean	SD	t	df	p
Right ear	1000	Pre	9.61	6.61	-0.734	12	0.477
		Post	10.91	2.68			
	1500Hz	Pre	14.24	5.28	-0.380	13	0.710
		Post	14.73	4.20			
	2000Hz	Pre	12.66	4.37	5.491	14	0.00**
		Post	5.33	5.95			
	3000 Hz	Pre	14.88	5.75	0.616	13	0.548
		Post	13.89	4.97			
	4000 Hz	Pre	16.85	7.43	0.065	12	0.949
		Post	16.78	6.17			
	6000 Hz	Pre	20.97	6.36	3.331	12	0.006**
		Post	16.31	4.84			

*paired samples t-test.

Table 4b. Distortion product otoacoustic emission (DPOAE)-left ear (pre/post- treatment)

Side	Frequency	Test time	Mean	SD	t	df	p
Left ear	1000 Hz	Pre	11.58	6.36	0.516	11	0.616
		Post	10.65	4.77			
	1500Hz	Pre	16.83	7.22	0.563	11	0.585
		Post	15.64	6.92			
	2000Hz	Pre	15.64	5.95	0.925	11	0.375
		Post	14.12	6.45			
	3000 Hz	Pre	15.46	6.78	0.027	11	0.979
		Post	15.40	7.25			
	4000 Hz	Pre	17.67	6.84	-0.593	11	0.565
		Post	18.58	6.96			
	6000 Hz	Pre	19.82	7.61	1.327	10	0.214
		Post	16.45	5.82			

*paired samples t-test.

Distortion product otoacoustic emission (DPOAE) measurements only showed a statistically significant difference between the two values for the right ear in 2000 Hz and 6000 Hz.

DISCUSSION

Although with a limited number of patients, this study is unique in nature, as all components of the auditory system have been evaluated with the latest up-to-date diagnos-

tic tests. In our study, no statistically significant difference was observed between the hearing assessment results obtained before therapy and those recorded within the first year after minimum six months of follow-up.

All the studies evaluating the audiologic side effects performed so far have had conflicting results and have been performed with limited tests that evaluated only specific parts of the auditory system. Case reports are the major source of information related to autotoxic side effects of antiepileptic drugs.[30]

Conflicting results have been reported by studies that performed ABR to evaluate the impact of ASM on the brainstem and peripheral auditory pathways.[31] Yuksel et al.[32] applied ABR to all patients who started to use carbamazepine or valproate before and after 13 months of treatment. They reported abnormalities in both earlier and late components of ABR results in patients using CBZ but not in any with valproate. They interpreted their findings as a possible interference effect of CBZ on synaptic transmission of neuronal membranes. Two more similar studies in the literature verified these findings regarding CBZ.[33,34] Our results are not consistent with these findings but, a relatively lower number of patients in our study might be a confounding factor.

Conducted studies with patients diagnosed with epilepsy and control groups of adults, report that individuals with epilepsy exhibited abnormal immittance findings and prolonged ABR component latencies compared to the control groups. Additionally, they observed that increasing CBZ dosage was associated with further latency prolongation in ABR components.[31]

In a study conducted by Koçak et al.,[26] no prolongation was observed in the absolute interwave latencies between waves I and V of ABR in epilepsy patients using CBZ, compared to the control group.[35]

The study that performed only pure tone air and bone thresholds to evaluate the effects of valproate on hearing did not find any abnormalities after 6 months of valproate use.[36] Our pure tone audiometry results are consistent with these results. Drug level monitoring was not performed in our study however all the patients were on therapeutic recommended dosages according to pediatric guidelines and none of them reported any side effects attributed to the used drug. Some studies have reported auditory side effects of antiepileptic drugs even in therapeutic drug doses.[12]

CBZ has been reported to cause tinnitus, changes in pitch perception, reversible sensorineural hearing disruption, and abnormalities in ABR even in therapeutic plasma drug levels. The proposed mechanism for these deleterious effects was through sodium channel blockage however, prospective experimental animal studies for elucidating the possible pathophysiology are still lacking.(9) Reversible sensorineural hearing loss confirmed by audiogram has been reported 6 days after intake of very high dose CBZ and the late effect has been attributed to delayed clearance of the active metabolite of the drug.[14]

LEV is one of the second-generation anti-seizure medication with presumed fewer side effects. The number of studies investigating the effect of LEV on hearing is very limited. One animal study has revealed a slight decrease in DPOAE levels post-treatment with LEV however these results were not statistically significant.[37] The main known mechanism of LEV is the inhibition of calcium channels which possibly affects cochlear neural response by affecting neurotransmitter release. This mechanism has been proposed as a benefit of this drug to prevent audiogenic seizures in therapeutic doses.[37] Application of extremely high doses (100mg/kg) of LEV has shown to decrease cochlear action potentials (CAP) in rats by a proposed mechanism of L-type calcium and potassium channel suppression in neurons of hippocampus in addition to glutamate release inhibition however studies in the literature evaluating effects of LEV on the auditory system are still lacking and more experimental and clinical studies are needed for more precise conclusions.[38]

It is known that there is a stepwise continuous development of human auditory system development beginning with the embryonic period and not completed till the late ages of childhood. The myelination process of the neuronal axons is reported to be prolonged till around age 12 as well as and ongoing maturation has been reported till early adulthood.[39] This knowledge brings to mind the question of how the antiepileptics might be affecting the incompletely developed auditory system in terms of multiple functional components like hearing, receptive language, sound discrimination, and speech capacity.

As studies about the effects of anti-seizure medications on the auditory system accumulate, cumulative knowledge about the side effects of the drugs will increase the clinician's awareness about drug selection, especially in childhood epilepsy syndrome where accompanying neurodevelopmental abnormalities are very common. This clinical approach will provide additional contribution in the prevention of additional losses related to speech and cognition.

Limitations of the study

This prospective study was designed with the aim of evaluating all aspects of the auditory system in patients who started antiepileptic drugs. Because of the nature of some audiology tests, only the patients who were able to perform all the tests could be included in the study, so patients under age 6 and those with poor cooperation were excluded. This limited the number of patients included in the study. Future studies including audiologic tests appropriate for age covering all aspects of the auditory system could add further valuable contribution to the literature.

Valproic acid (VPA) was the most commonly prescribed medication among patients eligible for inclusion within the planned study timeline (n=12; 75%). However, the limited number of patients receiving carbamazepine (CBZ) or

levetiracetam (LEV) precluded a meaningful comparative analysis of audiological outcomes across the three treatment groups.

Our study does not demonstrate the potential long-term effects of these medications on hearing; however, conducting future studies in this area would be beneficial.

Conclusion

Childhood epilepsy is a very common disease that can be controlled to a large extent with proper symptomatic treatment. Antiepileptic drugs still constitute the mainstay of the treatment strategies. Auditory side effects of antiepileptic drugs need to be taken into consideration at the process of drug initiation to prevent further possible neurodevelopmental regression. Further studies focusing on age-based auditory side effects of antiepileptics are needed to be held in the future.

Ethics Committee Approval

The study was approved by the Marmara University Medical Faculty Clinical Research Ethics Committee (Date: 04.01.2019, Decision No: 09.2019.111).

Informed Consent

Prospective study.

Peer-review

Externally peer-reviewed.

Authorship Contributions

Concept: G.B., N.O.A.; Design: G.B., N.O.A., N.H.; Supervision: D.T., O.U., A.C.; Fundings: G.O., N.O.A.; Materials: G.O., N.H., N.O.A.; Data collection &/or processing: G.O., O.U N.O.A.; Analysis and/or interpretation: D.T., A.C., O.U.; Literature search: D.T., A.C., O.U.; Writing: G.O., N.H., N.O.A.; Critical Review: D.T., O.U., A.C.

Conflict of Interest

None declared.

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Okul Çağındaki Çocuklarda En Sık Kullanılan Antiepileptik İlaçlardan Valproat (VPA), Karbamazepin (KBZ) ve Levetirasetam (LEV)'ın İşitsel Değerlendirmesi: Küçük Bir Kohortta Geniş Kapsamlı İşitsel Test Tasarımı ile Tek Merkezli Prospektif Çalışma

Amaç: Bu çalışmada, yaygın olarak kullanılan antiepileptik ilaçların (AEİ)—valproat (VPA), karbamazepin (KBZ) ve levetirasetamın (LEV)—yeni tanı konmuş epilepsili okul çağındaki çocukların işitme fonksiyonları üzerindeki etkilerinin değerlendirilmesi amaçlanmıştır.

Gereç ve Yöntem: 2017 ILAE kriterlerine göre idiopatik jeneralize veya kendi kendini sınırlayan fokal epilepsi tanısı almış, tedavi almamış 16 çocuk (ortalama yaş 11.5±3.7 yıl) üzerinde prospektif bir çalışma yürütüldü. Hastalara VPA (n=12), CBZ (n=2) veya LEV (n=2) tedavisi başlandı ve ilaç dozları bir ay içinde terapötik düzeylere çıkarıldı. İşitsel değerlendirmeler; tedavi öncesi ve ortalama 10 aylık takip sonrasında, saf ses odyometrisi (0.25–8 kHz), timpanometri ve akustik refleksler, distorsiyon ürünü otoakustik emisyonlar (DPOAE) ve işitsel beyin sapı yanıtı (ABR) testleri ile gerçekleştirildi. Başlangıç ve takip sonuçları eşleştirilmiş t-testi ile karşılaştırıldı (anlamlılık düzeyi $p<0.05$).

Bulgular: Başlangıçta tüm işitme eşikleri ≤25 dB HL idi. Tedavi sonrası işitme eşikleri genel olarak değişmedi, ancak sağ kulakta 4 kHz frekansında hafif bir artış gözlendi (+3.8 dB HL, $p=0.009$). ABR latansları ve pikler arası süreler stabil kaldı. Timpanometri ve akustik reflekslerde değişiklik gözlenmedi. DPOAE amplitüdlerinde sağ kulakta 2 kHz (−7.3 dB, $p=0.001$) ve 6 kHz (−4.7 dB, $p=0.006$) frekanslarında azalma saptandı. Sol kulak ölçümleri ise sabit kaldı. Hiçbir hastada işitsel semptom veya advers etki bildirilmedi.

Sonuç: Yaklaşık 10 aylık monoterapi ile uygulanan VPA, CBZ veya LEV tedavisi, çocuklarda klinik olarak anlamlı bir işitme bozukluğuna yol açmamıştır. Bununla birlikte, kohlear emisyonlarda frekansa özgü küçük düşüşler gözlemlenmiştir. Bu ön bulguların doğrulanması için daha geniş örneklemli, ilaçlara özgü çalışmalar gerekmektedir.

Anahtar Sözcükler: Anti-nöbet ilaçlar; distorsiyon ürünü otoakustik emisyonlar; işitsel beyin sapı yanıtı; ototoksisite; pediatrik epilepsi; saf ses odyometrisi.