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Retinal Pigment Epithelium Screening of Patients Treated with Anti-Epileptic Medications using Electrooculography

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Abstract

Aim: This study uses electrooculography (EOG) to identify the probable side effects of anti-epileptic medications on the retina. A seizure is a severe involuntary shrinkage state of the skeletal muscle and occurs spasmodically. There are certain anti-epileptic medications such as carbamazepine and valproic acid, which may affect retinal layers, mainly retinal pigment epithelium (RPE) of the visual system.

Methods: Twenty patients (10 males and 10 females) in the age range of 15-30 years old participated in this study (case group) and were treated with anti-epileptic medications. EOG was recorded in the population and the Arden Index (AI) of EOG in the patient group was compared to that of the control group with healthy retinas.

Results: We observed no statistical difference in the sex and age factors, while the variation for the best corrected visual acuity was significant. There was also a significant difference in the AI between the case and control groups ($p < 0.001$).

Conclusion: Anti-epileptic drugs may affect a certain retinal layer; RPE, which can be diagnosed by the AI in the EOG test.

Keywords: Seizure; Anti-epileptic medications; Electrooculography.

Introuduction

A seizure is a burst of uncontrolled electrical activity between brain cells that causes temporary abnormalities in muscle tone or behaviors, sensation, or status of awareness. On the other hand, anti-epileptic medications are known to have some side effects, especially on the visual system.

Visual electrophysiology is a series of tests that deals with different physiological and pathological conditions of the visual system. Electrooculogram (EOG), electroretinogram (ERG), and visual evoked potential (VEP) are the routine tests used for this purpose.

In this regard, Sanaie S et al (2014) adapted the EOG technique to study the effect of toxoplasmosis on the visual system, particularly the retina. They reported a significant difference between the Arden Index (AI) of the patient and control groups, indicating pathological changes in the retina, especially the retinal pigment epithelium (RPE) [1].

Sarzaeim F et al (2022) [2] also investigated the effect of hand-arm vibration on the retina of road drilling machinery operators. They found that the hand-arm vibration produced by road drilling machinery could affect the

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operator's retina. The range of this effect can be measured by ERG. In another research by the same group, flash VEP was measured in 10 patients with head trauma, where VEP pathological changes were observed, showing that visual pathway disturbances were produced by head trauma. These disturbances could be diagnosed by VEP [3]. There is sufficient evidence that verifies the usefulness of these techniques [4-25].

Furthermore, visual electrophysiology can also be applied to study the side effects of different medications on the visual system. Extensive research on the potentially toxic effects of amiodarone on various parts of the visual system like the retina and visual pathway corroborated the effect of consuming amiodarone. The range of this effect can be diagnosed by ERG and VEP [26, 27]. Accordingly, Allahdady F. et al (2016) studied the toxic effect of hydroxychloroquine (HCQ) on the retina of arthritis rheumatoid patients using the EOG test. They concluded that EOG is a suitable technique to evaluate retinal damage caused by HCQ [28].

Likewise, anti-epileptic medications such as carbamazepine and valproic acid can affect the visual system. In this regard, Sarzaeim F. et al (2022) investigated the toxic effect of anti-epilepsy medication on the visual pathway among 20 patients. The authors revealed that the patients might experience visual pathway disturbances which can be diagnosed by the VEP test [29]. Finally, using ERG, Abdolalizadeh S. et al (2022) studied the retina of patients treated with anti-seizure drugs. They showed that anti-seizure medications could affect the retinal layers. These drugs mainly affect bipolar and muller cells, which can be detected by reducing the b-wave amplitude of the ERG [30].

Considering the last two reports above, the current research was designed to use EOG to investigate the potentially toxic effects of anti-epileptic medication on the RPE of patients treated with anti-epileptic drugs.

Patients and Methods

In this study, 20 patients (40 eyes) between 15 and 30 years old suffering from seizures were assigned to the case group. In order to control their disease, they received either monotherapy or polypharmacy for over a year. The patients were then evaluated for visual acuity and brain magnetic resonance imaging (MRI). The case group had the best corrected visual acuity (BCVA) ranging from 7/10 to 10/10, and normal brain MRI reports. Further, EOG was performed on the case group and the control group which consisted of 20 subjects of the same age and sex with healthy retinas. To this end, the eye was pre-dark-adapted for 15 minutes. Then the subject was asked to rotate his/her eyes simultaneously between the three bulbs fixed in front of his/her eyes for 10 minutes and the corresponding potential changes were screened. The aim of this experiment was to measure light adaptation potential (LAP). Then the subject was dark-adapted for 10 minutes. The same procedure was followed to measure the dark adaptation potential (DAP). In the end, the LAP to DAP ratio which is called AI was calculated for both case and control groups, and the results were compared to extract differences between them.

Results

Demographic results in the case and control groups are demonstrated below (Table 1). There is no statistically significant difference between the two groups in age ($p = 0.84$) and sex variables whereas the difference in BCVA is significant ($p < 0.001$).

The AI in the case group was 1.61 ± 0.2 whereas it was 2.13 ± 0.33 in the control group. The difference between the two groups is statistically significant as far as AI is concerned ($p < 0.00l$).

Discussion

EOG was performed on patients taking anti-epileptic medications for seizure treatment. It was found that, compared to the control group, AI was reduced in the case group.

EOG originated from RPE [1,27] and therefore this layer of the retina gets affected in epileptic patients consuming anti-epileptic medications. The result of the present work may be supported by the findings of the following studies.

Jan Remi et al (2010) performed a prospective study on the effect of carbamazepine on eye movements and posture

Table 1: The demographic findings in the case and control groups

Variable		Groups (Mean ± SD)		*p*-value*
		Control	Case	
Age		20.40 ± 4.78	19.9 ± 4.38	0.84*
	Male	10 (50%)	10 (50%)	1**
Sex				
	Female	10 (50%)	10 (50%)	
Visual Acuity (LogMar)		0 ± 0	0.031 ± 0.036	0.000*
* Based on Mann-Whitney U test				
* Based on Chi-squared test				

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control. For this purpose, EOG was applied to 12 healthy carbamazepine-treated volunteers. The authors showed toxic effects of carbamazepine which resulted in impaired saccadic eye movements. In this respect, EOG serves as an objective mean to measure anti-epileptic central nervous system (CNS) side effects and could be used in the early stage of drug development [31].

In another research, Comaish I F et al (2002) worked on the effect of vigabatrin in patients suffering from epilepsy, where 14 epileptic patients treated with vigabatrin were examined by EOG. It was observed that AI was reduced in vigabatrin-treated subjects. Moreover, they found that the AI may recover after cessation of the drug, while the visual loss may persist [32].

Conclusion

Anti-epileptic medications affect the retina layers. They can particularly affect RPE, which can be detected by EOG.

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