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Study of Cognitive and Behavioral Impacts of Idiopathic Epilepsy and Antiepileptic Drugs (AEDs) in Children and Adolescents

Mohamed Ibrahim Aboeisa [a*], Mohammad Abdel Hakeem Seleem [b], Tarek Mohamed El Gohary [a] and Azza Kamal Al Shahawy [a]

[a] Pediatrics Department, Faculty of Medicine, Tanta University, Egypt.
[b] Neuropsychiatric Department, Faculty of Medicine, Tanta University, Egypt.

Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Background: Epilepsy is a common neurological condition that can have a detrimental impact on social, emotional, and cognitive functioning. Psychiatric and cognitive problems in children with epilepsy and antiepileptic drugs can affect quality of life. Long-term follow-up studies reveal that epilepsy that develops in childhood is more common than epilepsy that develops later in life. Has a marked impact on adult life even when the epilepsy is not complicated by intellectual disability or other neurological impairments. The aim of this study was to study cognitive and behavioral impacts of idiopathic epilepsy and antiepileptic drugs in children and adolescents compared to normal ones.

Methods: This prospective, case control study was conducted on 60 children or adolescents suffering from idiopathic epilepsy aged 6-16 years. Children were classified into four equal groups and were examined after 6 months from diagnosis: Group A subjected to valproic acid at a dose of 10-60 mg/kg/day, group B subjected to Carbamazepine at a dose of 10-30 mg/kg/day, group C subjected to levetiracetam at a dose of 10-60 mg/kg/day and group D subjected to Oxcarbazepine at a dose of 20-30 mg/kg/day. Thirty healthy children or adolescents of matched age and sex served as a control group who attended Pediatric General Outpatient Clinic of Tanta University Hospitals. The following was done to all of the patients: full history taking, complete physical

**Corresponding author: E-mail: Mohamed.aboessa@med.tanta.edu.eg;*

examination, routine laboratory investigations, electroencephalography, brain magnetic resonance imaging, specific tests for behavior and executive functions including the Child Behavior Checklist – school age, Stanford-Binet Intelligence Scales (fifth version), Wisconsin Card Sorting Test and Continuous Performance Test. Thirty healthy children or adolescents of matched age and sex served as a control group.

Results: Children with epilepsy who were treated with AEDs showed higher behavioral problems scales, lower mean IQ and lower executive functions as compared to controls. LEV and VPA had a more negative effect on behavior than CBZ and OXC while VPA and CBZ had a more negative effect on mean IQ and executive functions than LEV and OXC.

Conclusion: Antiepileptic drugs (AEDs) may be one of the causes of epilepsy-related cognitive and behavioral issues in children.

Keywords: Cognitive and behavioral impacts; idiopathic epilepsy; antiepileptic drugs; children and adolescents.

1. INTRODUCTION

Epilepsy is a prevalent chronic neurological illness that affects physical, social, and emotional function in children and adolescents. It's defined as a brain disorder marked by an enduring proclivity for epileptic seizures, as well as the neurobiologic, cognitive, psychological, and social repercussions of this illness [1]. Multiple seizures during a 24-hour period are included provided the child returns to baseline consciousness between episodes, according to the International League against Epilepsy (ILAE) definition [2].

The majority of these youngsters never have a recurrence. A seizure, on the other hand, could be the first sign of a more serious medical issue or the onset of epilepsy. Epilepsy has traditionally been described as a condition in which a kid experiences two or more seizures without a proximal cause (unprovoked seizures). The ILAE also accepted these two alternative requirements in 2013: 1) one unprovoked or reflex seizure with a 60% chance of recurrence in the next 10 years; or 2) a diagnosis of an epilepsy syndrome [3].

A quarter of all childhood epilepsy is linked to recognizable structural brain lesions, suspected early insults as demonstrated by cerebral palsy, or other metabolic-genetic encephalopathies. The most common structural abnormalities seen in children with epilepsy include prenatal and perinatal hypoxic-ischemic insults, stroke, and cortical deformities [4].

Relationships between cognitive status and a range of clinical epilepsy characteristics, such as aetiology, age of onset, seizure type and severity, duration, antiepileptic drugs, and other factors, have been studied for a long time [5].

Children with epilepsy are more prone than the general population to have mental health and developmental co-morbidities. Several studies have found that children with epilepsy have a greater prevalence of emotional disorders, attention deficit hyperactivity disorder (ADHD), and autistic spectrum disorders [6].

Long-term follow-up studies show that childhood-onset epilepsy has a marked impact on adult life even when the epilepsy is not complicated by intellectual disability or other neurological impairments [7]. Attention deficit hyperactivity disorder is one of the most prevalent epileptic comorbidities in children. It is commonly recorded in roughly 30% of children with epilepsy, compared to 3-6% of children without epilepsy [8]. The traditional medical goal in the management of epilepsy has been to achieve seizure control with minimum or no adverse drug effects, ignoring the necessity of monitoring QOL [9].

The aim of this study was to study cognitive and behavioral impacts of idiopathic epilepsy and antiepileptic drugs in children and adolescents compared to normal ones.

2. SUBJECTS AND METHODS

This prospective, case control study was conducted on 60 children or adolescents suffering from idiopathic epilepsy aged 6-16 years who attended Pediatric Neuropsychiatry Outpatient Clinic of Tanta University Hospitals after obtaining the approval of the Ethics Committee. The study period extended from April 2018 till October 2020.

Exclusion criteria were children and adolescents with 2 ry epilepsy, epileptic syndromes, chromosomal anomalies, any other chronic illness e.g. cardiac, pulmonary, renal, endocrinological, chronic malnutrition, etc. or who was subjected on drug intake other than antiepileptic medications for at least 2 months before starting antiepileptic drug.

2.1 Randomization

Sixty children or adolescents suffering from idiopathic epilepsy that was confirmed by normal examination of the physical and neurological systems with normal MRI of the brain. Children were divided into four subgroups and examined after 6 months; **Group A** subjected to valproic acid at a dose of 10-60 mg/kg/day **Group B** subjected to Carbamazepine at a dose of 10-30 mg/kg/day. **Group C** subjected to levetiracetam at a dose of 10-60 mg/kg/day **Group D** subjected to Oxcarbazepine at a dose of 20-30 mg/kg/day. Thirty healthy children or adolescents of matched age and sex served as a control group who attended Pediatric General Outpatient Clinic of Tanta University Hospitals.

2.2 Preoperative Assessment and Preparation

Routine preoperative assessment was done to all patients the following after an informed consent from parents; including full history taking, complete physical examination, and routine laboratory investigations, electrocardiogram (ECG), and MRI. Drug serum level of (Carbamazepine, Sodium valproate, Oxcarbazepine, and Levetiracetam) was measured one hour before the dose using high-performance liquid chromatography (HPLC) method for the used antiepileptic drugs (if available). Also, some specific investigations for cognition and behavior were done for patients and controls; including Child Behavior Checklist – school age, Stanford-Binet Intelligence Scales (fifth version), Wisconsin Card Sorting Test and Continuous Performance Test.

2.3 Statistical Analysis

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp). Qualitative data were described using number and percent. The Kolmogorov-Smirnov test was used to verify the normality of distribution. Quantitative data were described using range (minimum and maximum), mean, standard deviation, median and interquartile range (IQR). When comparing more than two groups, analysis of variance (ANOVA) with a post-hoc test is used for parametric data, while fisher's Exact or Monte Carlo correction for chi-square when more than 20% of the cells have expected count less than 5. Additionally, paired t- test for normally distributed quantitative variables, to compare between two periods and marginal homogeneity test to analyze the significance between the different stage. In terms of qualitative factors, the chi square test was performed to compare the groups. In parametric data, the Student t-test was employed to compare two groups in terms of quantitative variables. Statistical significance was defined as a P value < 0.05.

3. RESULTS

In this study, about 60 children or adolescents suffering from idiopathic epilepsy aged 6-16 with thirty healthy children or adolescents of matched age and sex served as a control group was included. In terms of age and gender, there was no statistically significant difference between the groups tested [Table 1].

There were insignificant differences regarding Clinical characteristics of studied epileptic patients and routine laboratory investigations among epileptic subgroups and control group.

Table 1. Age and sex of patients and control groups

		VPA (n = 15)	CBZ (n = 15)	LEV (n = 15)	OXC (n = 15)	Control (n = 15)	Test of Sig.	p
Age (years)		9.37 ± 2.24	9.47 ± 1.88	9.57 ± 2.41	9.30 ± 2.0	9.53 ± 2.20	F= 0.041	0.997
Sex	Male	7 (46.7%)	7 (46.7%)	8(53.3%)	7(46.7%)	8(53.3%)	χ^2= 0.320	0.988
	Female	8 (53.3%)	8 (53.3%)	7(46.7%)	8(53.3%)	7(46.7%)		

VPA: Valproate treated group, CBZ: Carbamazepine treated group, LEV: Levetiracetam treated group, OXC: Oxcarbazepine treated group, ⁄2: Chi square test, F: F for ANOVA test, IQR: Inter quartile range

There was no statistically significant difference among epileptic patients before treatment compared with control group as regards all CBCL scales. The mean of aggressive, overall difficulties, withdrawn / depressed, social problems, attention problems, aggressive, internalising, externalising, whole problems anxiety disorders, somatic disorders, ADHD and conduct disorders scales were statistically significantly higher in epileptic patients after treatment compared with before treatment and in epileptic patients after treatment compared with control group. However, the mean of social and total competence scales was statistically significantly lower in epileptic patients after treatment compared with before treatment and control group [Fig. 1].

The mean of ADHD scales was statistically significantly higher in VPA treated group after treatment compared with control groups. The mean of total competence scale was statistically significantly lower in both VPA and CBZ treated groups after treatment compared with each of control group and compared with LEV and OXC treated groups after treatment while the mean of anxiety, somatic, conduct disorders and ADHD scales were statistically significantly higher in LEV treated group after treatment compared with control group. The mean of anxiety and conduct disorders scales were statistically significantly higher in LEV treated group compared with CBZ and OXC treated groups after treatment. The mean of ADHD scale was statistically significantly higher in each of VPA and LEV treated groups compared with each of CBZ and OXC treated groups after treatment [Fig. 2].

The mean of social, attention, total problems scales were statistically significantly higher in VPA treated group after treatment compared with control groups. The mean of social, attention and total problems scales were statistically significantly higher in CBZ treated group after treatment compared with control group. The mean of social problems, thought problems, aggressive, externalizing and total problems scales were statistically significantly higher in LEV treated group after treatment compared with control group. The mean of social problems scale was statistically significantly higher in LEV treated group compared with each of VPA and OXC treated groups after treatment. The mean of thought problems, aggressive, disorders scales were statistically significantly higher in LEV treated group compared with CBZ and OXC treated groups after treatment. The mean of attention problems scale was statistically significantly higher in CBZ then VPA treated groups compared with each of OXC and LEV treated groups after treatment. The mean of externalizing problems scale was statistically significantly higher in each LEV treated group compared with VPA and CBZ treated groups after treatment [Table 3].

The mean of attention and total problems scales were statistically significantly higher in VPA treated group after treatment compared with before treatment. The mean of thought, attention and total problems scales were statistically significantly higher in CBZ treated group after treatment compared with before treatment. The mean of social, thought, externalizing, total problems, aggressive Behaviour scales were statistically significantly higher in LEV treated group after treatment compared with before treatment [Fig. 3].

The mean of anxiety disorders and ADHD scales were statistically significantly higher in VPA treated group after treatment compared with before treatment. The mean of anxiety disorders, somatic disorders, ADHD and conduct scales were statistically significantly higher in LEV treated group after treatment compared with before treatment [Fig. 4].

There was no statistically significant difference between epileptic patients before treatment and control group as regards mean IQ, mean percentage of perservative errors, mean non perservative error, mean omission errors, mean commission error. The mean percentage of preservative errors, non-preservative errors, omission errors, and commission errors were statistically significantly higher in epileptic patients after treatment compared with control group and higher in epileptic patients after treatment compared with before treatment. While the mean IQ was statistically significantly lower in epileptic patients after treatment compared with control group and lower in epileptic patients after treatment compared with before treatment [Table 4].

The mean IQ was statistically significantly lower in each of VPA and CBZ treated groups after treatment compared with control group and in each of VPA and CBZ treated groups after treatment compared with before treatment. The mean IQ was statistically significantly lower in each of VPA and CBZ treated groups after treatment compared with each of LEV and OXC after treatment. The mean percentage of

perservative errors was statistically significantly higher in each of VPA and CBZ treated groups after treatment compared with before treatment and control group and higher in each of VPA and CBZ treated groups after treatment compared with each of LEV and OXC after treatment. The mean percentage of non-preservative errors was statistically significantly higher in each of VPA and CBZ treated groups after treatment compared with before treatment and control group and higher in each of VPA and CBZ treated groups after treatment compared with each of LEV and OXC after treatment. The mean of omission errors was statistically significantly higher in each of VPA and CBZ treated groups after treatment compared with before treatment and control group and higher in each of VPA and CBZ treated groups after treatment compared with each of LEV and OXC after treatment. The mean of commission errors was statistically significantly higher in each of VPA and CBZ treated groups after treatment compared with before treatment and control group and higher in each of VPA and CBZ treated [Table 5].

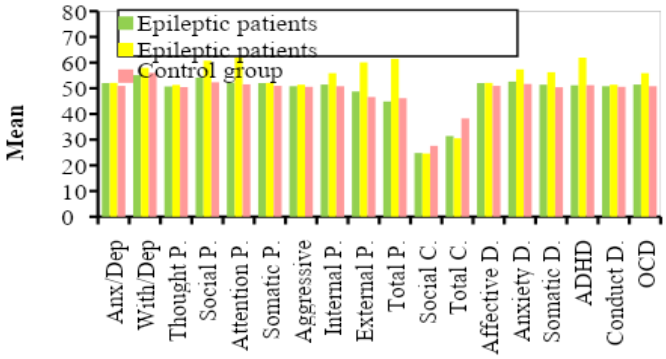

Fig. 1. Comparison of the mean of Child Behaviour Checklist scales among epileptic patients before and after treatment and control group

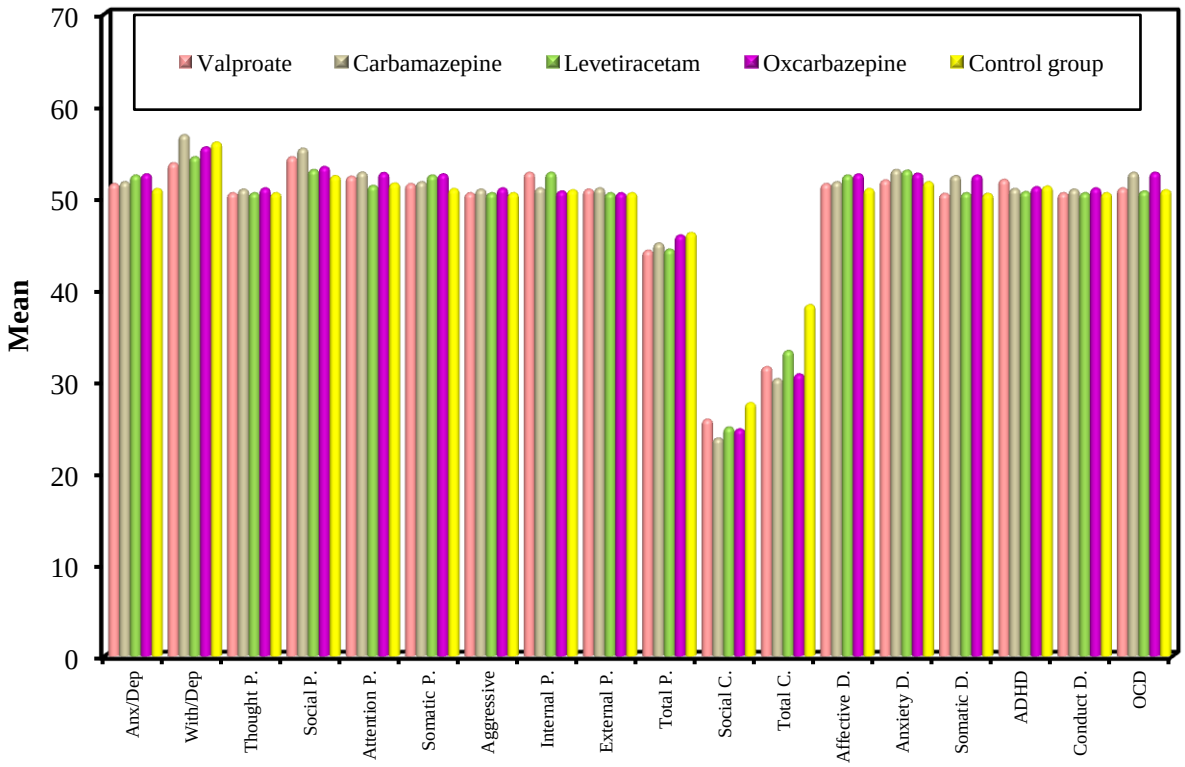

Fig. 2. Comparison of the mean of Child Behavior Checklist scales among epileptic subgroups after treatment and control group

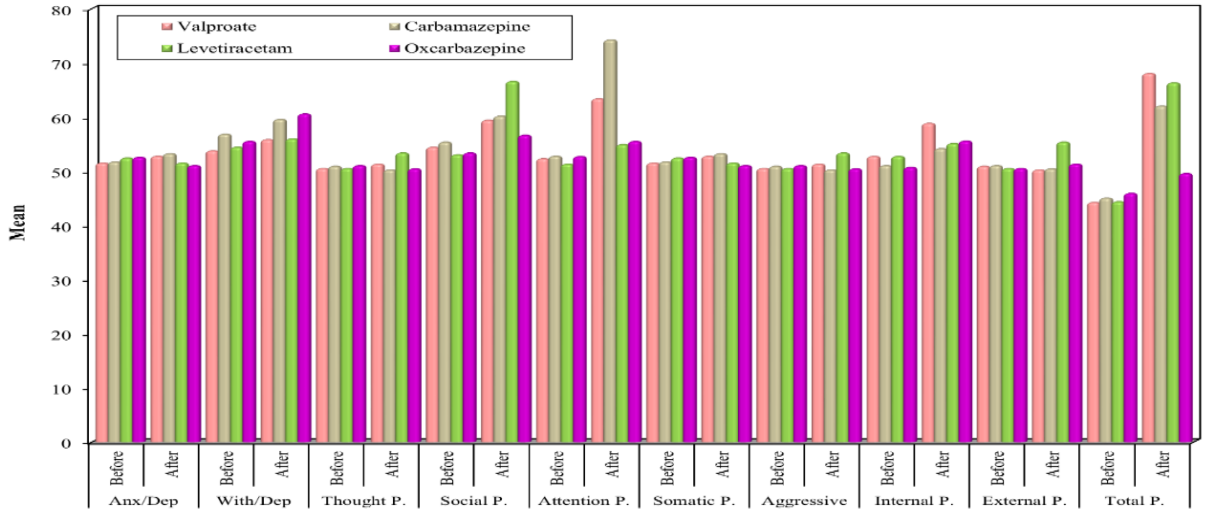

Fig. 3. Comparison of the mean of Child Behaviour Checklist scales among epileptic subgroups before and after treatment

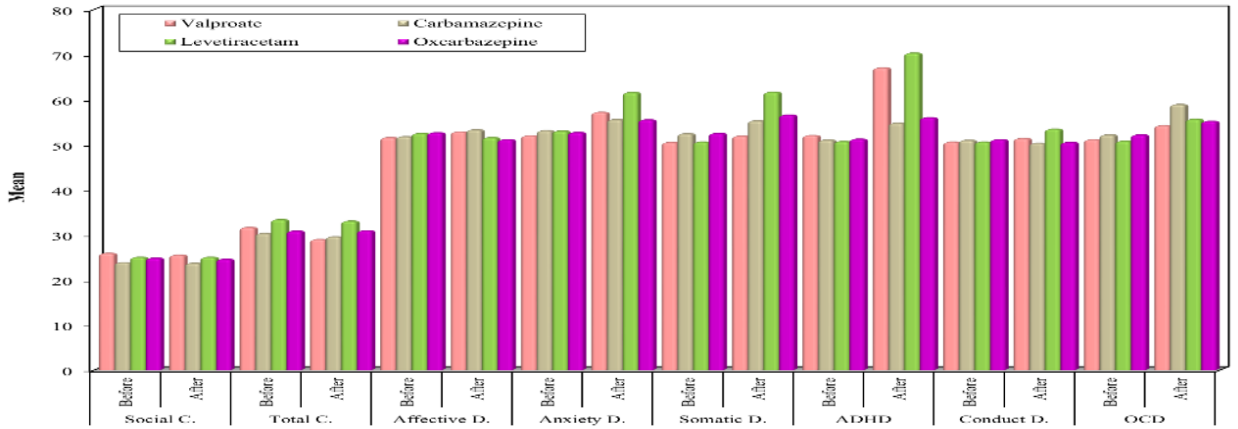

Fig. 4. Comparison of the mean of Child Behavior Checklist scales among epileptic subgroups before and after treatment

Table 2. Clinical characteristics of studied epileptic patients and routine laboratory investigations among epileptic subgroups and control group

		VPA (n = 15)	CBZ (n = 15)	LEV (n = 15)	OXC (n = 15)	Test of Sig.	p
Family history of epilepsy	Negative	12 (80.0%)	13(86.7%)	11(73.3%)	11(73.3%)	χ2=	MCp=
	Positive	3(20.0%)	2(13.3%)	4((26.7%%)	4(26.7%)	1.192	0.905
Age of onset of epilepsy (years)		9.53 ± 2.18	9.37 ± 2.04	9.30 ± 2.05	9.40 ± 2.32	F=	0.993
						0.031	
Types of seizures	Generalized	15 (100.0%)	0(0.0%)	9(60%)	0(0.0%)		
	Focal	0(0.0%)	15 (100.0%)	6(40%)	15 (100.0%)		
EEG changes N (%)	Abnormal	7(46.7%)	6(40.0%)	7(46.7%)	6(40.0%)	χ2=	MCp=
	Normal	8(53.3%)	9 (60.0 %)	8(53.3%)	9 (60.0 %)	0.382	1.000
Clinical data	VPA (n = 15)	CBZ (n = 15)	LEV (n = 15)	OXC (n = 15)	Control group (n = 15)	F	p
Hemoglobin (g/dL)	12.45 ± 1.05	12.45 ± 1.05	12.54 ± 0.77	12.31 ± 0.86	12.39 ± 0.78	0.134	0.969
Platelets (×109/L)	366.33 ± 56.74	347.67 ± 50.42	354.33 ± 49.13	361.0 ± 41.67	349.0 ± 44.85	0.397	0.810
WBCs (×109/L)	6.92 ± 1.54	6.89 ± 1.59	6.75 ± 1.54	6.91 ± 1.59	7.17 ± 1.69	0.138	0.968
ALT (IU/L)	22.93 ± 4.37	22.73 ± 6.32	22.07 ± 3.83	22.33 ± 4.97	20.33 ± 6.52	0.569	0.686
AST (IU/L)	20.93 ± 4.37	20.73 ± 6.32	21.57 ± 3.83	24.33 ± 4.97	19.33 ± 6.52	0.578	0.686
Blood urea(mg/dL)	21.93 ± 5.06	21.33 ± 5.46	21.73 ± 4.10	21.67 ± 4.53	20.27 ± 6.39	0.246	0.911
Serum Creatinine (mg/dL)	0.60 ± 0.28	0.64 ± 0.31	0.64 ± 0.20	0.65 ± 0.29	0.59 ± 0.25	0.160	0.958

χ2: Chi square test, MC: Monte Carlo, F: F for ANOVA test, IQR: Inter quartile range, p: p value for comparing between the studied groups, VPA: Valproate treated group, CBZ: Carbamazepine treated group, LEV: Levetiracetam treated group, OXC: Oxcarbazepine treated group, WBCs: White Blood Cells, ALT: Alanine aminotransferase. AST: Aspartate aminotransferase

Table 3. Comparison of the mean of Child Behaviour Checklist scales among epileptic subgroups before and after treatment

	VPA (n=15)	CBZ (n =15)	LEV (n = 15)	OXC (n=15)	Control group (n = 15)	F	P
Anxious/Depressed	52.73 ± 2.74	53.20 ± 4.54	51.47 ± 1.55	51.0 ± 1.36	50.93 ± 1.443	2.348	0.063
Withdrawn/Depressed	55.80 ± 5.14	59.53 ± 9.73	55.93 ± 3.71	60.53 ± 7.20	56.0 ± 3.84	1.946	0.112
Thought Problems	51.27 ± 1.75	50.20 ± 0.41	53.33 ± 5.12	50.40 ± 0.63	50.47 ± 0.74	4.135*	0.005*
Social Problems	59.73 ± 7.06	60.13 ± 8.87	66.53 ± 6.47	56.60 ± 5.83	52.33 ± 2.82	9.608*	<0.001*
Attention Problems	63.33 ± 4.48	74.20 ± 5.52	54.87 ± 6.59	55.47 ± 4.75	51.53 ± 1.60	52.166*	<0.001*
Somatic Problems	52.73 ± 2.74	53.20 ± 4.54	51.47 ± 1.55	51.0 ± 1.36	50.93 ± 1.44	2.348	0.063
Aggressive	51.27 ± 1.75	50.20 ± 0.41	53.33 ± 5.12	50.40 ± 0.63	50.47 ± 0.74	4.135*	0.005*
Internalizing Problems	58.80 ± 11.21	54.13 ± 6.38	55.07 ± 7.85	55.53 ± 8.58	50.80 ± 1.01	2.047	0.097
Externalizing Problems	50.20 ± 0.41	50.40 ± 0.63	53.33 ± 5.12	51.27 ± 1.75	50.47 ± 0.74	4.135*	0.005*
Total Problems	68.0 ± 2.04	62.0 ± 4.31	66.27 ± 2.91	49.53 ± 7.87	46.13 ± 3.50	70.424*	<0.001*

*t: Paired t-test. F: F for ANOVA test, pairwise comparison bet. each 2 groups were done using Post Hoc Test (Tukey). p: p value for comparing between the studied groups p0: p value for comparing between before treatment and after treatment in another group. *: Statistically significant at p < 0.05. VPA: Valproate treated group, CBZ: Carbamazepine treated group, LEV: Levetiracetam treated group, OXC: Oxcarbazepine treated group*

Table 4. Comparison of the mean IQ among epileptic subgroups before and after treatment and control group, the mean percentage of perservative, non- perservative, ommession and coomession errors in Wisconsin Card Sorting Test among epileptic patients before and after treatment and control group

	Epileptic patients (n = 60)		Control group (n = 15)	p1	p0	p2
	Before treatment	After treatment				
Mean IQ	93.97 ± 4.56	89.37 ± 4.61	95.33 ± 4.73	<0.001*	0.306	<0.001*
Perservative Errors %	9.76 ± 1.52	12.26 ± 2.61	9.09 ± 0.88	<0.001	0.106	<0.001*
Non-perservative Errors %	1.31 ± 1.38	2.81 ± 1.79	1.19 ± 1.31	0.002*	0.775	<0.001*
Omission errors	2.90 ± 1.12	4.38 ± 1.47	2.73 ± 1.22	<0.001*	0.613	<0.001*
Commission Errors	5.23 ± 1.18	6.72 ± 2.15	5.11 ± 1.16	<0.001*	0.061	0.004*

*p_0: p value for comparing between before treatment and Control group. p1: p value for comparing After and Control group. p2: value for comparing Before treatment and After treatment in Epileptic patients. *: Statistically significant at p < 0.05*

Table 5. Comparison of the mean IQ, preservative, non- preservative, omission, and commission errors among epileptic subgroups before and after treatment and control group

		VPA (n = 15)	CBZ (n = 15)	LEV (n = 15)	OXC (n = 15)	Control group (n = 15)	F	p
Mean IQ	Before treatment	94.73 ± 4.37	94.07 ± 4.45	92.87 ± 4.79	94.20 ± 4.89	95.33 ± 4.73	0.582	0.677
	After treatment	86.80 ± 2.70	85.0 ± 2.65	92.73 ± 3.53	92.93 ± 3.06	95.33 ± 4.73	25.043*	<0.001*
Perservatve errors %	Before treatment	9.63 ± 1.92	9.73 ± 1.20	9.95 ± 1.51	9.74 ± 1.51	9.09 ± 0.88	0.746	0.564
	After treatment	14.05 ± 2.01	14.03 ± 1.90	10.29 ± 1.58	10.65 ± 2.20	9.09 ± 0.88	24.787*	<0.001*
Non-perservative Errors %	Before treatment	1.41 ± 1.37	1.31 ± 1.42	1.31 ± 1.42	1.20 ± 1.46	1.19 ± 1.31	0.064	0.992
	After treatment	3.41 ± 1.57	3.73 ± 1.81	2.41 ± 1.80	1.69 ± 1.31	1.19 ± 1.31	7.140*	<0.001*
Omission errors	Before treatment	2.80 ± 1.21	2.87 ± 1.36	2.93 ± 1.10	3.0 ± 0.85	2.73 ± 1.22	0.124	0.973
	After treatment	2.90 ± 1.12	2.80 ± 1.21	2.87 ± 1.36	2.93 ± 1.10	3.0 ± 0.85	2.73 ± 1.22	<0.001*
Commission Errors	Before treatment	5.80 ± 1.21	5.87 ± 1.36	5.93 ± 1.33	5.73 ± 0.88	4.93 ± 1.16	1.743	0.150
	After treatment	8.53 ± 1.06	8.40 ± 1.18	4.93 ± 1.44	5.0 ± 1.31	4.93 ± 1.16	36.254*	<0.001*

*t: Paired t-test. F: F for ANOVA test, pairwise comparison bet. each 2 groups were done using Post Hoc Test (Tukey). p: p value for comparing between the studied groups p_0: p value for comparing between before treatment and after treatment in another group. p_1: p value for comparing between Control and each other group. p_2: p value for comparing between VPA and CBZ. p_3: p value for comparing between VPA and LEV. p_4: p value for comparing between VPA and OXC. p_5: p value for comparing between CBZ and LEV. p_6: p value for comparing between CBZ and OXC. p_7: p value for comparing between LEV and OXC. *: Statistically significant at p < 0.05. VPA: Valproate treated group, CBZ: Carbamazepine treated group, LEV: Levetiracetam treated group, OXC: Oxcarbazepine treated group*

4. DISCUSSION

Children with epilepsy experience disease symptoms, therapy side effects, recurrence risk, brain function impairment, and behavioral issues [10]. The aetiology of epilepsy, seizure type, frequency, and duration; localization of the epileptic focus; age at onset of epilepsy; physiological and structural changes in the brain secondary to seizures; and adverse effects of antiepileptic drugs are all factors that can contribute to a poor quality of life in epilepsy patients [11].

In the present study, it was found that children with epilepsy treated with AEDs had higher behavioral problems scales, lower IQ scores and lower executive functions as compared with control group after 6 months of treatment with AEDs. Valproate and LEV had a more negative effect on behavior than CBZ and OXC after 6 months of treatment. The effect of LEV on behavior was more significant than VPA while valproate and CBZ had a more negative effect on cognition and executive functions than LEV and OXC after 6 months of treatment. Additionally, both LEV and OXC showed no negative effect on in children with epilepsy, cognition and executive processes are impaired. After 6 months of treatment.

In consistent with our results, El Tantawi and Hamdey [12] reported that children with epilepsy under the age of five have higher mean scores in four of the seven behavior domains (withdrawal, sleep problems, attention, and aggression) than healthy children, indicating a higher prevalence of behavioral problems in epileptic children with mean CBCL scores for most of the domains significantly higher than controls.

In agreement with our results, Mishra et al. [13] found that mean CBCL scores for most domains were statistically substantially higher in children with epilepsy of both ages than controls. Clinical range anomalies were found mostly in the externalising domain (23.3%) in children aged 2 to 5, and in both the internalising (21.2%) and externalising (45%) domains in children aged 6 to 14. Parallel to our results, Sarhan et al. [14] demonstrated that patients with epilepsy who received VPA or CBZ, the attention problem scale (88.8 11.06), social problem scale (63.9 9.09), and thought problem scale (56.6 4.7) of the CBCL were considerably influenced, especially in the younger age groups. Also, Loutfi et al. [15] highlighted that patient diagnosed with ADHD clinically and according to DSM-IV criteria, when patients with clinical scores of ADHD and those with borderline scores were combined, the CBCL DSM-oriented scales revealed that ADHD was the most common disorder (56.6%), followed by affective problems (53.3%), anxiety problems (50%), conduct problems (50%), somatic problems (33.3%), and obsessive–compulsive problems (33.3%). (30 percent). In terms of the parents, 12.5 percent of those parents said their children's ADHD symptoms worsened after AEDs were introduced. 6.7% of them were using sodium valproate).

Furthermore, Ahmed and Mohamed [16] revealed that out of 720 children with epilepsy assessed using appropriate psychometric studies and ADHD test, 77 (10.6%) were found to be ADHD sufferers, thirty-five (45.5%) patients were on Sodium valproate.

Moreover, Piccinelli et al. [17] revealed worsening of the attention span at 12 months follow up (53.5% vs. 32.6%) in carbamazepine treated group than those who received VPA.

In accordance with our results, Lagae et al. [18] demonstrated that aggressiveness was one of the most typical negative effects of levetiracetam that occurred in 6% of children treated with the medication.

Parallel with our results, Thelenga et al. [19] detected behavioral abnormalities in at least one domain in 21 (35%) patients in the LEV group, In the LEV group, agitation/aggression was detected in 12 (20%) patients more frequently, and irritation was reported in 16 (26.7%) individuals.

Additionally, Tekgül et al. [20] also confirmed that irritability (67%) was the most commonly reported adverse effect, followed by hyperactivity (8%), somnolence (6%), behavioral abnormalities (5%), restlessness (5%), and ADHD (5%). (5 percent) In line with our results, Sarhan et al. [14] also reported that cognitive development was significantly delayed with significantly lower IQ in epileptic children who were receiving AEDs including VPA.

In consistent with our results, El-Sayed et al. [21] highlighted that preservative, and non-perservative errors are higher in group A under antiepileptic treatment than other groups. Also, they revealed higher omission and commission

errors in group A of epileptic patients under antiepileptic treatment compared with group B of epileptic patients without treatment and group C of healthy subjects.

However, Schiemann-Delgado et al. [22] demonstrated that in this long-term study, the mean changes in the Child Behavior Checklist scores from baseline were all negative, indicating improvement, including the aggressive behavior score. All of the improvements on the Child Behavior Checklist were statistically significant. Also, Donati et al. [23] stated that there was no cognitive function impairment with VPA, CBZ-treated children over a 6- month period of treatment. Also, they revealed also that there no impairment in cognitive functions with OXC-treated children which confirmed the results of the present study.

On the contrary, Hanci et al. [24] reported that there was no statistically significant difference between the mean IQ scores of carbamazepine-treated patients at the non-drug baseline, after six months of therapy, and after twelve months of treatment. However, our study has some limitations; Firstly, small number of patients included in this study. Secondly, refusal of some parents to fill the consent to incorporate their children in the study. Thirdly, poor compliance of the parents on treatment with loss of follow up of some cases. Finally, some cases also were excluded from the study due to poor seizures control and need for more than antiepileptic medication.

5. CONCLUSION

AEDs have the potential to have negative impacts on children with epilepsy's cognition and Behaviour, as well as other issues that could be more detrimental than the seizures themselves. As a result, selecting the appropriate AED for the treatment of paediatric epilepsy will aid in improving the children's quality of life and academic performance.

CONSENT

An informed written consent was obtained from all parents.

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that they have no known competing financial interests or non-financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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