Research Article

The effect of carbamazepine monotherapy on Intelligence in children with idiopathic epilepsy

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Abstract

Introduction: Effective treatment of epilepsy depends on medication compliance across a lifetime. Various studies indicate that drug tolerability is a significant limiting factor in medication maintenance. Available antiepileptic drugs have the potential to induce detrimental effects on cognitive function and therefore compromise patient wellbeing. On the other hand, some agents may serve to enhance cognitive function. **Aim**: To study the impact of some antiepileptic drugs on intellectual functions of idiopathic epileptic children. **Methods**: 15 children recently diagnosed with idiopathic epilepsy aged 3-17 years were included. All patients underwent full clinical and neurological examination, electroencephalography, brain CT and intelligence testing. The patients were treated with carbamazepine (CBZ). The Stanford-Binet – Fifth Edition (SB5) was applied before administration of CBZ, six months and 12 months after the start of antiepileptic therapy. **Results**: Epileptic children receiving CBZ had significantly impaired intellectual functions after 6 months and 12 months of monotherapy. **Conclusion**: Carbamazepine can adversely affect intellectual development of the children with idiopathic epilepsy

Keywords: Idiopathic epilepsy, Carbamazepine, intellectual functions, SB5, childhood.

Introduction

Epilepsy is the most common chronic neurological disorder in the general population and childhood. Epilepsy is considered to be present when two or more unprovoked seizures occur with an interval more than twenty four hours. A seizure is a transient paroxysmal pathophysiological disturbance of brain function resulting from spontaneous excessive discharge of neurons. Approximately one-third of seizures in children are due to epilepsy (Camfield & Camfield, 2015).

Pediatric epilepsy is strongly associated with neurocognitive impairment and behavioral issues ranging from minor attention and memory deficits to serious mental difficulties. This is of major concern as deficits in memory and attention during childhood can result in detrimental developmental effects with serious consequence for the child's social life and academic achievement (Lagae, 2017).

The etiology of cognitive decline in pediatric epilepsy is multifactorial, even within a particular patient. These contributing factors include underlying brain abnormalities and disorders that cause epilepsy, frequency of seizures, severity of epileptic activity, psychosocial issues and the antiepileptic drugs (Kim & Ko, 2016).

Antiepileptic drugs are the mainstay treatment modality for epilepsy. The primary goal of antiepileptic drugs for treatment of epilepsy is to reduce seizures and the secondary objective is to prevent the neuropsychological and cognitive disorders thus avoiding potential future poor academic performance (Moavero et al., 2017).

Intelligence testing represents a critical "first pass" in characterizing a child's cognitive functioning. These tests provide practitioners with a general sense about how a child is performing compared to his same-aged peers. In addition, they are critical in educational planning, occupational planning and care planning (MacAllister et al., 2019).

The aim of the current study is to assess the effects of carbamazepine on the intellectual functions of children with idiopathic epilepsy.

Subjects and methods

The study was conducted between December 2018 and May 2020 at Minia University Hospital for Children, Egypt. Approval for the study was granted by Minia University Medical Faculty Ethical Committee. Informed consent forms were obtained from parents of the patients.

Fifteen children newly diagnosed with idiopathic epilepsy were involved in the study. They hadn't received any AEDs until the beginning of the study and would be treated with carbamazepine. Their age range was 3-17 years. The diagnosis of epilepsy was done according to the International League Against Epilepsy (ILAE) classification and based on clinical data and electroencephalography (EEG) findings. In addition, brain CT was performed to exclude organic causes of seizures.

Inclusion criteria for epileptic children:

- Children newly diagnosed with idiopathic epilepsy according to the International League
  Against Epilepsy (ILAE) classification (Scheffer et al., 2018).
- Age range: 3-17 years.
- With no visual, hearing or speech problems
- Hadn't received any antiepileptic drugs prior to the study and would start] carbamazepine (CBZ) monotherapy

Exclusion criteria for epileptic children:

- Patients with reflex or secondary epilepsy.
- History of severe head trauma.
- Concomitant neurological, psychiatric, genetic or medical disorders.
- Receiving other neuroactive drugs.
- Previous exposure to any antiepileptic drug or start on poly-therapy antiepileptic drugs.
- Mental retardation or disability children.

Sociodemographic data forms were completed with the parents of all subjects with full history taking. Complete clinical and neurological examination was done. The Stanford-Binet – Fifth Edition (SB5) was applied to evaluate the intellectual functions of participants. It was applied three times for epileptic children, at time of presentation prior to starting antiepileptic drugs then six and 12 months after administration of (CBZ).

Statistical methods

The collected data were statistically analyzed using **SPSS program software version 25. Paired samples T test** was used to analyze quantitative data between different two times within the studied group. **Chi square test** was used for analyses of qualitative data. The level of significance was taken at (**P value < 0.05**).

Results

Demographic data of subjects are shown in table (1). They showed that the study was conducted on 15 children (11 males and 4 females). Their mean age was 9.3 years. About 47% of participants were living in rural areas and about 53% were living in urban regions.

Full scale intelligence scores (FSIQ) measured by Stanford–Binet Fifth Edition (SB5) of the studied subjects at day zero (before starting CBZ monotherapy), 6 and 12 months of treatment are shown in table (2).

Table (1): demographic data of participants:

		Descriptive statistics
		N=15
Age	*Mean ± SD*	9.3±1.8
Sex	*Male* *Female*	11(73.33%) 4(26.67%)
Residence	*Rural* *Urban*	7(46.67%) 8(53.33%)

Table (2): FSIQ scores of Participants at day zero, 6 and 12 months of treatment:

		Day 0	After 6 months	After 12 months	P value		
		N=15	N=15	N=15	D0 vs 6m	D0 vs 12m	6m vs 12m
FSIQ score	**Mean ± SD**	86.84±6.72	73.39±7.11	72.31±8.19	*<0.001**	*<0.001**	*0.703*

Discussion

It is known that antiepileptic drugs have a double-edged impact on cognitive functions. They can reduce the number of subtle and overt epileptic seizures causing improvement in the cognitive functions and other learning processes. On the other hand, they may cause excessive sedation and reduce psychomotor speed, vigilance, memory and attention leading to significant cognitive impairment and educational problems. These problems can sometimes arise even in the therapeutic ranges of AEDs (Helmstaedter & Witt, 2017).

The current study showed that patients treated with carbamazepine (CBZ group) had a significant negative effect on the intellectual functions of epileptic children after 6 months and 12 months of monotherapy relative to the day zero.

This finding is in disagreement with, Donati et al., (2007) and, Eun et al., (2012) who stated that carbamazepine monotherapy didn't significantly affect intellectual functions in epileptic patients 6 months of treatment.

Also, Anderson et al., (2015) found that the IQ scores of children on CBZ monotherapy was not significantly lower than IQ scors of those who were off treatment. Furthermore, there was no significant difference in the IQ score during treatment and after withdrawal.

Similarly, Hanci et al., (2019) reported that there was no statistical significant difference between the FSIQ scores of patients receiving carbamazepine at the nondrug baseline, after six or after 12 months of treatment.

The discrepancies in the results shown above may be due to variations in study design, duration of the study, patient characteristics and tests used for assessment of intelligence. Furthermore, some studies lacked a control group or baseline data.

Conclusion

Carbamazepine can adversely affect intellectual development of the children with idiopathic epilepsy.

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