European Institute of Knowledge & Innovation

Annals of Innovation in Medicine (AIM) ISSN: 2977-0335

Original Research Article

Evaluation of Side Effects of Anti-Seizure Drugs Among Sudanese Children with Epilepsy in Wad Medani Pediatric Teaching Hospital

Salma Hassan Mohammed Eltahir[1*], Haydar El Hadi Babikir [2], Ibrahim Osman M. Omer [2], and ImadEldeen Mohammed Taj El Deen [3]

[1] *Clinical Pharmacist, Wad Medani Pediatric Teaching Hospital, Ministry of Health, Gezira State;* Shani23101982@gmail.com
[2] *MD, CChN, FRCPCH. Consultant Paediatric Neurologist, Department of Paediatrics and Child Health, University of Gezira.;* hayder@uofg.edu.sd , haydarbabikir@yahoo.com
[2] *Department of Clinical Pharmacy and Pharmacy Practice, Faculty of Pharmacy, University of Gezira.;* ibrahim70814@yahoo.com
[3] *Department of Pharmacology, Faculty of Pharmacy, University of Gezira;* omdataj64@gmail.com
* *Correspondence:* Shani23101982@gmail.com*; Tel.: 00249121488003*

https://doi.org/eiki/10.59652/aim.v1i3.91

Abstract:

Background: Treatment of epilepsy with anti-seizure drugs (ASDs) for 2-5 years is important to control epileptic seizures. Side effects of ASDs are well recognised and affect treatment outcomes if ASDs are severe.

Methods: A cross-sectional descriptive hospital-based study was conducted on 67 children with epilepsy on follow-up visits at a neurology referral clinic in Wad Medani Pediatric Teaching Hospital, Central Sudan, from February 2022 to July 2022. Side effects of ASDs were measured using the Pediatric Epilepsy Side Effects Scale (PESQs). Data were entered into the Statistical Package of Social Sciences (SPSS) version 20, and descriptive analysis was done to calculate frequencies and percentages and chi-square test for association. The P-value of < 0.05 was considered statistically significant.

Results: Gender assessment showed that 36 (53.7%) of study patients were male. 43(64.2%) of participants had low severity of side effects, 14(20.9%) had low–moderate severity, and 8(11.9%) had no side effects. Significant associations were found between age and cognitive side effects (P-value .008); epilepsy type and cognitive side effects (P-value .026); seizure frequency and behavioural side effects (P-value .018); Type of ASD and behavioural side effects (P-value .000) and; type of ASD and neurological side effects (P-value .004).

Keywords: Anti-seizure drugs, epilepsy, paediatric, side effects, PESQ

Received: 06 Dec. 2023
Accepted: 16 Dec. 2023
Published: 19 Dec. 2023

1. Introduction

Treatment of epilepsy with anti-seizure drugs (ASDs) for 2-5 years is important to control convulsions. Antiseizure drugs decrease membrane excitability, increase postsynaptic inhibition or alter the synchronisation of neural networks to decrease excessive neuronal excitability associated with seizure development. Adverse effects were categorised into a lot of classes according to the Medical Dictionary for Regulatory Activities, which included nervous system disorders like dizziness, headache, and memory impairment, and psychiatric disorders like drowsiness, mood and behavioural changes (Alsfouk et al., 2020) Adverse effects can develop acutely or many years after starting treatment (Perucca & Gilliam, 2012). In

clinical practice, tolerability is a major issue and the choice of a certain (ASDs) is at least partially based on a comparison of tolerability profiles of the drugs (Ijff & Aldenkamp, 2013). Multiple new ASDs have been developed and introduced into the market in recent years. Many of these drugs have been promoted as having an advantage over older medications because of the smaller risk of side effects and better seizure control. Global changes in the CNS excitation levels, behavioural deficits and cognitive impairment associated with (ASDs) in children affect learning and school performance (Loring & Meador, 2004) (Ortinski & Meador, 2004). Three factors are clearly involved in cognitive impairment in patients with epilepsy: the underlying etiology of epilepsy, the effects of seizures or the epileptiform EEG discharges themselves, and the central nervous system effects of (ASDs) (Ijff & Aldenkamp, 2013). Phenobarbital and benzodiazepines are associated with the greatest risk of cognitive side effects. Valproic acid (VPA) is considered to be a drug of first choice and one of the most frequently prescribed antiseizure drugs worldwide and is usually well tolerated (Gerstner et al., 2008). Multiple new ASDs have been developed and introduced into the market in recent years. Lamotrigine showed better performance in memory, sedation, and cognitive speed than carbamazepine (Cavanna et al., 2010). Cognitive side effects are usually reversible after withdrawal of AED(Helmstaedter & Witt, 2020). Behavioral side effects (BSEs) associated with ASDs are often overlooked. Agitation, aggression, psychosis, behavioural disorders, hyperactivity, and restlessness are some ASD-related BSEs (Thigpen et al., 2013). Antiseizure medications (ASMs) may affect appetite, affecting normal growth and weight gain(Buraniqi et al., 2022).

2. Materials and methods

Study Design:

A cross-sectional descriptive, hospital-based study design was used for the assessment of side effects of ASDs in pediatric patients.

Study Area:

This study was conducted at Wad-Medani Pediatric Teaching Hospital, a tertiary hospital established in March 1987 in Wad-Medani city, the Capital of Gezira State in Central Sudan. The patients and their family members visited the outpatient referral clinic frequently for regular follow-ups where the study was carried out. The study was conducted in the period of February 2022 to July 2022.

Population of the study:

The study subjects were 2 to 16-year-old children with epilepsies visiting this hospital neurology refer clinic. Information on young children, that is, those of two to eight years old, was collected from their caregivers.

Inclusion criteria:

Children who were diagnosed with epilepsy and prescribed one or more ASD/s, were between 2 and 16 years of age, had no comorbid medical conditions requiring daily medication, and had no significant developmental disorders reported by their caregivers. Informed consent was obtained from family members.

Exclusion criteria:

Refused consent

Sample size:

The total number of study participants was 67.

Sampling techniques:

Probability sampling (systematic random sampling) was used.

Data Collection Method:

A patient within the inclusion criteria was assigned a patient identification number and then interviewed.

Descriptive medical data (type of epilepsy, disease duration, prescribed ASDs, and seizure frequency) and demographic data (child age and gender) were collected from patient's charts. The father's employment status was collected directly from the family member during the interview—Appendix A.

Seizures were classified according to the International League Against Epilepsy (ILAE) (Berg et al., 2010).

Patients and/or family members were interviewed using the pediatric epilepsy side effect questionnaire scale (PESQs), consisting of 19 questions involving cognitive, motor, behavioral, neurological and weight side effects. Likert scale type was used to give scores. The overall score began with zero (no side effects) to 114 (high severity of side effects, and then sub-scoring was measured for each type of side effect (cognitive, motor, etc) by the same scoring system.

Statistical analysis:

Collected data were entered into the Statistical Package of Social Sciences (SPSS) version 20, and descriptive analysis was conducted to calculate frequencies and percentages for categorical data chi-square tests for association. A P-value of < 0.05 was considered statistically significant in related tests.

3. Results

3.1. Socio-clinical demographic data:

Total number of patients who were studied was 67. There were 36(53.7%) of study patients were male and 31(46.3%) were female. Exactly 27(40.3%) of patients were between 2 and 6 years old, and 19(28.4%) were between 12 and 16 years old. The rest were aged 6 to 12. Fathers of 64 (95.5%) of patients were employed.

A total of 33 (49.3%) of study patients had 1-12 seizures/ year, 18 (26.9%) were seizure-free for > 12 months, 10(14.9%) had 2-4 seizures/ month, 3(4.5%) of had 1-7seizures / week, and 3(4.5%) had daily seizures. There were 39(58.2%) of participants had generalised seizures, 22 (32.8%) had focal seizures, 5(7.5%) had myoclonic seizures, and 1(1.5%) had unclassified seizures. Exactly 29 (43.5%) of study patients were prescribed valproate, 18(27%) received CBZ-IR, 7(10.5%) administered CBZ-CR, 6(9%) were prescribed levetiracetam and the rest received polytherapy involved clonazepam as add on therapy. 51 (76.1%) of participants had a seizure duration of> One year, 7(10.4%) of study patients had duration of 5-8 months. Exactly (89.6%) of study patients were prescribed monotherapy. Table (1)

Table 1 This is a table of **the** distribution of Study patients according to clinical demographic characteristics.

Variable	Frequency	Percent %
Seizure frequency		
Seizure free for > 12 months	18	26.9%
1-12 seizures/ year	33	49.3%
2-4 seizures/ month	10	14.9%
1-7seizures / week	3	4.5%

Daily seizures	3	4.5%
Type of epilepsy		
Generalised	39	58.2%
Focal	22	32.8%
Myoclonic	5	7.5%
Not classified	1	1.5%
Prescribed ASDs		
Valproate	29	43.3%
Carbamazepine	25	37.3
Levetiracetam	6	9%
Other ASDs	7	10.4%
Duration of epilepsy		
1-4 months	4	6%
5-8 months	7	10.4%
9-12 months	5	7.5%
> One year	51	76.1%
Other		
Monotherapy	60	89.6%
Polytherapy	7	10.4%
Total		
	67	100%

3.2. Overall Side effects of ASDs:

Exactly 43(64.2%) of the study population had low severity of side effects, 14(20.9%) had low –moderate severity of side effects, and 8(11.9%) had no side effects. See Figure1.

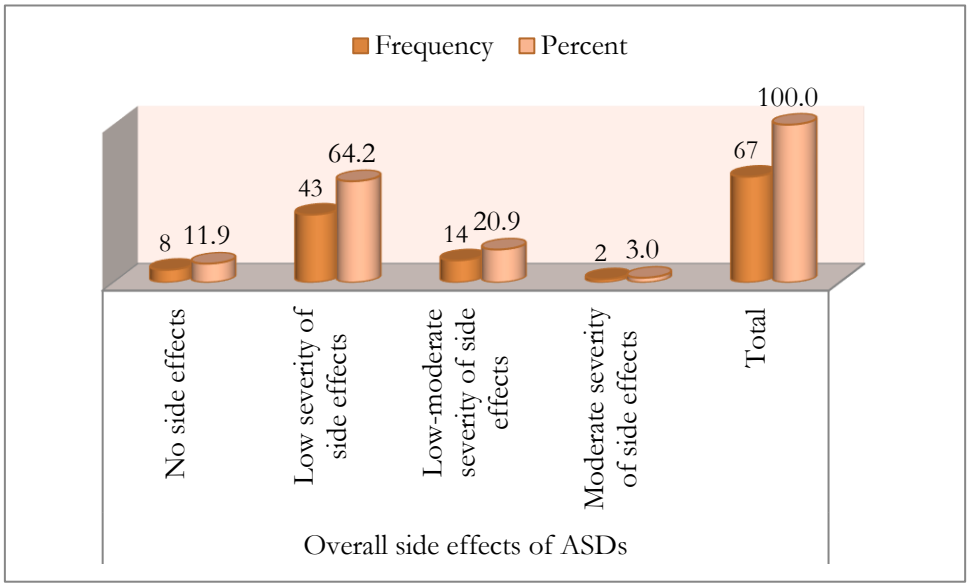

Figure 1 This is a figure of the distribution of study patients according to the overall side effects of ASDs

3.3. Subscales for side effects of ASDs

Of all the study participants, 24(35.8%) of study patients had cognitive side effects, 27(40.3%) had low-severity of cognitive side effects, and 10(14.9%) had low-moderate severity of cognitive side effects. Exactly 45(67.2%) of the study population had no motor side effects, and 15(22.4%) had motor side effects. Further, 31(46.3%) of patients had no behavioural side effects, and 20(29.9%) had low-severity side effects. Moreover, 31(46.3%) of patients had no neurological side effects, and 23(34.3%) had low-severity side effects. Precisely 39(58.2%) of study patients had no change in weight side effects, and 16(23.9%) had low severity of weight change side effects (See Table 2).

Table 2 This is a table of **the** distribution of study patients according to cognitive, motor, behavioural, neurological and weight change side effects.

Variable	Frequency	Percent
Cognitive ASDs side effects (subscale)		
No side effects	24	35.8
Low severity of side effects	27	40.3
Low – Moderate severity of side effects	10	14.9
Moderate severity of side effects	5	7.5
Moderate - high severity of side effects	1	1.5
Motor ASDs side effects(subscale)		
No side effects	45	67.2

Low severity of side effects	15	22.4
Low-moderate severity of side effects	7	10.4
Behavioural ASDs side effects(subscale)		
No side effects	31	46.3
Low severity of side effects	20	29.9
Low- Moderate severity of side effects	12	17.9
Moderate severity of side effects	3	4.5
Moderate-high severity of side effects	1	1.5
Neurological ASDs side effect (subscale)		
No side effects	31	46.3
Low severity of side effects	23	34.3
Low-moderate severity of side effects	6	9.0
Moderate severity of side effects	5	7.5
Moderate- high severity of side effects	2	3.0
Weight change-related ASDs side effects (subscale)		
No side effects	39	58.2
Low severity of side effects	16	23.9
Low-moderate severity of side effects	6	9.0
Moderate severity of side effects	2	3.0
Moderate-High severity of side effects	4	6.0
Total / each subscale		
	67	100

3.4. Age and cognitive side effects:

There were 17(65.4%) patients in the age group 2-6 years who had no cognitive side effects, and 8(30.8%) had low severity of cognitive side effects. 7(43.8%) of participants in the age group >6-12 years had low severity of cognitive side effects. Exactly 9(50%) of study patients in the age group >12-16 years had low severity of cognitive side effects.

3.5. Type of epilepsy and cognitive side effects:

There were 14(40.0%) and 14(40.0%) patients with generalised seizures with no cognitive side effects and low severity of cognitive side effects, respectively. Exactly 7(41.2%) and 7(41.2%) of study patients with focal epilepsy had no cognitive side effects and low severity of cognitive side effects, respectively. There were 2(50%) and 2(50%) of the study population with myoclonic seizures had low severity of cognitive side effects and moderate severity of cognitive side effects, respectively.

3.6. Seizure frequency and behavioural side effects:

There were 6(50.0%) study patients who were seizure-free for >12 months had no behavioural side effects, 14(51.9%) of the study population with 1-12 seizures/year had no behavioural side effects, and 9 (33.3%) had low severity of behavioural side effects. Two (66.7%) of patients with daily seizures had low severity of behavioural side effects.

3.7. Anti-seizure drug/s and behavioral side effects:

There were 8(61.5%) patients who were prescribed CBZ- IR and had no behavioural side effects, 3(23.1%) had low severity of behavioural side effects, and 2(15.4%) had low–moderate severity of behavioural side effects. There were 4(66.7%) patients who received CBZ-CR who had no behavioural side effects, and 2(33.3%) had low severity of behavioural side effects. Exactly 13(48.1%) of participants who administered VPA had no behavioural side effects, and 1(100%) of patients who received polytherapy (CBZ+ phenobarbital (PHN) + clonazepam (CLZ)) had high severity of behavioural side effects.

3.8. Anti-seizure drug/s and neurological side effects:

7(53.8%) of study patients prescribed CBZ-IR had no neurological side effects, and 4(30.8%) had low severity of neurological side effects. There were 4(66.7%) patients who were prescribed CBZ-CR who had low severity of neurological side effects. Three (75.0%) of patients who were prescribed levetiracetam (LEV) had low-moderate severity of neurological side effects and 16(59.3%) of the study population who received VA had no neurological side effects.

3.9. ASDs side effects and associated factors:

Statistically significant associations were found between: age and cognitive side effects P-value =.008, type of epilepsy and cognitive side effects P-value.026, Seizure frequency and Behavioral side effects P- value .018, type of anti-seizure drug/s and Behavioral side effects P-value .000, Type of anti-seizure drugs and neurological side effects P-value .004. Table 3

Table 3 This is a table of the distribution of study patients according to side effects and associated factors

Association Tests	
Socio-clinical demographic variable/side effects	Pearson Chi-Square / Asymp. Sig. (2-sided) (p-value)
Age * Cognitive	.008*
Type of epilepsy * Cognitive	.026*
Seizure frequency * Behavioral	.018*
Type of anti-seizure drug/s * Behavioral	.000*
Type of anti-seizure drugs * Neurological	.004*

***= significant. The P-Value is assumed statistically significant if it is < 0.05**

4. Discussion:

More than half of the study patients were males, which indicated that epilepsy was more common in males than in females in our setting. This result agreed with a result from a study by (Lee et al., 2016), which showed male predominance (64.9%) and (54.7%) in Southwest Ethiopia (Mohammed et al., 2022).

Epilepsy was more common in young children than in older children in the study setting. This result agrees with the fact that the resolution of epilepsy occurs spontaneously when the brain develops with the advancement of age. Around half of the study patients had 1-12 seizures/year.

More than half of the study patients were diagnosed with generalised seizures, which were the most common type of epilepsy stated by a study (Dima & Shibeshi, 2022). Another study from Sweden found that focal seizures alone or plus generalised seizures were more common (54.0%) in epileptic patients (Larsson & Eeg-Olofsson, 2006). Focal epilepsy was also common in the study setting but with fewer frequencies.

Valproic acid (VPA) for ASD was the most commonly prescribed, followed by CBZ. A similar result was found in many studies (Kwong et al., 2012) from China and (50.5%) from Jordon (Albsoul-Younes et al., 2016). Levetiracetam (LEV) as monotherapy was prescribed to a lesser extent despite the fact that it is one of the safest ASD and is recommended in the management of different types of epilepsy by international guidelines. In the study setting, LEV was not available as free, which may explain why it was less frequently prescribed.

The overall side effects were accepted in most patients. Around two-thirds of study patients had low severity of side effects, while less than a quarter had low-moderate severity of side effects.

Regarding cognitive side effects, nearly half of patients had low-severity side effects, about one of three had no side effects, and few had low-moderate severity side effects. The most common cognitive side effects were "finding difficulties in remembering" and "obtaining poor school results".

Motor side effects were not common in this study population. This was explained by the number of patients in this category: around two-thirds had no motor side effects, while the rest had low motor side effects. The most common motor side effect stated by the caregivers was hyperactivity. Near half of the study population had no behavioural side effects, while around one-third of them had low severity of behavioural side effects. The most common behavioural side effect was aggressiveness.

Neurological side effects were comparable to behavioral side effects, and the same results were observed. The patients experienced sleepiness, drowsiness, and headaches.

More than half of patients had no change in weight as a side effect of ASDs, and less than a quarter of them had low severity of weight change. Good appetite was more common than weight increase.

Low severity of cognitive side effects was common in most age groups except in the age group from 2- 6 years, where about two-thirds of them had no cognitive side effects, and the rest had low severity of cognitive side effects. Less than half of the age group >6-12 years had low severity of cognitive side effects, a quarter of them had no cognitive side effects, and another quarter had low-moderate severity of cognitive side effects. In the age group >12-16 years, half had low severity of side effects, while the other half involved other categories of cognitive side effects, with only one patient having moderate-high severity of cognitive side effects. The most common cognitive side effects of ASDs mentioned by patients/ family members were poor school results, memory problems and confusion. One

study found a similar result (33.8%) regarding poor school results (Kaushik et al., 2019). Another cohort study found that Slow thinking and decreased concentration were less likely with levetiracetam or carbamazepine than valproic acid ($p < .05$)(Egunsola et al., 2018).

Patients with generalised and focal seizures had equal percentages of no to low severity of side effects(less than half in each). Low –moderate severity of cognitive side effects of ASDs was found to be higher in generalised seizure than in focal seizure. Half of the patients with myoclonic seizures had low severity of cognitive side effects, and the other half had moderate severity of cognitive side effects. Not classified seizure involved only one patient who showed low-moderate severity of cognitive side effects of ASDs.

Half of the study patients who were free from seizures for > 12 months and half of those who had 1-12 seizures/ year had no behavioural side effects of ASDs. Two-thirds of the study population who had daily seizures experienced low severity of behavioural side effects, while the remaining third experienced moderate-high severity of behavioural side effects. Moderate-high severity of side effects was only shown in patients who had daily seizures. The most common behavioural side effects of ASDs stated by patients/ family members were "aggression" and "hyperactivity".

No behavioural side effects of ASDs were found in nearly two-thirds of patients who received CBZ-IR and in two-thirds of those who received CBZ-CR. There was a higher percentage of low severity of behavioural side effects in the study population who received CBZ-CR than those who received CBZ-IR (one-third to about a quarter, respectively). Some patients who received CBZ-IR showed moderate severity of behavioural side effects compared to no patients in the CBZ-CR category. Nearly half of the patients who received VPA experienced no side effects, while around one-third of them experienced low-severity of behavioral side effects. In the category of (CBZ+ PHN + CLZ) polytherapy receipts, there was one study patient (the only study patient in this category) who experienced moderate–high severity of behavioural side effects of ASDs.

Around one-third of the study population who received CBZ-IR had low severity of neurological side effects, compared to two-thirds of patients who received CBZ-CR. Low - moderate severity of neurological side effects were found in three-quarters of study patients who received levetiracetam, while no neurological side effects were shown in nearly two-thirds of those who received VPA. VPA and CBZ-IR receipts both showed comparable percentages of no neurological side effects and low severity of neurological side effects in this study. One published review article mentioned that the cognitive side effects of CBZ, phenytoin and VPA were comparable and associated with modest psychomotor slowing accompanied by decreased attention and memory (Loring, 2005).

Cognitive, behavioural, and neurological side effects of ASDs were found to be associated with many factors. Cognitive side effects were found to be associated with age and type of seizure, with the latter having a higher significance. Behavioural side effects of ASDs were associated with types of ASDs (higher significance) and seizure frequency. Neurological side effects of ASDs were associated with types of ASDs. Among all these factors, types of ASDs had the highest association with side effects. Motor and weight change side effects were not found to be associated with any factors. A published study found that LEV and VPA were associated with significant weight gain, TPM was associated with significant weight loss, and LTG and CBZ were not associated with significant weight change (Pickrell, 2013). A more recent review article found an association between weight change and the uses of VBA and no association with other antiepileptic drugs (Buraniqi, 2022)

5. Conclusions:

The overall side effects were tolerated by most patients. Most study patients experienced low severity of side effects, especially cognitive side effects. Neurological side effects were found to be comparable (similar percentages) to behavioural side effects. Motor and weight change side effects were not common. Cognitive, behavioural, and neurological side effects of ASDs were found to be associated with many factors, while Motor and weight change side effects were not found to be associated with any factors.

6. Patents:

Author Contributions: Conceptualisation, investigation, methodology: Prof. ImadEldeen Mohammed Taj El, Prof. Haydar El Hady Babikir, and Dr. Ibrahim Osman M. Omer. Data curation, software, formal analysis, writing original draft and visualisation: Dr. Salma Hassan Mohammed Eltahir. Resources (Patients): Prof. Haydar El Hady Babikir and Dr. Salma Hassan Mohammed Eltahir. Validation: Prof. ImadEldeen Mohammed Taj El Deen and Prof. Haydar El Hady Babikir. Writing-review and editing: Prof. ImadEldeen Mohammed Taj El Deen and Prof. Haydar El Hady Babikir.

Funding: "This research received no external funding."

Institutional Review Board Statement: This study was conducted after it had been approved by the Ministry of Health Gezira state and the Ethical Committee of the University of Gezira before patients were approached, recruited, and enrolled. This article was a part of another study carried out by the same authors. So, ethical approval was taken for the whole study, and it possessed the number: 5-22 on 22/2/2022; however, this article involved no experimental tests on humans or animals.

Informed Consent Statement: "Informed consent was obtained from all subjects involved in the study."

Conflicts of Interest: "The authors declare no conflict of interest."

Appendix A

Patient's clinical and socio-demographic characteristics (outpatient neurology refer clinic)

Variable	**Frequencies/percentages**			
Sex	Male ( )		Female ( )	
Age(Y)	2-6 ( )	6-12 ( )	12-16( )	
Father employment status	Employed ( )		Not employed( )	
Duration of epilepsy	1-4 month ( )	5-8 month ( )	8-12 month ( )	more than one year( )
Type of epilepsy	Generalised ( )	Focal ( )	Myoclonic ( )	Unclassified ( )
Seizure frequency	1–12 seizures per year ( )	2–4 seizures per month( )	1–7 seizures per week( )	Daily seizures( )
Anti-seizure drugs				
Monotherapy				
Polytherapy				
Total				

References

Albsoul-Younes, A., Gharaibeh, L., Murtaja, A. A., Masri, A., Alabbadi, I., & Al-Qudah, A. A. (2016). Patterns of antiepileptic drugs use in epileptic pediatric patients in Jordan. *Neurosciences Journal*, *21*(3), 264-267.

Alsfouk, B. A. A., Brodie, M. J., Walters, M., Kwan, P., & Chen, Z. (2020). Tolerability of antiseizure medications in individuals with newly diagnosed epilepsy. *JAMA neurology*, *77*(5), 574-581.

Berg, A. T., Berkovic, S. F., Brodie, M. J., Buchhalter, J., Cross, J. H., van Emde Boas, W., . . . Mathern, G. W. (2010). Revised terminology and concepts for organisation of seizures and epilepsies: report of the ILAE Commission on Classification and Terminology, 2005–2009. In: Wiley Online Library.

Buraniqi, E., Dabaja, H., & Wirrell, E. C. (2022). Impact of antiseizure medications on appetite and weight in children. *Pediatric Drugs*, *24*(4), 335-363.

Cavanna, A. E., Ali, F., Rickards, H. E., & McCorry, D. (2010). Behavioral and cognitive effects of antiepileptic drugs. *Discovery medicine*, *9*(35), 138-144.

Dima, S. A., & Shibeshi, M. S. (2022). Antiepileptic drug adherence in children in southern Ethiopia: a cross sectional study. *PLoS One*, *17*(2), e0263821.

Egunsola, O., Choonara, I., Sammons, H. M., & Whitehouse, W. P. (2018). Safety of antiepileptic drugs in children and young people: A prospective cohort study. *Seizure*, *56*, 20-25.

Gerstner, T., Bell, N., & König, S. (2008). Oral valproic acid for epilepsy-long-term experience in therapy and side effects. *Expert Opinion on Pharmacotherapy*, *9*(2), 285-292.

Helmstaedter, C., & Witt, J.-A. (2020). Anticonvulsant drugs and cognition. *NeuroPsychopharmacotherapy*, 1-12.

Ijff, D. M., & Aldenkamp, A. P. (2013). Cognitive side-effects of antiepileptic drugs in children. *Handbook of clinical neurology*, *111*, 707-718.

Kaushik, S., Chopra, D., Sharma, S., & Aneja, S. (2019). Adverse drug reactions of antiepileptic drugs in children with epilepsy: a cross-sectional study. *Current Drug Safety*, *14*(3), 217-224.

Kwong, K. L., Tsui, K. W., Wu, S. P., Yung, A., Yau, E., Eva, F., . . . Cheng, W. W. (2012). Utilisation of antiepileptic drugs in Hong Kong children. *Pediatric neurology*, *46*(5), 281-286.

Larsson, K., & Eeg-Olofsson, O. (2006). A population based study of epilepsy in children from a Swedish county. *European Journal of Paediatric Neurology*, *10*(3), 107-113.

Lee, Y. K., Ah, Y. M., Choi, Y. J., Cho, Y. S., Kim, K. J., & Lee, J. Y. (2016). Antiepileptic drug adherence and persistence in children with epilepsy attending a large tertiary care children's hospital. *Epileptic Disorders*, *18*(4), 408-417.

Loring, D. W., & Meador, K. J. (2004). Cognitive side effects of antiepileptic drugs in children. *Neurology*, *62*(6), 872-877.

Mohammed, H., Lemnuro, K., Mekonnen, T., & Melaku, T. (2022). Adherence to anti-seizure medications and associated factors among children with epilepsy at tertiary Hospital in Southwest Ethiopia: a cross-sectional study. *BMC neurology*, *22*(1), 310.

Ortinski, P., & Meador, K. J. (2004). Cognitive side effects of antiepileptic drugs. *Epilepsy & Behavior*, *5*, 60-65.

Perucca, P., & Gilliam, F. G. (2012). Adverse effects of antiepileptic drugs. *The lancet neurology*, *11*(9), 792-802.

Thigpen, J., Miller, S. E., & Pond, B. B. (2013). Behavioral side effects of antiepileptic drugs. *US Pharm*, *38*(11), 15-20.