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Factors influencing withdrawal of anti-epileptic drugs and management of recurrent seizure: A systematic review

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Abstract

Objective: This study aims to investigate the risk factors associated with seizure recurrence following the withdrawal of antiepileptic drugs (AEDs) in patients with epilepsy. Method: A systemic review of recent literature and clinical studies was conducted, focusing on variables such as patient demographics, epilepsy characteristics, treatment history, comorbid condition, adherence to treatment, withdrawal protocols and seizure outcomes were included. Results: factors like polypharmacy AED drugs, undesirable effects, cognitive impairment, cost, compliance are leads to withdrawal of antiepileptic drugs. which cause recurrence of seizure and severe risk. Only seizure free patient can slowly withdrawal the Anti-epileptic drugs. Management strategies for recurrent seizures post-withdrawal varied, including AED reinitiation, dose adjustment, adjunctive therapies, and epilepsy surgery. Conclusion: Healthcare were optimizing outcomes for epilepsy patients by using gradual tapering strategies, adjunctive therapies, patient education, and diligent follow-up to minimize seizure recurrence and ensure AED withdrawal efficacy.

Keywords: Anti-epileptic drugs; Seizure recurrence; Cognitive impairment; Cost; Compliance

1. Introduction

Epilepsy is a significant public health concern that has a direct impact on around 50 million of globally. Several types of epilepsy: Idiopathic generalized epilepsies, Symptomatic focal epilepsies, Mesial temporal lobe epilepsy, Frontal lobe epilepsy, Parietal and occipital lobe epilepsy. The most important etiologies in adulthood are cerebrovascular diseases, tumors, traumatic brain injuries, infections of the central nervous system, and neurodegenerative disorders1. The disturbance of nerve cell activity in the brain can lead to seizure in epilepsy chronic neurological disorder that tends to tip the balance between cerebral excitability and inhibition towards uncontrolled excitability is common. Temporary impairment of consciousness is often caused by epileptic seizure, which can pose a risk of bodily harm and disrupt education2. Epilepsy is more common in adults over 65 or in young children. conventional treatment like carbamazepine, diazepam, phenobarbital, phenytoin, Levetiracetam, valproic acid were primarily of anticonvulsant medication. Surgery may be considered in challenging instances even though these medications frequently control or low the frequency of seizure in some patients3. Medication adherence is a major complication due to the long term of treatment and the AED medications show undesired effect.50% of patients were withdrawal the AED drugs due to undesirable effects like neurotoxic, hepatotoxicity, psychiatric issues, haematological toxicity, and visual impairment. On the other hand, AED drugs are highly expensive so it is not economic free, this factor is included to withdrawal AED drugs by the patient4 .

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2. Determining to initiate an anti epileptic drug

Table 1 Anti Epileptic Drugs being utilized in the treatment of epilepsy

Seizure type	Conventional anti-seizure drug	Recently developed anti-seizure drug
I. Partial seizures (i) Simple partial	Carbamazepine Phenytoin Phenobarbital Primidone Valproate	Gabapentin Lamotrigine
(ii) Complex partial	Carbamazepine Phenobarbital Phenytoin Primidone Valproate	Gabapentin Lamotrigine
(iii) Partial with secondly generalized tonic clonic seizure	Carbamazepine Phenobarbital Phenytoin Primidone Valproate	Gabapentin Lamotrigine[3]

The optimal with respect to when to begin treatment with an antiepileptic sedate isn't Uninterruptedly direct, especially for patients with a single seizure, or patients with seizures of minor symptomatology. In polytherapy, the conventional combination of AEDs phenytoin, phenobarbital, carbamazepine, ethosuximide, valproic acid and primidone was frequently used in view of a widespread belief that polytherapy is superior to monotherapy. Polytherapy with AED controls seizure to minimal extent but it leads to increased toxicity extensively. In contrast to polytherapy, monotherapy lowers the risk of unfavourable medication interactions5.

The metabolism and excretion of several AEDs are greatly impacted by hepatic and renal impairment, which may lower the safety and tolerability of prolonged usage. Patients with epilepsy should have a complete medical examination before starting therapy in order to identify the type of seizure they are having and to take into account baseline patient features that may affect the decision of whether medication is required and, if so, which AED would be the best option6. For the successful management of new-onset epilepsy the following aspects should be considered before initiation of the therapy 1) The selected AED should be effective and specific for the type of seizure 2) The AED should have minimum adverse effects and admissible toxicity profile; and 3) The drug should be administered slowly to achieve desired dose and the patient's response to the treatment should also be considered. AED monotherapy may not work for a number of reasons, such as incorrect diagnosis (such as mistaking syncopal spells for seizures), incorrect seizure type diagnosis leading to ineffective AED choice (such as mistaking partial complex seizures for absence and prescribing carbamazepine instead of ethosuximide or valproate), intolerable side effects (such as depression, sedation, or cognitive impairments), idiosyncratic reactions (such as rash, aplastic anaemia, or hepatoxicity), noncompliance, overtreatment, and pharmacogenetic factors . Many factors can cause AED monotherapy to fail, such as incorrect diagnosis (such as mistaking syncopal spells for seizures), incorrect seizure type diagnosis leading to ineffective AED choice (such as mistaking partial complex seizures for absence and prescribing carbamazepine instead of ethosuximide or valproate), intolerable side effects (such as depression, sedation, or cognitive impairments), and idiosyncratic reactions (such as rash, aplastic anaemia)7. An alternative first-line AED can be used in place of a medication if the maximum tolerated dosage is ineffective in controlling seizures or if side effects occur. The second medication should be added to the first one gradually in order to achieve this. The first medication should be gradually stopped once the new medication's effective dosage has been established. The newer drugs are preferred if the initial therapy was failed8.

3. Monotherapy versus polytherapy

For the initiation of drug therapy with antiepileptic drug selection, administration, duration, monitoring of therapy is complicated. Because anti-epileptic drugs have severe adverse effects which affects both psychological (memory,

attention, concentration) and physiological (circadian rhythm, vision, sexual health) functions. These drugs also influence the behavioural and socio economical activities of patients. Most of the AEDs associated with narrow therapeutic index which leads to toxicity if there is no proper monitoring of AED drugs in patients. Polytherapy treatment with AEDs is critical because many AEDS are associated with the induction of hepatic enzymes and it affects the serum level of concurrently administrating drugs which results in decreased therapeutic efficacy, dosing and frequency adjustment of concomitant drugs. Monotherapy is the most utilized standard therapy for the treatment of epilepsy due to reduced adverse effects and drug-drug interactions. But in the other hand polytherapy with newly discovered drugs shows significant improvement in the treatment of epilepsy. In recent studies it is proved that polytherapy of AEDs with different mechanism of action shows synergistic effects. Polytherapy specifically with levetiracetam and valproate in the combination other anti-epileptic drugs has the evidence for potential synergistic effect. But the major barrier in the treatment with polytherapy is the high cost of AED drugs and complexity in drug monitoring. For these reasons, monotherapy is mostly recommended over polytherapy. Second and third generation AEDs has improved safety and therapeutic efficacy in clinical trials than the current first-generation AEDs in the market. But only second-generation AEDs are approved by FDA to utilize in the monotherapy for epilepsy. Many researches have been conducted for the implementation on 'Rational polytherapy' with AED (9,10,11).

4. Considering withdrawing an AED

There are many reasons to consider discontinuation of AED in seizure – free patient, these reasons are mostly related to the negative impact of AEDs on health, cognition, and ultimately on quality of life (QOL). There is increasing evidence on the benefits of AED withdrawal on psychosocial well-being and, most importantly, on the economic burden of these patients. Finally, the patient plays a crucial role in this decision. Older AEDs with effects on hepatic enzyme induction or inhibition can prove particularly problematic for patients taking multiple medications for other conditions. Likewise, certain medications are associated with undesirable long term side effects, such as, gumal hypertrophy, hirsutism, and weight gain. Additional disadvantages of continuing treatment indefinitely include the risk of teratogenicity.

The cost of antiepileptic drugs continues to increase, especially with the advent of newer patented medications. So, medications were discontinued because of patient can't afford for the expensive medications. Similarly, patient under the medication of AED, suffers Behavioral and cognitive side effects while in the epileptic treatment. Discontinuation of AED drug may report neuropsychological improvement. So, this may cause recurrence of seizure12 .

5. Factors leads to AED withdrawal

Anti-epileptic drugs (AEDs) are mainly used in the patients for the treatment of epilepsy. But prolonged use of AED is associated major adverse reactions and other complication which may negatively influences the patient's quality of life and health status. In this scenario where AED withdrawal is comes under consideration. AED withdrawal should be considered depends on many factors which includes age at onset, epilepsy types, seizure frequency, EEG, patient adherence and health conditions. If all the criteria and conditions are met consultants may initiate the AED withdrawal with close monitoring. Prior to the withdrawal of AED, consultants must provide counselling to the patients(1,13,21,22).

Here are the few reason that leads to AED withdrawal:

- Decreased seizure frequency: AED withdrawal can be considered if a patient is free of seizure for a period of 2-5 years for adults and 6 months to 2 year in children with normal EEG. During AED withdrawal patients should be cautiously monitored for the recurrence of seizure and changes in EEG (1,14,22).
- Psychotropic effects: AEDs are associated with many mental issues which affects cognition and behaviour of patients. In this case consultants may withdraw AED or changes the dosage regimen to minimize these effects (15,16).
- Multiple medications: Many individuals need multiple AEDs for the control of seizure. Polytherapy with AEDs are associated with numerous adverse effects and drug related complications. It can be reduced by the withdrawal of unnecessary AEDs and simplify the AED drug regimen with less adverse reactions and effective therapeutic effects (17,11,18).
- Teratogenicity: AEDs are associated with risks in women of child bearing potential. So, it is essential to consider the health care provider about the withdrawal of AED or to change medication with no teratogenic effects for the optimization of AED therapy and to reduce potential risks in the unborn child (19,20).
- Financial burden: Epilepsy is a chronic disorder. Generally, long term use of drugs is expensive which becomes a major reason for patients to withdraw AED therapy. In such cases, AED withdrawal can be considered depends on the control of seizure and other criteria which includes EEG. Once all the criteria are met and no other reason

for the continuation of AED therapy, withdrawal of AED drugs can be taken into account to decrease financial burden and to increase patients' compliance. Before considering to withdraw AEDs, patients should consult with the health care provider and consultant should counsel the patient about the risk (21,22,12).

6. During the period of AED withdrawal state

Deciding whether to discontinue antiepileptic medications (AEDs) for patients who have been seizure-free for two years is critical. However, some individuals may experience seizures again after stopping AEDs. The role of electroencephalograms (EEGs) in predicting seizure recurrence after AED withdrawal is uncertain. A meta- analysis, the first of its kind, investigates the potential of EEGs in guiding AED discontinuation. By pooling data from studies that examined EEG results before AED cessation and subsequent seizure recurrence, the study assessed the quality of each study using the Newcastle–Ottawa Scale. The analysis, which included 15 studies comprising 2349 participants, underscores the importance of abnormal EEG findings in predicting seizure relapse. Specifically, abnormal EEG patterns such as paroxysmal activity, slowing, and spike and wave activities were associated with a higher risk of relapse. In conclusion, our findings highlight the utility of EEGs, particularly in detecting paroxysmal abnormalities, as a valuable tool for predicting seizure relapse after reducing AEDs, thus providing essential insights for managing epilepsy. Thus, It is recommended to withdraw AEDS if there is no reoccurrence of epilepsy for minimum of 2 years with normal mentality, normal IQ, normal EEG and normal behavioural activities (23,24.25,26,21).

7. Neuropsychological dysfunction: while taking AED

Both classical drug and newer antiepileptic drug has shown positive effects and undesirable effects. it causes cognitive and behavioural impairment. Studies found that polytherapy cause more side effects than monotherapy.

7.1. Classical drugs

Especially barbiturates and benzodiazepines cause severe side effects. Also affects the patient's daily routine, this makes polytherapy of AED were convert into monotherapy by physicians to reduce the impact of polytherapy classical drugs.

7.2. Newer drugs

When newer AEDs with placebo are directly compared with few older AEDs, the newer AEDs shows promising results. Newer drugs like Gabapentin, lamotrigine, tiagabine, topiramate, and vigabatrin are mostly preferred now a days. Comparison of each classic drugs and newer drugs were done. Overall, preliminary studies implies that several newer generation AEDs elicit minimal cognitive impairments and shows more favorable results than older AED (27,28,29).

Table 2 Classification of Anti Epileptic Drugs and their potential side effects

Classification of AED drugs	Drug name	Side effects
CLASSICAL DRUGS	Carbamazepine	Phonophobia, Atrioventricular block, CHF, stevens- Johnson syndrome, hypocalcemia, pancreatitis.
	Clonazepam	Depression, suicidal thought, fatigue, ataxia, upper respiratory infection.
	Diazepam	suicidal thought, Depression, ataxia, dizziness, headache, euphoria.
	Ethosuximide	suicidal thought, Depression, ataxia, dizziness, headache, loss of appetite, aplastic anemia, agranulocytosis, SLE.
	Phenytoin	suicidal thought, nephrotoxicity, cardiac arrest, ataxia, slurred speech, confusion, feeling nervousness.
	Valproic acid	Disturbance in thinking, depression, peripheral edema, ecchymosis, rhinitis.
	Lamotrigine	Aseptic meningitis, indigestion, xerostomia, dizziness, tremor, pain throat.

NEWER DRUGS	Vigabatrin	suicidal thought, arthralgia, aggressive behavior, liver failure, confusion, memory impairment.
	Gabapentin	Nausea, ataxia, stevens-Johnson syndrome, disturbance in thinking, hostile behavior, mood swings.
	Topiramate	suicidal thought, stevens-Johnson syndrome, drug induced encephalopathy, glaucoma, loss of appetite.
	Tiagabine	Palpitation, syncope, stevens-Johnson syndrome, tachycardia, hypertension, edema, pruritus, sweating, gingivitis, diarrhea.
	Zonisamide	Schizophrenic form disorder, suicidal thought, encephalopathy, agitation, depression, abnormal weight loss[8].

8. Risk of a seizure recurring, if an AED is stopped

Patients who become seizure free during the epilepsy treatment tends to discontinue the AEDs before completion of the therapy. However, withdrawal has certain risks that are difficult to predict. Predictors includes age at onset, etiology, types of seizure, idiopathic epilepsy syndrome, Brain MRI abnormalities .Also predicting the recurrence of seizure risk after AED withdrawal is possible by taking EEG .After taking EEG it shows some effects of interictal epileptiform discharge(IEDs),so it is recommended to monitor EEG frequently to predict risk of AED withdrawal.According to LICE guidelines, the patients with an abnormal EEG should be informed of the higher risk recurrence of seizure after AED withdrawal (30,31).

9. Conclusion

Epileptic seizure is defined by the ILAE as a "Transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain". It is classified as partial seizure and generalised seizure. Comorbidities like psychiatric worse to response to initial treatment with anti-epileptic drugs and increased risk of death. The disturbance of nerve cell activity in the brain can lead to seizure in epilepsy chronic neurological disorder that tends to tip the balance between cerebral excitability and inhibition towards uncontrolled excitability is common. Several factor like polypharmacy, neuropsychological dysfunction, to avoid teratogenic effect, cognitive impairment, compliance of medications, cost, etc, are the purpose to withdrawal of AED. Thus, withdrawal of AED seems recurring seizure to the patient. In some case, to prevent recurrence of seizure and during pregnancy AED drug should not withdraw, the only way to alternate the drugs with less adverse effects were preferred to the patients. Proper counselling should be given about the drugs to the patient. Moreover, polytherapy were converted to monotherapy for optimal dosage regimen. Thus, AED management were depended upon the individuals. lifestyle changes can help manage side effects from AED like getting regular exercise, eating a healthy diet, maintaining a consistent sleep schedule, and reducing stress can improve overall well-being and may alleviate some side effects. Also, complement therapies like meditation, yoga is help to overcome from the side effects. Likewise cost of AED is a crucial aim for withdrawal, patient should get proper guidance from the health care professionals under their knowledge should explore another brand of drug, check about health insurance for the management. If the patient were seizure free, from the guidance of health professional AED can withdrawal. The decision to withdraw AEDs should be made carefully, weighing the potential benefits of discontinuation against the risk of seizure recurrence and the impact on the individual's quality of life. patients should be educated about the importance of adherence to their tapering plan, as well as the need for ongoing monitoring and follow-up care after AED withdrawal to ensure optimal seizure management and safety.

Compliance with ethical standards

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The authors have no conflict of interest regarding this investigation

References

[1] Verrotti A, Trotta D, Salladini C, Morgese G, Chiarelli F. Risk factors for recurrence of epilepsy and withdrawal of antiepileptic therapy: a practical approach. Ann Med [Internet]. 2003;35(3):207–15. Available from: http://dx.doi.org/10.1080/07853890310008260

[2] Lado FA, Rubboli G, Capovilla P, Avanzini G, Moshé SL. Pathophysiology of epileptic encephalopathies. Epilepsia [Internet]. 2013 [cited 2024 Aug 13];54(s8):6–13. Available from: http://dx.doi.org/10.1111/epi.12417

[3] Au - Mukhopadhyay T-. J, Au - Kandar H, Au - Das C, Au - Ghosh S, Au - Gupta L. SP - 20 EP - 26 T1 - Epilepsy and its Management. Epilepsy and its Management: A Review VL - 1 JO - Journal of PharmSciTech ER.Researchgate.net. [cited 2024 Aug 13]. Available from: https://www.researchgate.net/publication/286200646_Epilepsy_and_its_Management_A_Review

[4] Toledano R, Gil-Nagel A. Adverse effects of antiepileptic drugs. Semin Neurol [Internet]. 2008 [cited 2024 Aug 13];28(03):317–27. Available from: https://pubmed.ncbi.nlm.nih.gov/18777478/

[5] Marson AG. When to start antiepileptic drug treatment and with what evidence? Epilepsia [Internet]. 2008 [cited 2024 Aug 14];49(s9):3–6. Available from: https://pubmed.ncbi.nlm.nih.gov/19087111/

[6] St. Louis E, Rosenfeld W, Bramley T. Antiepileptic drug monotherapy: The initial approach in epilepsy management. Curr Neuropharmacology [Internet]. 2009 [cited 2024 Aug 14];7(2):77–82. Available from: http://dx.doi.org/10.2174/157015909788848866

[7] St. Louis E. Editorial [hot topic: Monotherapy to polytherapy: Antiepileptic drug conversions through the spectrum of epilepsy care (guest editor: Erik K. st. Louis)]. Curr Neuropharmacol [Internet]. 2009;7(2):75–6. Available from: http://dx.doi.org/10.2174/157015909788848910

[8] Walker R, Whittlesea C. Clinical pharmacy and therapeutics. Elsevier Health Sciences UK; 2011.

[9] Deckers CLP, Hekster YA, Keyser A, Van Lier HJJ, Meinardi H, Renier WO. Monotherapy versus polytherapy for epilepsy: A multicenter double-blind randomized study. Epilepsia [Internet]. 2001 [cited 2024 Aug 14];42(11):1387–94. Available from: https://pubmed.ncbi.nlm.nih.gov/11879339/

[10] Mutanana N, Tsvere M, Chiweshe MK. General side effects and challenges associated with anti-epilepsy medication: A review of related literature. Afr J Prim Health Care Fam Med [Internet]. 2020 [cited 2024 Aug 14];12(1). Available from: http://dx.doi.org/10.4102/phcfm.v12i1.2162

[11] St. Louis E. Truly "Rational" Polytherapy: Maximizing efficacy and minimizing drug interactions, drug load, and adverse effects. Curr Neuropharmacol [Internet]. 2009 [cited 2024 Aug 14];7(2):96–105. Available from: http://dx.doi.org/10.2174/157015909788848929

[12] Alsaadi T, Shakra M, Turkawi L. Discontinuation of AEDs: When and how? Health [Internet]. 2013;05(06):21–7. Available from: http://dx.doi.org/10.4236/health.2013.56a1004

[13] Raymond AA. How to stop antiepileptic drugs [Internet]. Neurology-asia.org. [cited 2024 Aug 14]. Available from: http://neurology-asia.org/articles/20073_027.pdf

[14] Hixson JD. Stopping Antiepileptic Drugs: When and why? Current Treatment Options in Neurology [Internet]. 2010 Jun 26;12(5):434–42. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2918788/

[15] Ortinski P, Meador KJ. Cognitive side effects of antiepileptic drugs. Epilepsy Behav [Internet]. 2004;5:60–5. Available from: http://dx.doi.org/10.1016/j.yebeh.2003.11.008

[16] Nadkarni S, Devinsky O. Psychotropic effects of antiepileptic drugs. Epilepsy Curr [Internet]. 2005 [cited 2024 Aug 14];5(5):176–81. Available from: http://dx.doi.org/10.1111/j.1535-7511.2005.00056.x

[17] St. Louis E. Minimizing AED adverse effects: Improving quality of life in the interictal state in epilepsy care. Curr Neuropharmacol [Internet]. 2009 [cited 2024 Aug 14];7(2):106–14. Available from: https://pubmed.ncbi.nlm.nih.gov/19949568/

[18] Lee JW, Dworetzky B. Rational polytherapy with antiepileptic drugs. Pharmaceuticals (Basel) [Internet]. 2010 [cited 2024 Aug 14];3(8):2362–79. Available from: http://dx.doi.org/10.3390/ph3082362

[19] Tomson T, Battino D, Perucca E. Teratogenicity of antiepileptic drugs. Curr Opin Neurol [Internet]. 2019 [cited 2024 Aug 14];32(2):246–52. Available from: https://pubmed.ncbi.nlm.nih.gov/30664067/

[20] Güveli BT, Rosti RÖ, Güzeltaş A, Tuna EB, Ataklı D, Sencer S, et al. Teratogenicity of Antiepileptic Drugs. Clinical Psychopharmacology and Neuroscience [Internet]. 2017 Feb 1;15(1):19–27. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5290711/

[21] Laue-Gizzi H. Discontinuation of antiepileptic drugs in adults with epilepsy. Aust Prescr [Internet].2021;44(2):53–6. Available from: http://dx.doi.org/10.18773/austprescr.2021.005

[22] Lossius MI, Alfstad KÅ, Aaberg KM, Nakken KO. Discontinuation of antiepileptic drugs in seizure-free patients – when and how? Tidsskrift for Den norske legeforening [Internet]. 2017 Mar 22; Available from: https://tidsskriftet.no/en/2017/03/klinisk-oversikt/discontinuation-antiepileptic-drugs-seizure-free-patients-when- and-how

[23] Ruiz NV. Deciding when less is more: The Crossroads of withdrawing antiepileptic drugs. Epilepsy Curr [Internet]. 2018;18(1):21–3. Available from: http://dx.doi.org/10.5698/1535-7597.18.1.21

[24] Javier Gilbert Jaramillo, José María, Pedro J, Óscar López, Gadea D, Diaz H, et al. Corrigendum to "Effectiveness and safety of perampanel as early add-on treatment in patients with epilepsy and focal seizures in the routine clinical practice: Spain prospective study (PERADON)" [Epilepsy Behave 102 (2020) 106655]. Epilepsy & Behaviour. 2020 Jan 28;

[25] Piña-Garza JE, Rosenfeld W, Saeki K, Villanueva V, Yoshinaga H, Patten A, et al. Efficacy and safety of adjunctive perampanel in adolescent patients with epilepsy: Post hoc analysis of six randomized studies. Epilepsy Behav [Internet]. 2020;104(106876):106876. Available from: http://dx.doi.org/10.1016/j.yebeh.2019.106876

[26] Welton JM, Walker C, Riney K, Ng A, Todd L, D'Souza WJ. Quality of life and its association with comorbidities and adverse events from antiepileptic medications: Online survey of patients with epilepsy in Australia. Epilepsy Behav [Internet]. 2020;104(106856):106856. Available from: http://dx.doi.org/10.1016/j.yebeh.2019.106856

[27] Loring DW, Marino S, Meador KJ. Neuropsychological and behavioral effects of anti-epilepsy drugs. Neuropsychol Rev [Internet]. 2007;17(4):413–25. Available from: http://dx.doi.org/10.1007/s11065-007-9043-9

[28] Hirsch E, Schmitz B, Carreño M. Epilepsy, antiepileptic drugs (AEDs) and cognition: Epilepsy, AEDs and cognition. Acta Neurol Scand [Internet]. 2003;108:23–32. Available from: http://dx.doi.org/10.1034/j.1600-0404.108.s180.4.x

[29] Drane DL, Meador KJ. Cognitive and behavioral effects of antiepileptic drugs. Epilepsy Behav [Internet]. 2002;3(5):49–53. Available from: http://dx.doi.org/10.1016/s1525-5069(02)00502-9

[30] Dm AV, Frcp SMDM. Risk of seizure recurrence after antiepileptic drug withdrawal, an Indian study [Internet]. Neurology-asia.org. 2006 [cited 2024 Aug 14]. Available from: http://neurology-asia.org/articles/20061_019.pdf

[31] Yang W, Zhang X, Long J, Wu Q, Han Y. Prediction of the recurrence risk in patients with epilepsy after the withdrawal of antiepileptic drugs. Epilepsy Behav [Internet]. 2020;110(107156):107156. Available from: http://dx.doi.org/10.1016/j.yebeh.2020.107156