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Anti-Seizure Drug Discontinuation in Individuals with Epilepsy: Single-Centre Experiences – When, How Long, How?

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Abstract

Aims: The present study aimed to evaluate seizure recurrence rates after anti-seizure medication (ASM) discontinuation in adults with epilepsy and to identify clinical and treatment-related factors associated with relapse.

Study Design: Retrospective observational single-center study.

Place and Duration of Study: This study was conducted at the Department of Neurology, Hitit University Faculty of Medicine Hospital. Patient data collected between December 2013 and January 2025 were retrospectively analyzed.

Methodology: Adult patients with epilepsy who had been seizure-free for at least 2 years and whose ASM therapy was gradually discontinued under neurologist supervision were included. Only patients with normal neurological examination findings, normal cranial Magnetic Resonance Imaging (MRI), and regular follow-up data were analyzed. Demographic characteristics, age at onset, seizure type, duration of seizure-free period prior to discontinuation, treatment modality (monotherapy vs polytherapy), Electroencephalography (EEG) findings before withdrawal, tapering duration, and seizure recurrence were evaluated.

Results: Out of 1,538 epilepsy patient files reviewed, ASM therapy was discontinued in 424 patients (27.6%). The cohort included 189 females (44.6%) and 235 males (55.4%), with a mean age of 46.8±15.2 years. Seizure recurrence occurred in 88 patients (20.8%) either during dose reduction or after complete withdrawal. Recurrence was significantly associated with shorter seizure-free duration, polytherapy, abnormal EEG findings, and shorter tapering periods.

Conclusion: ASM discontinuation is a critical stage in epilepsy management and remains a complex clinical decision. Individualized withdrawal strategies considering clinical risk factors may help reduce relapse rates and improve long-term outcomes.

Keywords: epilepsy, antiseizure medication withdrawal, seizure recurrence, relapse risk, polytherapy, electroencephalography

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Introduction

Epilepsy is one of the most common chronic neurological disorders worldwide, affecting approximately 50 million people globally [1]. Long-term treatment with anti-seizure medications (ASMs) allows many patients to achieve sustained seizure control and maintain a good quality of life [2]. However, prolonged drug use may lead to cognitive, behavioural, cosmetic, and systemic side effects, which may negatively influence treatment adherence and patient well-being [3,4].

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Approximately 70% of individuals with epilepsy can become seizure-free with appropriate treatment [5]. For these patients, discontinuation of ASMs becomes a major clinical consideration after a certain period of remission. Current clinical guidelines suggest that withdrawal may be considered after at least two years of seizure freedom in selected patients [2]. However, the decision to discontinue medication remains complex due to the risk of seizure recurrence and the potential consequences of relapse, including injury, loss of employment, and reduced quality of life.

Previous studies have reported varying relapse rates following ASM withdrawal, ranging between 20% and 40%, depending on patient characteristics, epilepsy type, and follow-up duration [6,7,8]. Several factors have been associated with recurrence risk, including abnormal EEG findings, polytherapy, focal epilepsy, shorter seizure-free duration, and rapid tapering schedules [9–12].

Despite the growing body of literature, there is still no universal consensus regarding the optimal timing and method of ASM discontinuation. Predicting which patients will remain seizure-free after withdrawal remains one of the most challenging aspects of epilepsy management.

Research Problem

Although ASM discontinuation represents an important therapeutic milestone, identifying patients who can safely stop treatment remains difficult.

Research Aim

This study aimed to evaluate seizure recurrence rates after ASM discontinuation and to determine the clinical factors associated with relapse in a large single-centre cohort.

Research Questions

1. What is the frequency of seizure recurrence after ASM withdrawal?
2. Which clinical variables are associated with relapse?
3. Does treatment modality influence recurrence risk?
4. Are EEG findings predictive of seizure recurrence?

Methods

Study Design and Population

This retrospective observational study was conducted at the Department of Neurology, Hitit University Faculty of Medicine Hospital. Medical records of patients with epilepsy followed between December 2013 and January 2025 were reviewed.

Patient Selection

Among 1,538 patients with epilepsy, 424 individuals in whom ASM therapy was discontinued under neurologist supervision were included in the analysis. Patients were required to have been seizure-free for at least 2 years before discontinuation. Only patients with normal neurological examination findings and normal cranial MRI were included to ensure a more homogeneous study population.

Data Collection

Demographic data, age at seizure onset, epilepsy type, treatment modality (monotherapy or polytherapy), duration of seizure freedom before discontinuation, EEG findings before withdrawal, tapering duration, and recurrence status were recorded. Previous studies have emphasised the importance of these variables in predicting relapse risk (6,7,11,12).

Withdrawal Protocol

ASM discontinuation was performed gradually, in accordance with clinical practice and recommendations from the available literature (9,13). The tapering duration varied among patients depending on drug type, treatment duration, and clinical judgment.

Outcome Measures

The primary outcome of the study was seizure recurrence during dose reduction or after complete drug withdrawal. Time to relapse and associated risk factors were analysed in detail.

Results

A total of 1,538 patient records with a diagnosis of epilepsy were reviewed retrospectively. Among these, anti-seizure medication (ASM) therapy was discontinued in 424 patients (27.6%) who met the inclusion criteria and had

been followed regularly in our outpatient clinic. The demographic and clinical characteristics of the study population are presented in Table 1.

Table 1. Demographic and Clinical Characteristics of Patients (n=424)

Variable	Value
Age (mean ± SD)	46.8 ± 15.2
Female	189 (44.6%)
Male	235 (55.4%)
Mean seizure-free duration before withdrawal	2–3 years
Monotherapy	301 (71.0%)
Polytherapy	123 (29.0%)
Relapse	88 (20.8%)
No relapse	336 (79.2%)

The study cohort consisted of 189 females (44.6%) and 235 males (55.4%), with a mean age of 46.8±15.2 years. The mean duration of seizure freedom before discontinuation was 2-3 years. Most patients had normal neurological examination findings and normal cranial MRI, as defined in the inclusion criteria. Before withdrawal, the majority of patients were receiving monotherapy, while a smaller proportion required polytherapy for seizure control.

Seizure recurrence occurred in 88 patients (20.8%), whereas 336 patients (79.2%) remained seizure-free during the follow-up period. Recurrence occurred either during the tapering phase or after complete discontinuation of ASM therapy. These findings are consistent with previously reported relapse rates of 20% to 40% across different patient populations (6,7,8,12).

Demographic and clinical characteristics of patients with and without seizure recurrence were compared (Table 2). Patients who experienced relapse were more likely to have shorter seizure-free duration before discontinuation, abnormal EEG findings, and a history of polytherapy. The relapse group also included a higher proportion of patients with focal epilepsy compared to the non-relapse group.

Table 2. Comparison of Patients With and Without Seizure Recurrence

Variable	Relapse (n=88)	No relapse (n=336)
Male sex	51	184
Polytherapy history	43	80
Monotherapy history	45	256
Abnormal EEG before withdrawal	45	96
Seizure-free period <3 years	55	121
Focal epilepsy	49	142

Treatment modality appeared to be an important factor. Patients receiving polytherapy before withdrawal had a higher relapse rate compared to those treated with monotherapy. This observation is consistent with previous studies indicating that the need for multiple ASMs may reflect a more severe disease course and an increased risk of recurrence (10,12).

EEG findings before drug withdrawal were also associated with recurrence. Patients with epileptiform discharges on pre-withdrawal EEG showed a higher relapse frequency compared to those with normal EEG recordings. This finding supports earlier evidence suggesting that EEG abnormalities may be important predictors of seizure recurrence [11].

The duration of tapering was another relevant variable. Patients who underwent shorter tapering periods showed relatively higher recurrence rates. Previous research has suggested that slower withdrawal schedules may reduce relapse risk in selected populations [9,13].

Table 3. Timing of Seizure Recurrence After ASM Withdrawal (n=88)

Time interval	Number of patients	Percentage
During tapering period	18	20.5%
0–3 months	24	27.3%
3–6 months	19	21.6%
6–12 months	15	17.0%
After 12 months	12	13.6%

The timing of seizure recurrence after ASM discontinuation was also analysed (Table 3). Most relapses occurred within the first year following drug withdrawal. In particular, a considerable proportion of recurrences occurred within the first 6 months, and a significant number occurred within the first 3 months. These results indicate that the early period following withdrawal is the most critical phase in terms of relapse risk. Similar findings have been reported in earlier studies examining long-term outcomes after ASM discontinuation [14,15].

Figure 1. Distribution of Seizure Recurrence According to Time After ASM Withdrawal

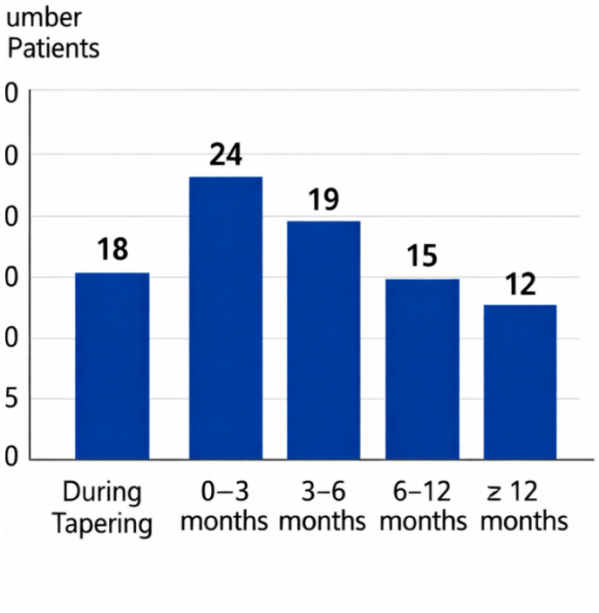
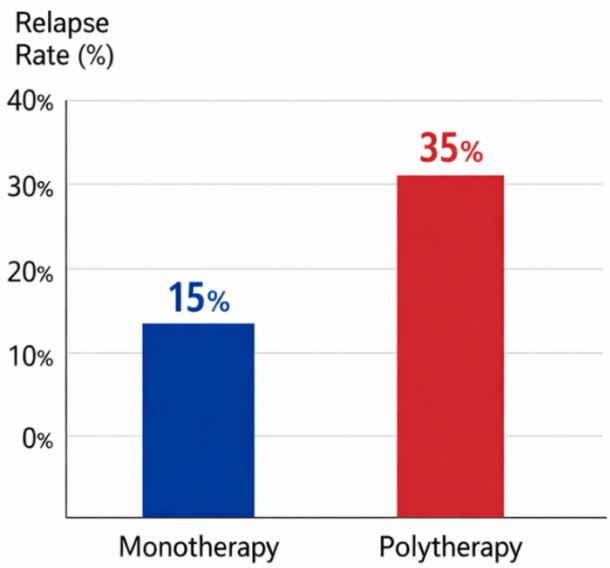


Figure 2. Comparison of Seizure Recurrence Rates in **Monotherapy** vs. **Polytherapy**



The distribution of recurrence over time is illustrated in Figure 1. The highest peak in relapse incidence was observed during the early post-withdrawal period, followed by a gradual decline in recurrence frequency over time.

Additionally, relapse rates were compared across treatment modalities. As shown in Figure 2, patients previously treated with polytherapy had higher recurrence rates than those on monotherapy before discontinuation. This pattern supports the hypothesis that patients requiring multiple medications represent a higher-risk subgroup.

Overall, these findings indicate that while a substantial proportion of patients can successfully discontinue ASM therapy, a considerable minority remains at risk of relapse. Clinical factors such as treatment modality, EEG abnormalities, and duration of seizure freedom before withdrawal appear to play important roles in determining recurrence risk.

Discussion

The present single-centre retrospective study evaluated seizure recurrence following ASM discontinuation and explored clinical factors associated with relapse. In our cohort, the mean seizure-free period before withdrawal was approximately 2–3 years, and recurrence rates were consistent with those reported in the literature. These findings contribute to the growing body of evidence suggesting that ASM discontinuation is a feasible strategy in selected patients but remains associated with a substantial risk of relapse.

Epilepsy is one of the most common chronic neurological disorders worldwide, affecting over 50 million people and posing a major public health burden [1]. Although long-term pharmacological treatment is effective in achieving seizure control in many patients, prolonged ASM exposure may be associated with cognitive, cosmetic, and systemic

side effects [3,4]. For this reason, withdrawal of therapy after a sustained seizure-free period is frequently considered in clinical practice. However, the major concern during this process is seizure recurrence and its potential psychosocial and medical consequences.

Previous studies have reported recurrence rates ranging between 20% and 40% after ASM withdrawal, depending on patient characteristics and duration of follow-up [6,7,8]. In our study, relapse rates were comparable to these reported ranges, supporting the external validity of our findings. The observed recurrence risk highlights that drug discontinuation remains a clinically sensitive decision that must be individualised.

One of the most important determinants in the decision to discontinue ASMs is the duration of seizure freedom. Clinical guidelines commonly recommend at least two seizure-free years before considering withdrawal (2,16). Our cohort aligns with this recommendation, as the average seizure-free duration before discontinuation was approximately 2–3 years. Earlier prospective studies demonstrated that longer seizure-free periods are associated with lower relapse risk, particularly in pediatric populations [17,18]. Similarly, adult studies have also confirmed that longer remission duration is a favourable prognostic factor [12,19].

Electroencephalographic findings have also been investigated as predictors of recurrence. Abnormal EEG activity before withdrawal has been consistently associated with increased relapse risk [11]. Although EEG data were not uniformly available across all patients in this retrospective cohort, the existing literature suggests that epileptiform discharges remain a significant marker of underlying cortical hyperexcitability and should be considered in decision-making.

Structural abnormalities represent another key factor. Imaging-detected lesions, particularly hippocampal pathology, have been linked to increased recurrence risk after withdrawal [20]. Patients with non-lesional epilepsy generally have a more favourable prognosis compared to those with focal structural abnormalities. This supports the importance of neuroimaging in evaluating candidates for treatment discontinuation.

Treatment-related variables also appear to influence outcomes. In our dataset, relapse rates differed notably between monotherapy and polytherapy groups, with higher recurrence observed in patients who required multiple drugs for seizure control. This finding is consistent with prior studies showing that patients treated with polytherapy often have more severe or refractory epilepsy and therefore carry a higher relapse risk [10]. Similarly, previous reports indicate that the need for multiple ASMs may reflect underlying disease severity rather than treatment effect alone.

The tapering process itself has been debated in the literature. Some studies suggest that rapid withdrawal may increase the risk of recurrence, whereas others show no significant difference between fast and slow tapering strategies [9,13]. Although tapering protocols varied in our cohort due to real-world clinical practice, gradual discontinuation was generally preferred to minimise withdrawal-related seizure risk.

Age at onset, epilepsy syndrome, and seizure type have also been proposed as prognostic indicators. Pediatric cohorts, especially those with benign epilepsy syndromes, often demonstrate better outcomes after withdrawal compared to adults [5,21]. Conversely, focal epilepsies, particularly those with structural etiologies, have been associated with higher recurrence rates [12,15]. These findings emphasise the need for syndrome-specific risk stratification.

Another important aspect is the timing of relapse. Previous studies have shown that most recurrences occur within the first year after withdrawal [14]. This observation underscores the importance of close follow-up during the early post-withdrawal period. In clinical practice, patients should be counselled about relapse risk, driving restrictions, occupational implications, and the importance of adherence to follow-up visits.

The results of our study are consistent with prior retrospective and prospective analyses that identified multiple clinical and treatment-related factors influencing recurrence risk. Our findings also align with regional data reported from Türkiye, supporting the generalizability of our observations within similar populations [6-8, 21-23].

This study has several strengths. It reflects real-world clinical practice in a tertiary neurology centre and provides insight into treatment discontinuation patterns in routine care. Additionally, the sample size and the inclusion of both monotherapy and polytherapy groups enabled comparative analysis.

However, several limitations must be acknowledged. First, the retrospective design may introduce selection bias and limit data completeness. Second, EEG and imaging findings were not uniformly available for all patients. Third, variability in tapering schedules and follow-up duration may have influenced outcomes. Despite these limitations, our findings remain clinically meaningful and consistent with the broader literature.

In conclusion, ASM discontinuation can be considered in carefully selected seizure-free patients, particularly those with favourable clinical profiles. However, relapse remains a significant risk, especially among patients with shorter remission periods, structural abnormalities, or a history of polytherapy. Individualised decision-making, guided by clinical features and patient preferences, remains essential. Future prospective multicenter studies with standardised protocols are needed to refine predictive models and optimise treatment strategies.

Limitations

This study has several limitations that should be considered when interpreting the results. First, the retrospective and single-centre design inherently introduces the possibility of selection bias and limits the generalizability of the findings. Patient records were reviewed based on available documentation, and some clinical variables, such as detailed EEG findings, exact tapering protocols, and adherence data, were not uniformly recorded for all individuals.

Second, the average seizure-free duration before discontinuation was approximately 2–3 years, but this period was not standardised across all patients. Variability in clinical decision-making regarding when to discontinue treatment may have influenced recurrence outcomes. Similarly, tapering schedules differed between patients due to real-life clinical practice, which may have affected relapse rates.

Third, although the total sample size was adequate for observational analysis, subgroup analyses—particularly comparisons between monotherapy and polytherapy groups—may have been influenced by differences in baseline disease severity. Patients on polytherapy likely represented a population with more refractory epilepsy, which itself may be a confounding factor associated with higher recurrence risk.

Fourth, imaging and electrophysiological data were not consistently available in all patients, limiting the ability to perform detailed predictive modelling based on structural or EEG abnormalities. In addition, the study did not include standardised neuropsychological or quality-of-life assessments, which could provide further insight into the benefits and risks of medication discontinuation.

Finally, the duration of follow-up after ASM withdrawal varied among patients. Since seizure recurrence can occur even years after discontinuation, longer and more uniform follow-up periods would provide a more accurate estimation of long-term outcomes.

Conclusion

Antiseizure medication discontinuation remains a complex clinical decision that requires careful patient selection and individualised risk assessment. In this single-centre retrospective study, seizure recurrence rates following treatment withdrawal were consistent with previously reported data, particularly among patients with shorter seizure-free periods and those receiving polytherapy.

Our findings suggest that a seizure-free duration of approximately 2–3 years may be a reasonable threshold for considering withdrawal in selected patients, although relapse risk remains significant. Treatment type also appears to play an important role, with higher recurrence observed in individuals who required multiple drugs for seizure control, likely reflecting greater underlying disease severity.

These results emphasise the importance of a structured and cautious approach to ASM discontinuation, including gradual tapering, close clinical follow-up, and thorough patient counselling regarding potential relapse risks. Future prospective multicenter studies with standardised withdrawal protocols and longer follow-up periods are needed to better define predictors of successful discontinuation and to improve individualised decision-making in epilepsy management.

Declarations

Ethics Approval and Consent to Participate

This study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki. Due to the retrospective design of the study and the use of anonymised data obtained from routine clinical records at Hitit University Faculty of Medicine Hospital, formal ethics committee approval was not required according to institutional policies in effect at the time of data collection. No patient-identifiable information was collected or recorded. Therefore, the requirement for written informed consent was waived.

Availability of Data and Materials

The datasets generated and/or analysed during the current study are not publicly available due to institutional data protection policies, but are available from the corresponding author on reasonable request.

Competing Interests

The author declares that there are no competing interests.

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Authors' Contributions

SE contributed to the study's conception and design, data collection, statistical analysis, interpretation of results, and drafting of the manuscript. The author read and approved the final version of the manuscript.

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