

WHO SHOULD HAVE DRUGS STOPPED AND WHO SHOULD BE CONTINUED?

Çiğdem Özkara

Turkey

According to ILAE definition, epilepsy is a chronic condition of the brain characterized by an enduring propensity to generate epileptic seizures, and by the neurobiological, cognitive, psychological, and social consequences of this condition. Antiepileptic drugs (**AEDs**) can prevent seizures but do not capable of eliminating the cause of epilepsy. Therefore patients should remain on drugs until there is no evidence that enduring propensity continues enabling risk of having a seizure. AEDs should be tapered due to unnecessary continuous drug intake, AED related side-effects, teratogenicity, drug interactions, financial burden and burden of daily intake of medications. However risks of continuation or stopping AEDs need to be analyzed meticulously. First of all one should be sure that person is completely seizure free although almost half of the seizures are not noticed by patients which indicates that information provided solely by patients may be unreliable. Secondly the diagnosis must be reviewed and presence of epilepsy should be proved to avoid unnecessary drug administration to patients with psychogenic nonepileptic seizures, the great mimicker of epilepsy. Those patients definitely should be tapered if they are on AEDs.

Physicians manage their patients according to some guidelines, experience and various drug trials. Unfortunately drug withdrawal studies have several limitations which disable interpretation of conclusions. Most studies enrolled a heterogeneous group of patients, many of them do not classify epilepsy types, many of them before MR era, and pediatric population is more studied and different than adult patients where extrapolation of results is not valid. Finally data pertaining to quality of life, morbidity, and socioeconomic and medicolegal issues are generally insufficient. Relapse rate differs from one study to another from 15 to 40 % but metaanalyses demonstrated low risk of recurrence at most 40%. Nevertheless risk of developing drug resistant epilepsy is 7-23% after discontinuation of drug therapy which may avoid the physician to take the risk.

Seizure related injuries, SUDEP are other important factors such as teratogenicity and adverse effects of AEDs while thinking about drug withdrawal or continuation. Duration of seizure freedom is another challenging subject yet not completely agreed upon. In children 2 years remission seemed to be reasonable where the data for adults is more weak but general suggestion is not to be less than 2 years or as more as 5 years. Etiology should also be taken into consideration whereas symptomatic and cryptogenic etiology is less successful than idiopathic group.

There is inconclusive data on EEG's role in predicting relapse. In one study, patients with an abnormal EEG before drug withdrawal were twice more likely to relapse than were patients with a normal EEG. In another study, the relapse rate in patients with an abnormal EEG before drug withdrawal was 47%, compared with a 33% relapse rate in patients with a normal EEG. Moreover sensitivity of EEG is limited in the epilepsy population in general. Epileptiform EEG activity may be suppressed by medication in some patients, which may lead to a false-negative result. EEG abnormalities may not occur until medication is reduced, which may have prognostic value in patients during withdrawal. In one study, relapse occurred in 83% of patients who's EEG worsened during dose reduction, compared with a relapse occurrence of 54% in patients who's EEG remained unchanged. Furthermore, some studies suggest that a rapid taper poses a higher risk for relapse than slow taper (over 6 month) and there is some speculation on certain AEDs posing a higher risk for relapse with taper.

Unfavorable prognostic factors for antiepileptic drug withdrawal are age at onset >12 years, symptomatic vs idiopathic etiology, mental retardation, abnormal neurologic examination, family history of epilepsy, poor initial response to

treatment, more than 1 drug being used at time of withdrawal, epileptiform EEG changes, slowing on EEG, emergence of EEG abnormalities during drug withdrawal and juvenile myoclonic epilepsy.

Before tapering patient counseling is essential: all risk factors which may present for a given patient must be identified, the patient must be informed of his individual risk, and that no test or risk factor analysis available allows flawless prognostication, they should be informed about the low but potential risk existing for status epilepticus and also they must know that the period of greatest risk of relapse is during the first year after initiation of drug withdrawal, particularly during the taper. The patient's motivations and goals need to be determined to ensure they are realistic, women who cite concerns regarding the teratogenic potential of antiepileptic drugs must be provided with education about the true risks as substantiated in the literature, parents who attribute a child's neurocognitive deficits to medication must be cautioned that these problems may not improve after drug withdrawal and that the problems may be due to other factors. Lastly, patients must be warned about avoidance of risky behavior (sleep deprivation, video/tv games), and dangerous practices (excessive alcohol consumption).

In conclusion, prescribed withdrawal of AED's is a reasonable consideration for a selected group of patients, risk factors that help predict and counsel patients are reasonably well defined. The decision to withdraw AEDs should only be taken after careful consideration of the risks and benefits, and informed discussion and must be discussed in each patient individually according to their own circumstances.