Antipsychotics and **seizure threshold** – review and case report

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Introduction

Almost all **first** or **second generation antipsychotics** have been implicated in **decreasing the seizure threshold** with a higher convulsive risk suggested in second generation ones in particular **Clozapine** but also Olanzapine. Studies also demonstrate that psychiatric syndromes are more frequent in people with neurological pathology like epilepsy than in general population.

Clozapine was developed in the 1960s and was the first atypical antipsychotic. It has been associated with a convulsive risk (myoclonus and generalized tonic-clonic seizures), which is **dose dependent** (as in the other antipsychotics) being the convulsive events more frequent than in the other drugs of the same class, with an estimated prevalence of 3%. The factors that were associated with an increased risk are **high doses** of the drug, **rapid titration**, **concomitant use of drugs with epileptogenic potential,** and **personal or family history of neurological disturbances**. The dose with more reported cases is 600mg but the risk exists from much lower doses, such as 300mg a day.

Objectives

Collect and review the most recent data on antipsychotics and their potential to decrease seizures threshold. Risk and precautions differences between antipsychotics were also a purpose of this work.

A **clinical case** of a patient in a high dose of clozapine who developed a seizure event is going to be described as well.

Methods

A literature research was carried out on **antipsychotics**, **convulsive threshold**, specifically on **Clozapine** related **seizures** and **risk factors** associated.

Results/Clinical Case

The case involves a **22-year-old man** with a 2-year history of **schizophrenia** with comorbid psychoactive drugs dependency and a poor therapy adherence. It is also worth mentioning that **his mother has epilepsy** without regular follow-up.

After several relapses due to treatment resistance and lack of adherence the patient had an involuntary admission. **Clozapine was titrated** 50mg per week until **500mg,** dose with which he **had a generalized tonic-clonic seizure**. At this time a therapeutic adjustment was made to 250mg of clozapine daily in association with Valproate 1000mg.

Conclusions

The **seizures' risk** of antipsychotic drugs is likely to be related to **patient features** that should always be thoroughly investigated in the clinical and personal history. To minimize the risk of neurological adverse effects, the **lowest effective dose** of antipsychotic, **slow titration** and **polypharmacy avoidance** should be recommended. The use of drugs of the same class or with potential for lowering the convulsive threshold must be closely monitored. A routine **electroencephalogram** should be done in patients who will initiate Clozapine especially if epileptic activity is suspected or if doses above 600mg are weighed.

The **introduction of an anticonvulsant drug** such as Valproate, which may work as a Clozapine augmentation strategy, has also been suggested by some authors.

It is **not mandatory to discontinue Clozapine** after a neurological event and a history of epilepsy is not an absolute contraindication to the use of this drug.

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