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Review

Pharmacotherapy in patients with epilepsy and psychosis☆

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ABSTRACT

The recognition and treatment of psychosis in persons with epilepsy (PWE) is recommended with the apparent dilemma between treating psychosis and opening the possibility of exacerbating seizures. The pooled prevalence estimate of psychosis in PWE is 5.6%. It has been proposed that a 'two hit' model, requiring both aberrant limbic activity and impaired frontal control, may account for the wide range of clinical phenotypes. The role of antiepileptic drugs in psychosis in PWE remains unclear. Alternating psychosis, the clinical phenomenon of a reciprocal relationship between psychosis and seizures, is unlikely to be an exclusively antiepileptic drug-specific phenomenon but rather, linked to the neurobiological mechanisms underlying seizure control. Reevaluation of antiepileptic treatment, including the agent/s being used and degree of epileptic seizure control is recommended. The authors found very few controlled studies to inform evidence-based treatment of psychosis in PWE. However, antipsychotics and benzodiazepines are recommended as the symptomatic clinical treatments of choice for postictal and brief interictal psychoses. The general principle of early symptomatic treatment of psychotic symptoms applies in epilepsy-related psychoses, as for primary psychotic disorders. In the authors' experience, low doses of antipsychotic medications do not significantly increase clinical risk of seizures in PWE being concurrently treated with an efficacious antiepileptic regimen.

1. Introduction

Rational pharmacological treatment of psychoses in persons with epilepsy (PWE) should ideally be based upon mechanisms linking the two disorders. However, the neurobiological understanding of these mechanisms remains incomplete, with the absence of a satisfactory explanatory model to guide drug treatment. The empirical evidence is also insufficient. These guidelines for the treatment of Psychoses in PWE (Fig. 1) are therefore based on the cumulative clinical experience of the authors and some systematic study.

A two-step procedure, not necessarily consecutive, is recommended. The first step requires reevaluation of the antiepileptic treatment, an integral and underrecognized component of assessment in the authors' view. The second step requires initiation of pharmacotherapy including antipsychotic drugs (APD) and benzodiazepines. In this review, we discuss contextually-relevant translational neuroscience in psychoses in PWE, recommended pharmacotherapy, and closely related topics such as alternating psychosis and the impact on seizure threshold of APD. While the level of evidence remains low, partly because of challenges inherent in performing multisite randomized control trials, prompt empirically based treatment of patients with psychosis is strongly recommended. Untreated psychotic episodes in PWE can have devastating effects on the patients and those supporting them [1].

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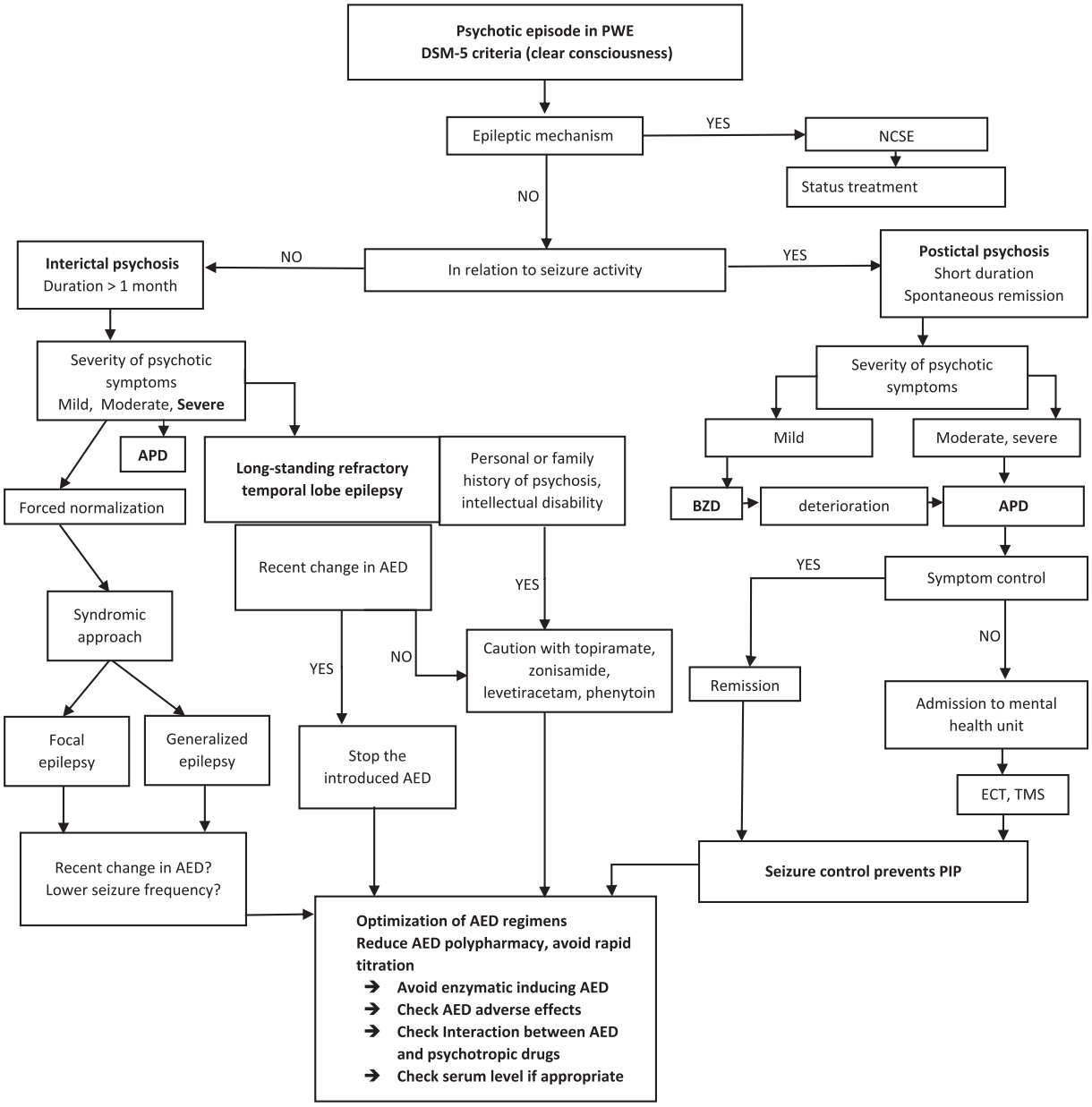

PWE: person with epilepsy. AED: Antiepileptic drug. APD: antipsychotic drug (neuroleptics). ECT: electroconvulsive therapy. TMS: transcranial magnetic stimulation. BZD: benzodiazepines. PIP postictal psychosis. NCSE: nonconvulsive status epilepticus

Fig. 1. Guidelines for treating psychotic episode in PWE.

2. Clinical classification of psychoses in PWE

Psychotic disorders are defined by the presence of delusions, hallucinations, disorganized thinking, and grossly disorganized and/or abnormal motor behavior, and may include negative symptoms Diagnostic and Statistical Manual of Mental Disorders (DSM-5). Consciousness is typically preserved. Psychoses in PWE can be clinically characterized into two main categories depending upon the temporal relationship of symptom emergence to seizures: interictal psychosis (IIP) and postictal psychosis (PIP) [2] (Table 1). Interictal psychosis refers to psychosis that occurs in clear consciousness in PWE with temporal onset *not* during or immediately following a seizure. A personal or family history of psychosis, intellectual disability, and the sum of previous seizures are recognized vulnerability factors [3]. Interictal psychosis can be further