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Treatment strategies in the postictal state

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Abstract

Postictal behaviors and symptoms often require special assessment and treatment. We review risk factors for postictal delirium and psychosis and management of agitated and confused behaviors in patients after seizures. Medical and emergency staff require careful training to manage behaviors associated with postictal delirium and psychosis in order to protect patients while their confusion resolves. Treatment of postictal states requires recognition of underlying neurological and systemic disorders associated with seizures and delirium such as metabolic disorders and nonconvulsive seizures. There is incomplete information about the causes and optimal treatments for seizure-related psychosis, however, postictal behaviors can usually be managed safely.

Keywords

Seizures; Delirium; Postictal; Psychosis; Epilepsy; Treatment

1. Introduction

Potential complications experienced during the postictal period include headache, functional deficits, neuropsychological deficits, and behavioral manifestations. Whether specific intervention is necessary (or possible) depends not only on the symptoms themselves, but also their place in the overall context of the patient's epileptic syndrome. Perhaps the most important step in evaluating patients with postictal complications, and deciding on appropriate treatment, is obtaining a full history, in advance if possible. A patient who has experienced severe postictal headache frequently, for example, is less likely to need urgent imaging studies than one who has never had such a headache before. Details of the seizure immediately preceding the postictal period are very important as well, as injury may have occurred or the seizure may have been unusually long or severe.

Management is straightforward for some clinical manifestations. Postictal migraines are common in patients with epilepsy and may respond to triptan therapy [1]. In contrast, more extensive evaluation may be needed. If a new focal deficit appears, especially if the precedent seizure has not been observed fully, imaging may be required to exclude intracranial injury. The type of evaluation may depend on the baseline diagnostic data available. When patients have prolonged confusion, and do not return to their pre-ictal function, nonconvulsive status may be present, and an EEG should be obtained. New metabolic derangements may have occurred, and clinical chemistry studies are important. Patients with initial seizures and prolonged confusion need thorough evaluations, usually

with cerebrospinal fluid examinations to exclude infections and inflammatory disorders. These data should also be obtained if a patient appears to have new, or persistent, neuropsychological deficits.

Behavioral syndromes, although usually brief, can pose special challenges for medical and nursing management, as well as for patients' family and friends. We discuss evaluation and treatment of two particularly troubling postictal phenomena, delirium and psychosis.

2. Postictal delirium

Postictal delirium is common and usually resolves rapidly; occasionally, however, it is prolonged and severe and may require special assessment. In a large British survey of patients with epilepsy and acute psychological disorders, 35% had complications of severe delirium, with behavioral or affective disorders [2]. Males predominated in the series; most patients had underlying cognitive and psychiatric disorders that appeared to leave them susceptible to developing postictal symptoms. Prolonged delirium should be attributed to seizures alone only after excluding other possible medical conditions associated with seizures and delirium [3]. These include complications of antiepileptic drug therapy (e.g., overdoses and valproic acid-induced hyperammonemia) and other structural, metabolic, and endocrine disturbances [4,5]. Some patients have multiple neurological conditions and may need broad medical screening for persisting delirium. Occasionally missed disorders include posterior reversible encephalopathy syndrome, withdrawal states, meningitis/encephalitis, complications of metabolic/endocrine disorders such as pontine myelinolysis and hypoglycemic injury, and phenytoin toxicity. Subtle ictal states are also often mistaken for "postictal" delirium: in a typical series of 22 elderly patients with apparent protracted postictal confusion (up to 5 days), EEGs were eventually obtained and revealed nonconvulsive status epilepticus [6].

For the majority of patients, the severity and duration of postictal delirium closely parallel the severity of their seizures [7]. Patients with prolonged convulsions and repetitive complex partial seizures often have severe and prolonged delirium, typically lasting from hours up to 1–2 days. A small group of patients, most with mental retardation and diffuse underlying cortical abnormalities, have been reported to have even longer periods—4 to 10 days—of postictal delirium after repetitive seizures [8].

After seizures most patients have "hypoactive" forms of delirium with confusion and withdrawn behavior. These may occasionally evolve into a "hyperactive" form of postictal delirium with agitated or unusual behaviors. Patients may require protection from wandering behaviors and can display reactive, aggressive behaviors if held [9,10]. Hyperactive postictal delirium is particularly common in patients with recurring or prolonged partial onset seizures and focal lesions. Most patients with postictal delirium do not require specific treatments, but simply need to be protected as their postictal confusion resolves. Patients need supportive care to avoid injuries; for example, windows should be closed and dangerous objects removed; bedrails with padding can be raised around the patient. Patients should be held down only if they require protection or may harm others. Police sometimes inappropriately struggle with patients in postictal states. Practical steps for managing uncontrolled behaviors in patients with hyperactive delirium have been detailed in a recent review [11]. Key points are that underlying cerebral disorders that contribute to delirium should be identified, if possible, prior to the episode, for example, hyponatremia, infections, and withdrawal states. Family members often can help calm and reassure confused patients. Patients with delirium should usually be restricted to a safe place, such as their hospital room; several staff standing in the doorway will usually convince even confused patients to remain in their room. Patients should have restraints placed only to protect them from

harming themselves or others, and this should be done through an approved hospital protocol. Even agitated patients will often cooperate in having temporary restraints placed if a staff member speaks to them in a direct, calm manner. If patients have very uncontrolled behaviors and need to be immediately restrained, they are best “overwhelmed” by a team of several staff members working together. Agitated, delirious patients usually “give up” and permit themselves to be kept in bed until their confusion subsides. Staff members need to be carefully trained on patient safety and to follow temporary restraint protocols; patients with postictal delirium have been held down improperly and suffered fractures and near asphyxiation. Agitated behaviors should not be permitted to escalate to the point that patients develop a severe “excited delirium” with autonomic hyperactivity and possible cardiac complications [12]. Patients with extremely violent, agitated behavior may occasionally require treatment with medications; however, doses should be titrated carefully to avoid sedation and worsened delirium. Haloperidol in 0.5- to 1-mg oral doses is usually effective for treating severely uncontrolled behaviors, with repeated or higher oral or intramuscular doses occasionally needed. Some patients with prolonged, moderately agitated delirium can be treated for several days with quetiapine fumarate (Seroquel). When agitated delirium is clearly due to recurring seizures, seizures and agitation can be treated with one or two 1-mg doses of lorazepam (oral or intravenous); however, repeated dosing may worsen delirium. If postictal delirium unexpectedly persists, nonconvulsive status epilepticus and other causes of delirium should be screened.

3. Postictal psychosis

Postictal psychosis can cause diagnostic confusion as well as therapeutic dilemmas. Does it represent a transient phenomenon, requiring only temporary treatment, or reveal previously undetected psychiatric illness? Are the clinical phenomena due to drug toxicity, another intervention such as epilepsy surgery, or a physiological change independent of the particular therapy that provoked it?

Hughlings Jackson suggested that “there is a transient epileptic paroxysm in every case of mental automatism occurring in epileptics before their mental automatism sets in” [13]. In a study of 536 “psychotic episodes,” about 25% were associated with disappearance of EEG discharges and may have occurred in the postictal period [14]. However, the same study found that patients who appeared “confused” were much more likely to have either bisynchronous spike-and-slow-wave discharges or diffuse delta activity than focal discharges [14]. An EEG should be obtained when a patient presents with “postictal” psychosis.

Could postictal psychoses or the phenomenon known as “forced normalization” be associated with ongoing seizure activity not detectable at the surface [15]? Only a few studies bear on this possibility. Two patients with implanted electrodes did not have clear ictal discharges during postictal psychoses [16,17]. In contrast, several small studies found patients with postictal psychosis had increased frontal or temporal perfusion on technetium-99m single-photon-emission computed tomography, suggesting the possibility of ongoing seizure activity associated with increased cerebral blood flow [18–20]. Are postictal psychoses really postictal? Clearly, additional research is needed to investigate their pathophysiology and treatment. Additional antiepileptic drug treatment, rather than antipsychotic drugs, might be needed.

Some clinical features predict onset and prognosis of postictal psychoses. In a recent study, postictal psychosis was associated with extratemporal seizure onset, bilateral interictal epileptiform activity, secondary generalization, and history of encephalitis, as well as a family history of psychiatric disorder [21]. Postictal psychosis was a predictor of subsequent

interictal psychosis on univariate but not multivariate analysis [22]. Most episodes resolve in about a week [23]. In a study of 151 episodes, mean duration was 9–10 days, and 95% resolved within 1 month [24]. History of interictal psychosis, family history, and impaired neuropsychological function predicted longer duration. An initial episode may not predict the need for long-term maintenance therapy.

Antiepileptic drugs (AEDs) implicated in the onset of psychoses, or “mania,” often associated with overdoses, in up to 15% of cases include phenytoin, ethosuximide, and carbamazepine among the older AEDs, and topiramate, vigabatrin, levetiracetam, and possibly zonisamide among the newer drugs [25,26]. There have been case reports and small series associating gabapentin with aggressive behavior in children [27]. However, there are few controlled data, except for vigabatrin [26]. Potential factors that might interact with AEDs and affect the risk of AED-induced behavioral disturbances include rapid escalation to high doses, history of febrile convulsions or status, and previous psychiatric history. Despite the experience with vigabatrin, it has been suggested that “GABAergic” AEDs might ameliorate symptoms such as insomnia, agitation, anxiety, and racing thoughts [28]. In one controlled trial, tiagabine did not increase the incidence of psychosis [26].

The value of antipsychotic treatment in postictal psychosis requires further study. Despite their role in symptomatic relief, there is no clear effect of neuroleptics on duration or prognosis of postictal psychoses [23]. For psychoses associated with epilepsy in general, a review of the literature up to 2008 revealed only one underpowered, randomized controlled trial from which few conclusions could be drawn [29]. Some studies report that postictal psychoses are triggered by seizure clusters, particularly during AED withdrawal for video/EEG monitoring [30,31]. Restarting AEDs may help these patients, but evidence is anecdotal.

One study prospectively investigated psychopathology in patients whose AEDs were withdrawn during video/EEG monitoring [32]. Anxiety and depression ratings, as well as seizures, increased significantly. In patients restarted on AEDs, psychiatric ratings returned to baseline within 2 weeks. AED withdrawal-emergent psychopathology was only weakly related to increased seizures. AEDs with potential “mood-stabilizing” effects such as carbamazepine, valproic acid, and lamotrigine might be of potential benefit during postictal psychoses.

Some psychotropic drugs, in addition to their other side effects, have the potential disadvantage of lowering seizure thresholds. The anti-depressants maprotiline and clomipramine and the neuroleptics chlorpromazine and clozapine are associated with increased risk [33,34]. Phenelzine, tranylcypromine, fluoxetine, paroxetine, sertraline, venlafaxine, trazodone, fluphenazine, haloperidol, pimozide, perphenazine, trifluoperazine, and risperidone appear to be associated with low seizure risk.

Drug interactions may be an issue in treating, or triggering, postictal psychosis. AEDs that induce CYP 3A4 can reduce concentrations of some selective serotonin reuptake inhibitors (SSRIs) [35]. Withdrawal of these AEDs during video/EEG monitoring might lead to sudden increases in antidepressant levels for patients on SSRIs and possibly contribute to a postictal psychosis. Restarting an enzyme-inducing AED in the postictal period might reduce the levels of antipsychotic drugs such as haloperidol [34].

One particularly difficult management issue is postictal violence, reported to be higher during postictal (suicide attempts were as well) than interictal psychoses [36]. A systematic study found that violence during seizures was rare, nondirected, and almost always brief [37]. Six of 1300 patients in an epilepsy clinic had a history of postictal aggression; in two, the episodes were associated with psychoses [38].

As a large proportion of postictal psychosis episodes occur out of hospital, it is very important to instruct families, and, if possible, patients themselves, to recognize their onset and take appropriate measures, such as making sure patients are not left alone.

The best therapy for postictal psychosis is uncertain. Clinical trials need to be performed, with patients stratified for potential precipitants such as AED withdrawal, using standardized rating scales. Sublingual lorazepam or rectal valproic acid could be tested for episodes occurring out of hospital.

In addition to psychotropic medications and AEDs, a number of other therapeutic modalities could be considered. Vagus nerve stimulation, because it requires surgical intervention, could not be started during a psychotic episode, but if a patient has a vagus nerve stimulator or another system implanted already, stimulation parameters could be adjusted in a manner that could test the hypothesis that postictal psychosis actually may be related to ongoing seizure activity. Another modality, repetitive transcranial magnetic stimulation (rTMS), can enhance (via rapid stimulation) or reduce (via slow stimulation) cortical excitability [39]. rTMS is noninvasive and can be applied acutely at the bedside. Stimulation at 1 Hz or less has been shown to have at least some antiseizure effects, which might be beneficial if the psychotic manifestations are related to unrecognized or undetected seizure activity. Stimulation at more rapid rates, in contrast, may rarely induce seizures. This therapeutic approach should be considered only in the context of a controlled clinical trial.

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