Strategies and Rationale for Management of Postictal Psychosis

Among patients who have had epilepsy for a prolonged period of time, seizures may produce psychosis. Controlling seizures is key to management.

What is Postictal Psychosis?
Postictal psychosis (PP) has been recognized for more than a century. Although the exact definition of PP varied from author to author, most agree that it occurs in people who have chronic epilepsy—often a person has had epilepsy for more than 10 years. In one series, the average time from onset of seizures to onset of PP was 15-22 years. The average age of the persons affected was 32-35. In other words, PP is common, affecting as many as 25-50 percent.

PP occurs most often after generalized tonic-clonic seizures (GTCs). In one series of patients, a GTC preceded the PP in 86 percent. It has also been reported after a cluster of complex partial seizures. When it occurs, it does not begin immediately after the seizure. Instead, it starts within one to six days after the seizure has ended. On average, the onset of PP was 2.5 days after the seizure. In between the seizure and PP, after the patient had recovered from the seizure itself, there was a lucid period.

What Causes PP?
The cause of postictal psychosis is unclear. Alper evaluated 59...
consecutive patients with refractory partial epilepsy. All of them had been admitted for video-EEG monitoring for the purpose of a presurgical evaluation. All experienced seizures (as required for the evaluation for epilepsy surgery), and all 59 developed PP. He compared this group to 94 people who had been admitted for the same reason but who had not developed PP.

When Alper examined where the seizures started, he discovered that people with extratemporal epilepsy were more likely to develop PP than those with temporal lobe epilepsy (P<0.036). Interestingly, this is the exact opposite of what others have found. The presence of bilateral interictal epileptiform discharges, possibly indicating bilateral cerebral injury or dysfunction, was significantly associated with PP (P<0.017). As other investigators had found, Alper noted that PP occurred more often after GTCs (P<0.049), after encephalitis (P<0.018), and if there was a family history of psychiatric illness (P<0.007).

The fact that people who have bilateral cerebral dysfunction are more likely to experience PP may be significant. Further, it is interesting that PP occurs more often after a generalized tonic-clonic seizure. A generalized tonic-clonic seizure, by definition, is an abnormal electrical discharge that involves both sides of the brain. In other words, PP tends to occur when both hemispheres are affected (whether by the injury, seizure, or both). It seems likely that large, interconnected networks of neurons are needed in order for PP to occur.

Metabolic studies have shown increased metabolism in both the frontal and temporal lobes during PP. Some have proposed that the increased metabolism is due to a “rebound” effect. After a seizure, there is postictal depression of cerebral activity. Later, as the PP develops, there may be a compensatory increase in cerebral metabolism. This is analogous to the situation that occurs when a person withdraws from a CNS depressant. For instance, benzodiazepine withdrawal can cause delirium and psychosis. Further research is needed in order to better understand why and how PP develops.

Treatment
Fortunately, PP often responds very rapidly to low doses of medication; however, the best treatment for PP is to control the seizures! When PP occurs, benzodiazepines and antipsychotic medications are most often used (Figure #3). The use of several antipsychotics has been proposed, and it seems that all are effective. One concern that many physicians have with the use of these medications is that they have been reported to cause seizures. Of course, this is exactly the patient population in which the medication is being prescribed, and so the fear is that seizures will worsen when an antipsychotic is started.

Almost all antipsychotic medications are mildly epileptogenic, with seizures occurring 0.1 to 1.5 percent of the time. In one series, the incidence of seizures was 0.3 percent for resperidone and 0.9 percent for quetiapine and olanzepine. It is thought that this effect is dose-related: an increased rate of seizures may occur at higher doses of antipsychotic medications. For instance, the incidence of seizures was one percent for clozapine at low doses (< 300 mg), 2.7 percent at moderate doses, and 4.4 percent at high doses (600-900mg/d). In contrast, Devinsky described no dose effect in 5,000 patients taking clozapine. In addition to seizures, antipsychotic medications have been reported to affect the EEG. The EEG may change in up to seven percent of individuals; however, a change in the EEG does not translate into a clinical problem.
Although there is appropriate concern for worsening seizures, the likelihood that this will occur is very small. First, the antipsychotic medications are usually needed in low doses. If there is a dose-related effect, using low doses minimizes this risk. Further, persons with epilepsy are already taking antiseizure medications, which likely will help to protect them to some degree. In short, given the morbidity and mortality associated with postictal psychosis, the benefits of treatment far outweigh the risks.

Conclusions
PP may occur in 25 percent of people with refractory epilepsy. It occurs most often after bilateral cerebral injury, and after one or more generalized tonic-clonic seizures. PP does not start immediately after the seizure(s); instead, there is usually a lucid period of one to six days before PP begins. Once present, PP lasts from several hours to as long as two to three months. Fortunately, it responds very well to treatment with either benzodiazepines or antipsychotic medications, often at low doses. As PP is short-lived, long-term use of antipsychotics is usually not needed. Instead, the best treatment for PP is to prevent it by eliminating its cause: seizures.

Table 3. Frequently used Treatments for Postictal Psychosis (PP)

Common side effects of antipsychotic medications include sleepiness and weight gain. Clozapine requires special monitoring, due to problems with agranulocytosis.

<table>
<thead>
<tr>
<th>Antipsychotic</th>
<th>Start Dose</th>
<th>Dose Range</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>clozapine</td>
<td>12.5mg</td>
<td>300-700mg</td>
<td>900mg</td>
</tr>
<tr>
<td>olanzepine</td>
<td>5mg</td>
<td>5-15mg</td>
<td>20mg</td>
</tr>
<tr>
<td>quetiapine</td>
<td>25-100mg</td>
<td>400-600mg</td>
<td>800mg</td>
</tr>
<tr>
<td>risperidone</td>
<td>2mg</td>
<td>4-6mg</td>
<td>16mg</td>
</tr>
</tbody>
</table>

Adapted from Elliott 2009

1. Devinsky O. Postictal psychosis: common, dangerous, and treatable. Epilepsy Currents 2008:8(2);31-34.