Addressing Psychiatric Comorbidities in Patients With Epilepsy

October 01, 2006 | ADHD [1], Bipolar Disorder [2], Comorbidity In Psychiatry [3], Major Depressive Disorder [4], Alcohol Abuse [5], Amphetamine Related Disorders [6] By Dee Rapposelli [7] and Dee Rapposelli [7]

In a presentation given at the midyear meeting of the American Epilepsy Society, Andres Kanner, MD cited studies from the literature showing that the rates of depression, anxiety, psychosis, and attention-deficit/hyperactivity disorder (ADHD) are significantly higher among persons with epilepsy than among the general population.

Persons with epilepsy have a high incidence of psychiatric comorbidities, and these comorbidities have a direct effect on treatment outcome, according to Andres Kanner, MD, professor of neurological sciences, senior attending physician in neurology, and director of the Laboratory of Electro-encephalography and Video-EEG-Telemetry at Rush University Medical Center in Chicago. In a presentation given this past June during the midyear meeting of the American Epilepsy Society in Oak Brook, Illinois, Kanner cited studies from the literature showing that the rates of depression, anxiety, psychosis, and attention-deficit/hyperactivity disorder (ADHD) are significantly higher among persons with epilepsy than among the general population (Table) [1-5]. Kanner provided a strong argument that epilepsy and depression, in particular, are closely tied and that effective treatment of the epilepsy is often contingent on appropriate identification and treatment of the psychiatric comorbidity as well.

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<thead>
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<th>TABLE</th>
<th>Prevalence of psychiatric disorders in the general and epileptic populations</th>
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<td></td>
<td>General population (%)</td>
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<tr>
<td>Major depression</td>
<td>2 - 4</td>
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<tr>
<td>Anxiety disorder²</td>
<td>2.5 - 6.5</td>
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<tr>
<td>Psychosis³</td>
<td>0.5 - 0.7</td>
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<tr>
<td>ADHD⁴,⁵</td>
<td>2 - 10</td>
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ADHD, attention-deficit/hyperactivity disorder.

"Psychiatric disorders are having a direct effect on treatment of seizures," he contended. "Not only is severe epilepsy associated with a higher risk of depression, but we are now asking whether depression may be a biologic marker for severe epilepsy," he said.

A study by Kanner and colleagues at Rush confirmed published findings suggesting that epilepsy and depression often go hand in hand. They found a history of psychiatric comorbidity in 49 (54%) of 90 patients who underwent surgery (temporal lobe resections) for seizure control. Major depression was the most common psychiatric disorder, affecting 84% of patients who had a history of psychiatric intervention. Of crucial import was that, among the 90 patients who underwent surgery for management of epilepsy, postoperative transient seizures occurred in twice as many patients who had a history of depression as patients who lacked such a history. Furthermore, disabling...
postoperative seizures were more than twice as likely to occur in patients with depression as in patients without depression (51% vs 22%).

**What to do?**

Proper treatment of epilepsy in patients with comorbid psychiatric conditions requires identification of the psychiatric disorder and either treating it or referring the patient to a mental health specialist, Kanner said. SSRIs are the first choice for depression, followed by serotonin-norepinephrine reuptake inhibitors (SNRIs). Kanner strongly urged neurologists to rule out bipolar disorder (BPD) in seemingly depressed patients and equally urged neurologists to refer, rather than troubleshoot, patients suspected of having BPD, patients who are suicidal, and patients who do not respond to second-line (ie, SNRI) therapy.

Kanner noted that SSRIs are safe in patients with epilepsy, but the agents should not be discontinued abruptly to avoid a flare of depression. He also cautioned that, although monoamine oxidase inhibitors are classic antidepressants, "they are drugs that neurologists should not be using. Dispensing of such agents should be left to psychiatrists."

To allay fears that antidepressants might trigger seizures, Kanner related data from placebo-controlled trials showing that seizure episodes were much more likely to occur among patients receiving placebo than an antidepressant (535 seizure episodes per 100,000 years among patients receiving antidepressants, compared with 1502 seizure episodes per 100,000 years among patients receiving placebo). However, certain agents should be avoided in patients with epilepsy, including maprotiline (Ludiomil), bupropion (Wellbutrin, Zyban), and clomipramine (Anafranil). He reminded the audience that depression and anxiety disorders often coexist. "SSRIs are very effective," he said, although no studies have looked into their use for treating anxiety in patients with epilepsy. Although benzodiazepines and SNRIs might be other therapeutic choices, they may cause additive toxicities when given with certain antiepileptic drugs. **Postictal psychosis**

A separate comorbid problem is the psychosis that can emerge as a complication of an epileptic event. A key symptom of an impending psychotic episode during the postictal period is insomnia. "Always alert the patient's family to call you if the patient reports having insomnia. Insomnia during this time heralds psychosis," Kanner told the audience.

"Postictal psychosis can be aborted with early pharmacologic intervention," he said, and related a case study in which the patient's family was instructed to administer 2 mg of risperidone (Risperdal) to the patient at the first sign of insomnia after a cluster of generalized tonic-clonic seizures and titrate up to 4 mg/d for the next 2 days, followed by 1 mg/d for an additional 2 days. Postictal psychosis can also evolve into interictal psychosis, necessitating regular use of an antipsychotic.

In patients with epilepsy who experience psychotic episodes, atypical antipsychotic agents are recommended over conventional agents because the risk of extrapyramidal adverse effects is low, they do not raise serum prolactin levels, and they may have mood-stabilizing properties—none of which can be said for conventional agents. Antipsychotic agents in general can exacerbate seizure activity, however. Chlorpromazine (Thorazine) at dosages exceeding 1000 mg/d and clozapine (Clozaril) at dosages exceeding 600 mg/d are the worst offenders, said Kanner. He added that among the older agents, haloperidol (Haldol) and molindone (Moban) are less likely to aggravate seizure activity.

In addition, antipsychotic agents can have additive toxic effects in combination with antiepileptic agents, such as phenytoin (Dilantin, Phenytek). "Therefore, when antipsychotic drugs are used in patients with epilepsy, the dose should be escalated slowly, and with certain drugs, lower doses should be used," Kanner instructed. **ADHD and epilepsy**

The prevalence of ADHD in children with epilepsy is particularly high and it may also be high in adults with epilepsy, although documentation about its prevalence in adult patients with epilepsy is lacking. Whereas ADHD prevalence in the general pediatric population is 4% to 12%, prevalence among children with epilepsy is 20% to 60%, reported Kanner. The prevalence of adult ADHD in the general population is 2% to 7%. "The high rate of ADHD among persons with epilepsy leads us to ask—as we are asking about depression—are ADHD and epilepsy linked?" said Kanner.

"The DSM-IV criteria for diagnosis of adult ADHD are based on 3 critical elements: childhood onset; presence of significant symptoms; and impairment in at least 2 domains, including school or work, social interaction, or home life," he continued. It can be treated with CNS stimulants, "which don't cause seizures, although the idea has been that they do." He noted, however, that enzyme-inducing antiepileptic drugs increase clearance of amphetamine compounds such as dextroamphetamine (Dexedrine) and magnesium pemoline (Cylert). Other interventions include atomoxetine (Strattera) and tricyclic antidepressants such as imipramine (Tofranil) and desipramine (Norpramin, Pertofrane). Tricyclics should be started at low doses and slowly titrated up. Furthermore, it should be noted that enzyme-inducing antiepileptic drugs will
cause tricyclic levels to drop.
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References:

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