

# SUICIDE IN PATIENTS WITH EPILEPSY

**Epilepsy and Risk of Suicide: A Population-Based Case–Control Study.** Christensen J, Vestergaard M, Mortensen PB, Sidenius P, Agerbo E. *Lancet Neurology* 2007;6(8):693–698. BACKGROUND: Studies have linked epilepsy with an increased suicide risk, but the association might be modified by psychiatric, demographic, and socioeconomic factors. METHODS: Suicide cases were identified in the Cause of Death Register in Denmark from 1981 to 1997. Up to 20 controls, matched by sex, birth year, and calendar date, were assigned to each suicide case. FINDINGS: We identified 21,169 cases of suicide and 423,128 controls. In total, 492 (2.32%) individuals who committed suicide had epilepsy compared with 3,140 (0.74%) controls, corresponding to a three times higher risk (rate ratio [RR] 3.17 [95% CI 2.88–3.50];  $p < 0.0001$ ). The RR remained high after excluding those with a history of psychiatric disease and adjusting for socioeconomic factors (1.99, 1.71–2.32;  $p < 0.0001$ ). The highest risk of suicide was identified in patients with epilepsy and comorbid psychiatric disease, even after adjusting for socioeconomic factors (13.7, 11.8–16.0;  $p < 0.0001$ ). In individuals with epilepsy, the highest risk of suicide was found during the first half year after diagnosis was made (5.35, 3.43–8.33;  $p < 0.0001$ ), and was especially high in those with a history of comorbid psychiatric disease (29.2, 16.4–51.9;  $p < 0.0001$ ). INTERPRETATION: Individuals with epilepsy have a higher risk of suicide, even if coexisting psychiatric disease, demographic differences, and socioeconomic factors are taken into account. Our study identifies people with newly diagnosed epilepsy as a vulnerable group that require special attention.

**Depression and Suicide in Epileptic Victims: A Population-Based Study of Suicide Victims during the Years 1988–2002 in Northern Finland.** Mainio A, Alamäki K, Karvonen K, Hakko H, Särkioja T, Räsänen P. *Epilepsy Behav* 2007; 11:389–393. Patients with epilepsy are known to have comorbid affective disorders and a higher risk for suicide compared with the general population. Epilepsy, depression, and suicidal behavior have been shown to have common pathogenic mechanisms in their etiology. We evaluated the association between epilepsy, suicidal behavior, and depression by using the comprehensive database of all suicides ( $n = 1,877$ ) committed in northern Finland during the years 1988–2002 with information on all hospital-treated somatic and psychiatric disorders. Hospital-treated epilepsy occurred in 1.3% of the victims. Compared with other suicide victims, those with epilepsy were more often female, were older, and had significantly more often suffered from depression. Epilepsy was first diagnosed 8.8 (3.9–11.6) years before suicide, and depression, about 1 year after epilepsy diagnosis. Interictal depression among patients with chronic epilepsy is often classified as atypical or chronic depression, or it can mimic a dysthymic disorder. Therefore, diagnosis and treatment of depression among patients with epilepsy constitute a great challenge in clinical practice.

## COMMENTARY

In 2003, the United States Agency for Healthcare Research and Quality concluded that there was insufficient evidence

to determine whether patients with refractory epilepsy are at increased risk of suicide (1). A recent meta-analysis reviewed 29 studies with 187 suicides out of a total of 50,814 patients (2). They found that suicide in patients with epilepsy is more frequent than in the general population, but variance in the results, including some cohorts with lower suicide rates for epilepsy patients than for patients with other disorders, limited a definitive conclusion.

Christensen et al. conducted a large population-based, case-control study of 21,169 individuals (492 with epilepsy) who committed suicide from 1980 to 1997 in Denmark. These cases were matched to 423,128 controls in order to assess the association between epilepsy and suicide, controlling for psychiatric, demographic, and socioeconomic factors. They found that suicide was increased over threefold for people with epilepsy and that this increase was still significant after adjusting for psychiatric and socioeconomic factors. The risk of suicide was particularly high in those patients with comorbid psychiatric disease (over 29-fold), although it was high even in those without history of psychiatric diagnosis (almost twofold). The risk was increased for individuals diagnosed in the prior half year (over fivefold) and decreased with increasing duration of epilepsy. The authors did not examine the timing of suicide in relationship to last seizure or to the influence of seizure type, frequency, and severity. In addition, the possible effects of treatments for seizures and depression were not investigated.

In evaluating 1,877 suicides committed in northern Finland from 1988 to 2002, Mainio et al. compared 25 patients with epilepsy treated in the hospital setting to the other 1,852 suicide victims. They found that suicide victims with epilepsy were slightly older (48 vs 43 years old), more likely to have depression (40% vs 19%), and less likely to be under the influence of alcohol at the time of suicide. Diagnosis of epilepsy occurred, on average, 1 year before diagnosis of depression and 8.8 years before suicide. There was an atypically large proportion of patients with generalized (92%) compared with partial (8%) seizure diagnosis, leading the authors to conclude that patients with generalized seizures may be at increased risk. Limitations included the small sample size, lack of patients treated solely as outpatients, and additional factors noted above for the Christensen et al. study.

Depression is a common problem for patients with epilepsy. The prevalence of depression in epilepsy has been reported to range from 3 to 60 percent compared with 2 to 4 percent in the general population (3). The risk of depression is highest for those individuals with refractory epilepsy. The presence of depression is more predictive of a patient's quality of life than seizure frequency and has been linked to increased use of health resources (3,4). Epilepsy is a chronic disorder that impacts psychosocial functioning; thus, one might conclude that depression in epilepsy is simply reactive or situational.

The prevalence of depression in epilepsy, however, appears to be higher than depression in other chronic diseases of similar severity. For example, a population-based study of 181,000 individuals found that lifetime prevalence of depression for patients with epilepsy was 29% compared to 17% in diabetes, 16% in asthma, and 8.7% in those without chronic disease (5). In addition, there appears to be a bidirectional relationship between epilepsy and depression (6). Not only is epilepsy a risk factor for depression, but it also appears that depression is a risk factor for epilepsy. In a case-control study of patients with new onset epilepsy in Sweden, patients with epilepsy were found to be seven times more likely to have a history of depression (i.e., preceding the onset of epilepsy) than controls (7). Similarly, elderly patients with new onset epilepsy were four times more likely to have a history of depression prior to epilepsy onset, when compared with controls in a population-based study (8). Another study of children and adults with epilepsy also found that depression was a risk factor and that suicide attempt was an even greater risk factor for subsequent unprovoked seizure (9). It is possible that epilepsy and depression are both symptoms of dysfunction within overlapping neuronal networks (e.g., limbic regions).

Given the relationship of depression to quality-of-life perceptions, healthcare utilization, compliance, and risk of suicide, it would seem appropriate to routinely evaluate epilepsy patients for depression and, when present, consider therapeutic interventions. However, depression in patients with epilepsy is frequently unrecognized and untreated (3,6). In a refractory group of patients undergoing video-EEG monitoring, 50% were depressed and 19% had experienced recent suicidal ideation; however, only 17% of these individuals were being treated with antidepressant medication (6). A survey of randomly selected neurologists from the American Academy of Neurology found that 83% did not routinely screen patients with epilepsy for depression, but 85% of these physicians answered that they would routinely screen if a well-controlled study demonstrated that treatment of depression could improve compliance and quality of life in epilepsy (3).

Factors that contribute to the under-recognition and inadequate treatment of depression for patients with epilepsy include: 1) an apparent lack of appreciation of the common occurrence and impact of depression, 2) the failure to screen or even consider depression as an important issue for clinical care, 3) a lack of well-conducted studies demonstrating the effect of cognitive-behavioral or pharmacological therapies directed at depression, and 4) an increased difficulty in diagnosis because depression in epilepsy appears different or has features that are attributed to the epilepsy itself. For example, depression in epilepsy commonly has an atypical presentation, which may resemble dysthymic disorder and fail to meet DSM-IV diagnostic criteria for depression (6). Dysthymic-like

disorders in epilepsy are characterized by symptoms of irritability and reduced frustration tolerance but fewer symptoms of anhedonia.

How might the rate of suicides be reduced in patients with epilepsy? Although additional research is needed, there are some actions that would seem logical. An awareness of the increased risk of depression and suicide in patients with epilepsy is important for clinicians who care for these patients. Identifying those patients with epilepsy who suffer from depression will allow initiation of treatment interventions for mood disorder and also will assist in identifying those individuals at particular risk for suicide so that preventive measures can be taken.

by Kimford J. Meador, MD

## References

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