Suicide Risk Tied to Acne Severity, Not Treatment

Study on association between isotretinoin use, suicidal behavior focuses on timing of treatment.

BY JENNIE SMITH

FROM BMJ

A large, retrospective cohort study is the latest to look at the association between isotretinoin and attempted suicide. Concerns about a link between isotretinoin and suicidal behavior have abounded for years, although previous studies have failed to show a conclusive link.

By studying when (before, during, or up to 15 years after treatment) suicidal behavior is most likely to occur in relation to treatment, researchers found that although the risk is increased during and up to 1 year after treatment, such risk is more likely related to the psychological effects associated with the disease – severe acne – than with the isotretinoin, and may be affected by treatment failure.

Pharmacoepidemiologist Anders Sundström of the Karolinska Institute in Stockholm and colleagues examined named records for 5,756 Swedish patients (aged 15-49 years) who were prescribed isotretinoin in 1980-1989. The men had a mean age of 22.3 years (women, 27.1 years) at first prescription, and were taking mean daily doses of 44.5 mg and 39.2 mg isotretinoin, respectively, for severe acne. Mean length of treatment was 4 months for men and 3.9 months for women. The patients' clinical records were compared with hospital-discharge and cause-of-death registers for the 1980-2001 period.

In all, 128 patients in the cohort were hospitalized for attempted suicide on 210 occasions during the study period; there were 24 completed suicides during this time. When the study cohort was compared with the general population, the standardized incidence ratios for suicide attempts rose from 0.89 (95% confidence interval, 0.54-1.37) at 3 years before treatment to 1.36 (95% CI, 0.65-2.50) in the year before treatment for first attempts, and from 0.99 (95% CI, 0.65-1.44) at 3 years before treatment to 1.57 (95% CI, 0.86-2.63) in the year before treatment for all attempts.

The risks were shown to be highest within 6 months after the start of treatment: 1.93 (95% CI, 1.08-3.18) for first attempts and 1.78 (95% CI, 1.04-2.85) for all attempts. The investigators also found that women who made suicide attempts received two or three treatments more often than did women who did not attempt suicide, suggesting treatment failure as a possible contributor.

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After treatment, the standardized incidence ratio declined to 0.97 (95% CI, 0.64-1.40) for first attempts and 1.04 (95% CI, 0.74-1.43) for all attempts within 3 years. After 3 years and for the duration of follow-up, the rate remained on par with the background rate for the population.

The investigators concluded that "an increased risk of attempted suicide was apparent up to six months after the end of treatment with isotretinoin." However, they wrote, "the risk of attempted suicide was already rising before treatment, so an additional risk due to the isotretinoin treatment cannot be established." Patients with a history of suicide attempts need not be denied treatment with isotretinoin, they wrote, but "close monitoring of patients for suicidal behavior for up to a year after treatment has ended" would be advisable (BMJ 2010 Nov. 12 [doi:10/1136/bmj.c5812]).

The investigators acknowledged some limitations of their study, including a lack of data on potential confounding factors other than age, sex, and calendar year. Low statistical precision was also a limitation: Although standardized incidence ratios were clearly rising before treatment, they wrote, "we found no statistical significance until six months after treatment. In the internal cohort crossover analysis – that is, analyzing outcomes before and after treatment in the same population – the differences in incidence did not reach statistical significance, making the estimated number needed to harm uncertain."

Also, they wrote, "we had no information on the effect of treatment. A bias would exist if the patients who made suicide attempts had a poorer effect of treatment than did those who did not make such attempts. In that case, the suicidal behavior should be attributed to the treatment resistant acne and not to the treatment. However, such bias would only strengthen the assumed association between severe acne and suicidal behavior."

In an editorial comment, Dr. Parker Magin of the University of Newcastle in Callaghan, New South Wales, Australia, and Dr. John Sullivan of the University of New South Wales in Sydney, said that clinicians could draw important practical conclusions from the study – namely, that during and after treatment with isotretinoin (and especially when treatment is unsuccessful), "patients should be carefully monitored for depression and suicidal thoughts. Patients probably have an increased risk before treatment, however, so all patients with acne of a severity for which isotretinoin is indicated should have psychosocial factors and suicidal intent monitored."

As for who should perform the monitoring, Dr. Magin said that although dermatologists generally take on that role, general practitioners "have more appropriate training and experience in psychological medicine … and could add invaluable expertise in the psychological aspects of management in a shared care model with dermatologists." Families of patients, Dr. Magin added, may also help with monitoring. (BMJ 2010 Nov. 12 [doi:10.1136/bmj.c5866])

The study was funded by the Swedish Research Council. Mr. Sundström and his coauthors declared that they had no conflicts of interest. Dr. Magin and Dr. Sullivan have been members of All About Acne, an organization supported by unrestricted educational grants from drug companies. Neither Dr. Magin nor Dr. Sullivan received payment from the organization, and the drug companies that provide support do not manufacture isotretinoin. ■

Previous Findings on Epilepsy, Psych Comorbidities Confirmed

BY PATRICE WENDLING

FROM THE EPILEPSY AND DEPRESSIVE DISORDERS CONFERENCE

CHICAGO – A past psychiatric history, depressive disorder diagnosis, and current use of psychotropic medications were significantly associated with a higher potential for suicidal behavior.

"Suicide risk in patients with epilepsy reflects the higher incidence of psychiatric comorbidity in this population rather than any neurologic or demographic factor," reported Robert C. Doss, Psy.D., and Dr. Patricia E. Penovich, of the Minnesota Epilepsy Group in St. Paul. This finding confirms what has been established in previous research.

VITALS

Major Finding: SPI-positive patients were significantly more likely than were SPI-negative patients to have a depressive disorder diagnosis (80% vs. 19%, respectively), previous psychiatric history (90% vs. 27%), and to currently use psychotropic medications (50% vs. 13%), all risk factors for suicide.

Data Source: Analysis of 58 consecutive adults at an inpatient epilepsy service.

Disclosures: The authors disclosed no conflicts of interest.

About 30% of people with epilepsy have a major depressive disorder, and research suggests that about 50% of the time they are never treated for the problem, according to the Epilepsy Foundation.

Moreover, the suicide rate in persons with epilepsy is on average 12%, compared with about 1% in the general population (Epilepsy Behav. 2003;4:[Suppl. 3]S31-8). Given the prevalence of this problem and the 2008 warning by the Food and Drug Administration regarding the association between suicidality and antiepileptic drugs, further understanding of this matter is urgently needed, Dr. Doss and Dr. Penovich reported in a poster at the conference.

Upon admission, the 58 patients in the sample underwent long-term video-EEG, neuropsychological testing, personality assessment using the Personality Assessment Inventory, social work evaluation, and if indicated, psychology and/or psychiatry consultation.

Ten patients (mean age, 36 years) showed clinical elevations on the inventory's Suicide Potential Index (SPI) and 48 patients (mean age, 38 years) did not. The SPI consists of 20 features on the inventory that tap what are described as key risk factors for completed suicide in the suicidality literature.

Patients with a positive SPI were significantly more likely than were those with a negative SPI to have a depressive disorder diagnosis (80% vs. 19%, respectively), to have a previous psychiatric history (90% vs. 27%), and to currently use psychotropic medications (50% vs. 13%), Dr. Doss and Dr. Penovich reported.

No other variables, including age, gender, education, duration of epilepsy, temporal lobe epilepsy, complex partial seizures, other neurologic history, epilepsy surgery, number of anti-epileptic drugs, seizure frequency, anxiety disorder diagnosis, or cognitive status were found to significantly differentiate the two groups.

The lifetime prevalence rate of suicide and suicide attempts has been reported to be particularly high in patients with temporal lobe epilepsy and those who have had epilepsy surgery when compared with the general population, but neither risk factor stood out in the current analysis. Temporal lobe epilepsy was present in 30% of the SPI-positive group, compared with 55% of the SPI-negative group, and epilepsy surgery in 20%, compared with 10%.

Also, the number of antiepileptic drugs was similar in both groups at 2.0 and 1.8.

"Routine care of persons with epilepsy should include screening for both current and past psychiatric symptoms," the authors concluded. "Particular attention should be paid to persons with epilepsy with a clear psychiatric history."

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