

Study finds lithium cuts bipolar suicides

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An inexpensive drug for bipolar disorder that has been shunted aside in favor of newer, more heavily marketed drugs is actually much more effective at preventing suicides and should be the drug of choice for first treatment of such patients, researchers will report today.

Lithium is just as effective as the newer Depakote at preventing the mood swings associated with the widespread, disabling disorder, but patients who take Depakote are 2.7 times as likely to commit suicide as those who take lithium. That is a major difference because suicide is 10 to 20 times more common among bipolar patients than in society at large.

"Psychiatry has never been able to say that what we do saves lives, which is the ultimate goal of medicine," said Dr. Frederick Goodwin, of the George Washington University Medical Center, who led the study of more than 20,000 patients. "With lithium, now we can."

The new study was funded by Belgium's Solvay Pharmaceuticals, manufacturers of Lithobid, a slow-release lithium preparation approved for the treatment of the mood swings associated with the disorder.

The findings, in today's *Journal of the American Medical Association*, "makes an argument that lithium should be reconsidered as the first-line treatment (for bipolar disorder), which is probably where it should have been all along," added Dr. Norman Sussman, a psychopharmacologist at New York University who was not involved in the study. "If we can reduce the risk of suicide, that is a good argument for using the drug."

Bipolar disorder — in which patients swing between deep depression and manic highs — is one of the most common mental problems in the U.S., affecting 1.3 to 1.5 percent of the population. Up to one in every five bipolar patients attempts suicide.

Thirty years ago, there were no drugs to treat the disorder. Then researchers discovered that lithium smoothed the mood swings in up to two-thirds of patients. It was the first important drug for mental problems of any sort. But the drug could not be patented, so pharmaceutical companies couldn't afford research and promotion. Nonetheless, lithium was widely used until Depakote — generically known as divalproex — became available in the early 1990s.

A spokesman for Abbott Laboratories, which manufactures Depakote, dismissed the findings. Abbott's John Leonard, a vice

president in charge of pharmaceutical development, said the study contained many flaws. It was a retrospective analysis. It did not take into account that doctors may have been more likely to prescribe divalproex, and not lithium, to more severely ill patients or to those with suicidal risk factors such as illegal drug use, he said.

"You need a prospective study," Leonard said. He noted that among patients switched from one drug to the other — the closest the study came to a fair comparison — suicide rates were comparable.

As recently as 1994, Goodwin said, lithium accounted for 80 percent of prescriptions for bipolar disorder. In 2001, divalproex accounted for more than 70 percent. Annual sales of lithium are about \$43 million a year, while those of Depakote are more than \$1 billion, he said.

Many young psychiatrists, he noted, have not even received training in using lithium. Some have been swayed by reports of excessive side effects associated with lithium, Goodwin added, but the two drugs actually have about the same risks.

Goodwin and his colleagues studied the records of 20,638 bipolar of two health-maintenance organizations, the Kaiser Permanente Medical Care Program in Oakland, Calif., and the Group Health Cooperative in Seattle.

They did not consider the efficacy of the two drugs but rather looked at deaths and hospital admissions resulting from suicide attempts. They found 31.3 suicide attempts per 1,000 people a year among those taking divalproex, compared with 10.8 attempts among those taking lithium. There were 1.7 successful suicides per 1,000 people per year in the first group, compared with 0.7 in the second group.

Goodwin conceded it's unknown why lithium was better. It is effective at reducing depression, and most suicide attempts occur during the depressive stages of bipolar disorder. But other effective antidepressants do not reduce suicide risk.

Studies have shown lithium is good at reducing impulsive and aggressive behavior. "Suicide is a very aggressive act," Goodwin said, and also an impulsive one, so the answer might lie in that direction.

Neither Goodwin nor Sussman is advocating stopping the use of divalproex. "There is no single drug that is best for everyone," Goodwin said. "Some patients respond better to one than to the other."

The two drugs are often used now in combination.

Material about who funded the study and criticism of the study came from Reuters.