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Combination therapy better than leading drug for bipolar disorder



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Health

People with bipolar disorder are less likely to suffer a relapse if they are taking both lithium and sodium valproate rather than the drug valproate alone, an Oxford University study has shown.

Sodium valproate (available as Depakote) has been increasingly prescribed over lithium

(Priadel) as a long-term therapy for bipolar disorder, particularly in North America. But the findings of the randomised trial, published in the medical journal *The Lancet*, suggest that those who have been prescribed valproate would fare better if lithium was added to their therapy, or if they changed to lithium alone.

' Our study indicates that a combination therapy of lithium plus valproate may be preferable for people with bipolar disorder over valproate alone, as there were significantly fewer relapses among those on both drugs over the two year period of the trial,' says Professor John Geddes of the Department of Psychiatry at the University of Oxford, who led the research.

About 1 in 100 people are diagnosed as having bipolar disorder (also known as manic depression), a mood disorder characterised by swings in a person's mood, including depression and mania. During a severe depressive episode, people may have feelings of hopelessness and despair, and have difficulty in carrying on with daily activities and work. In the manic phase,



Bipolar disorder is characterised by swings in a person's mood, including episodes of depression and mania.

Further information

- › The Lancet
- › Department of Psychiatry
- › Stanley Medical Research Institute



people may be overactive, lose judgement, become sexually uninhibited, and have grandiose ideas or delusions.

For many years, the standard therapy was lithium carbonate, a mood-stabilising drug. However, the dose must be carefully managed so anyone taking lithium must have regular blood tests, and it can cause adverse side-effects that some patients can't tolerate.

As a result anticonvulsant and antipsychotic drugs have been proposed as alternatives – most of these are drugs already used for epilepsy, schizophrenia or depression, rather than new treatments for bipolar

“ It’s clear that there is room for great improvements in therapies for bipolar disorder. ”

Professor John Geddes

disorder itself. Sodium valproate is an effective anticonvulsant agent, and it has been increasingly prescribed for bipolar disorder since the 1990s. There are also non-drug, psychological or ‘talking’ treatments that have been shown to have some benefit in bipolar disorder.

The Oxford team investigated whether a combination therapy including both lithium and valproate would be better than either drug alone in preventing relapse in bipolar disorder.

330 people with bipolar disorder and aged over 16 were randomised to receive valproate, lithium, or both in combination, with 110 people in each group. The trial was carried out at 41 standard clinical centres in the UK, USA, Italy and France, so that the results would be as clinically relevant as possible. The trial team recorded any relapses among the participants that required new treatment or admission to hospital over a two-year period.

Relapses occurred in 76 people on valproate therapy (69% of the 110 people in this treatment group), 65 people on lithium (59%), and 59 people on the combination therapy (54%).

The results showed that the combination of lithium plus valproate is more likely to prevent relapse than valproate alone. Lithium by itself is also slightly more effective than valproate. The study also suggests that the combination therapy may be better than lithium alone, but the differences are not statistically significant.

‘ Lots of people are prescribed valproate for a manic episode,’ says Professor Geddes. ‘Once the acute episode has settled, their doctor might then consider whether valproate might be considered long-term. Actually, our work shows that a better outcome would be more likely if lithium is added in. And if a monotherapy is to be used, lithium is better than valproate at preventing relapses.’

He adds: ‘Even with the combination therapy, most people needed additional treatment within the two years of the trial. It’s clear that there is room for great improvements in therapies for bipolar disorder. In particular, we would like to know why lithium

the simple light metal element – is superior to other drugs we've tried. We need to reinvigorate research to understand exactly what lithium does in the body and come up with new medicines that are as effective, but that are safer and easier to take.'

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