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Add-on lamotrigine enhances bipolar depression treatment

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By Lucy Piper, Senior medwireNews Reporter

Combining lamotrigine with quetiapine improves the treatment of depressive symptoms in patients with bipolar disorder, with the benefits maintained for at least a year, show findings from the CEQUEL trial.

Scores on the Quick Inventory of Depressive Symptomatology–self report version 16 (QIDS-SR16) at 12 weeks were, on average, 1.73 points lower among 101 moderately depressed bipolar patients randomly assigned to receive lamotrigine (25 mg/day titrated to 200 mg/day) in addition to quetiapine, compared with 101 assigned to receive add-on placebo.

By 52 weeks, the difference was significant at an average of 2.69 points lower for those taking add-on lamotrigine, after taking into account age, bipolar disorder type and dose of quetiapine (< or ≥300 mg/day), the researchers led by John Geddes (University of Oxford, UK) report in *The Lancet Psychiatry*.

They also found that significantly more patients taking lamotrigine plus quetiapine were in remission at 12 weeks (31 vs 16%) and 52 weeks (36 vs 13%), with relative risks of 2.11 and 3.73, respectively.

Discussing the findings in a related comment, Gin Malhi (University of Sydney, New South Wales, Australia) says: "[T]he investigators skillfully take advantage of the synergy between quetiapine and lamotrigine that arises from their differing, but complementary, mechanisms of action and the separate timescales over which they exert their effects."

He explains that quetiapine is often given in the short term to ameliorate acute symptoms, whereas lamotrigine is more effective over the longer term. The drug is therefore able to "achieve a therapeutic level and exert its actions under the initial cover of the antipsychotic, which can then be gradually tapered and withdrawn", he writes.

Geddes et al also considered the effects of folic acid, which is often given as a supplement to some patient groups taking lamotrigine, such as pregnant women and those with mood disorders, and found it interacted with the drug diminishing its additive effect.

As a result, when they restricted the analysis at 12 weeks to patients not allocated to folic acid, the estimated lamotrigine effect was greater, with a significant 4.1-point difference on the QIDS-SR16, compared with patients given add-on placebo.

The combination treatment was generally well tolerated and health-related quality of life improved for all groups, although there was no benefit due to lamotrigine, which the researchers say may be due to the study being under powered for this secondary outcome.

"CEQUEL is an important addition to the evidence base that informs clinical practice", say the authors, "it suggests that adding lamotrigine to quetiapine may be an effective and well tolerated option for many patients with bipolar depression."

Malhi agrees that the findings are "clinically relevant", but calls for replication and corroboration of the findings.

"[L]et's hope that there are more sequels to come, and that CEQUEL is simply the first of many such studies that aim to improve the treatment of bipolar depression", he concludes.

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