The addition of olanzapine to valproate or lithium for acute manic or mixed bipolar episodes reduced manic symptoms


QUESTION: In patients with acute manic or mixed bipolar episodes, is a combination of olanzapine with valproate or lithium more effective than valproate or lithium alone?

Design
6 week randomised [allocation concealed†,‡, blinded [patients, clinicians, data collectors, and outcome assessors]†,§, placebo controlled trial.

Setting
33 centres in the US and 5 in Canada.

Patients
344 patients (mean age 41 y, 52% women) who had bipolar disorder, manic (48%) or mixed (52%) episodes with or without psychotic episodes; had a score >16 (mean score 22) on the Young Mania Rating Scale (YMRS) at baseline; and had received treatment with a therapeutic blood concentration of lithium (0.6–1.2 mmol/l) or valproate (50–125 ìg/ml) for ≥2 weeks before visit 1. Follow up was 97%.

Intervention
Patients were allocated (2:1) to olanzapine, 5, 10, 15, or 20 mg/day (n=229) or placebo (n=115). All patients received valproate or lithium. Adjunctive use of benzodiazepine (≤2 mg/d of lorazepam equivalents) was permitted for ≤14 days cumulatively. Anticholinergic therapy (benztropine mesylate, ≤2 mg/d) could be used for extrapyramidal symptoms but not for prophylaxis.

Main outcome measures
Severity of manic symptoms (YMRS score), clinical response (improvement of ≥50% in YMRS score), and adverse events.

Main results
Analysis was by intention to treat. Patients in the olanzapine combination group had a greater mean decrease in YMRS score than patients in the control group (table). More patients in the olanzapine combination group than in the control group had a clinical response. Olanzapine combination therapy led to increased weight gain, somnolence, tremor, dry mouth, and speech disorder (table). The groups did not differ for dropouts (table).

Conclusion
In patients with acute manic or mixed bipolar episodes, the addition of olanzapine to valproate or lithium reduced manic symptoms but increased some adverse events.

See glossary.
†Information provided by author.
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‡††Information provided by author.
§†††Information provided by author.

Therapeutics
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