Olanzapine/Fluoxetine Combination Affirmed for Bipolar Depression

By Kenneth J. Bender, PharmD, MA [2]

A recent meta-analysis supports evidence of the effectiveness of the fixed olanzapine/fluoxetine combination (Symbyax) in treating the depressive phase of bipolar disorder. Response was ranked higher, but with no more adverse effects, than with treatment with olanzapine alone.

Dr Marcus Silva, University of Brasilia, and colleagues relate in the April issue of Journal of Affective Disorders that their findings “support a therapeutic role for OFC as an alternative for bipolar depressed patients with indications for olanzapine use.”

The investigators characterize their study, which included data on lamotrigine, as the only meta-analysis to address the efficacy of OFC in acute bipolar depression that was not focused on a single-drug class comparison. It comes 4 years after OFC became the first FDA-approved acute treatment of bipolar depression—a condition that can burden patients with bipolar disorder for 3 times as many days as other mood episodes and often recedes, rather than resolves, to persistent subtherapeutic depressive symptoms.

Treatment guidelines for bipolar depression have differed on the recommended agents, on the level of risk for antidepressants to promote switching to mania or rapid cycling, and on the measure with which to balance therapeutic benefit against risk. In a 2012 published review of antidepressant treatment for acute bipolar depression, Ben Amit, MD, and Abraham Weizman, MD, of Tel Aviv University lamented, “It is astounding how, despite numerous trials and meta-analyses conducted on the subject in recent years, the role of antidepressants in the treatment of bipolar depression still remains unclear.”

In 4 of the 5 major consensus-developed guidelines, however, OFC or some combination of an SSRI antidepressant and an antimanic agent is recommended among first-line treatments. In one example, guidelines from the World Federation of Societies of Biological Psychiatry include OFC among first-line treatments along with quetiapine adjunct and monotherapy, olanzapine, valproate, lamotrigine, and lamotrigine with lithium. In the one contrasting guideline, the International Consensus Group on the Evidence-Based Pharmacological Treatment of Bipolar I and II Depression includes OFC among second-line treatments for bipolar I depression, behind lithium, lamotrigine, and quetiapine; that guideline offers no first-line recommendation for bipolar II depression.

Response, remission, relapse with OFC

In this most recent meta-analysis, Silva and colleagues identified 4 randomized clinical trials that met inclusion criteria. They involved 1330 patients with follow-up periods that ranged from 8 to 25 weeks. Response rate was statistically significantly greater with OFC than with olanzapine or placebo, but not in comparison with lamotrigine. Similar results were found with remission rates, although the number of remissions were insufficient to fully power statistical comparison and the investigators acknowledged that “the quality of this body of evidence was low.” Severity of symptoms measured with Clinical Global Impression scales was reduced to a statistically significantly greater extent with OFC than with placebo and lamotrigine. Relapse rates were statistically significantly lower with OFC than with olanzapine alone but not lower than with...
lamotrigine, albeit there was low statistical power in this comparison. There was no significant difference between OFC, placebo, olanzapine, and lamotrigine in the risk for mania or in rates of hospitalization for psychiatric reasons.

Adverse effects occurred more frequently with OFC than with lamotrigine, although with fewer serious adverse events. Weight gain was greater with OFC than with lamotrigine or placebo, and comparable with olanzapine alone. The investigators attributed the similar incidence of adverse effects in the OFC and olanzapine groups to the olanzapine component, noting, “weight gain, somnolence, and tremor were less frequent in the controls without olanzapine.”

The investigators noted that their findings are based on a small number of studies that were affected by attrition and possibly reporting bias. They conclude, however, that “the use of OFC instead of some existing monotherapies, particularly olanzapine, shows benefits in response, remission, quality of life, severity of symptoms, relapse, and discontinuation. No increased risk of mania, the most important contradiction to its use, was observed.”

References:


Source URL:  

Links: