P04.04

Olanzapine cotherapy in prevention of recurrence in bipolar disorder

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This study examines whether olanzapine cotherapy with lithium or valproate reduces symptomatic recurrence compared to lithium or valproate monotherapy in patients suffering from bipolar disorder. Patients in syndromic remission of bipolar disorder after 6 weeks of acute therapy with olanzapine plus lithium (0.6–1.2 mEq/L) or valproate (50–125 microg/mL) were randomized to receive olanzapine (5–20 mg/day) or placebo with continued cotherapy for 18 months of double-blind therapy. Among patients who were in symptomatic remission of mania and depression, time to recurrence to either pole significantly favored the olanzapine cotherapy group (cotherapy, 124 days; monotherapy, 15 days, p=.023). Recurrence into mania following remission of mania was also significantly longer for olanzapine cotherapy-treated patients (n=46, 362 days) compared to monotherapy-treated patients (n=48, 63 days, p=.005). Time to recurrence into depression was not significantly different between cotherapy (n=30) and monotherapy (n=38) groups, but was numerically favorable for the cotherapy group (155 vs 27 days, respectively; p=.071). The results indicate that the combination of olanzapine plus lithium or valproate effectively prolongs time in remission in comparison to lithium or valproate monotherapy.

P04.05

Olanzapine versus divalproex sodium for bipolar mania: a 47-week study

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Objective: Compare olanzapine and divalproex for longer-term efficacy and safety in mania.

Method: This 47-week, randomized, double-blind study compared olanzapine (5–20 mg/day) to divalproex sodium (500–2500 mg/day) for bipolar I disorder (N=251). Young-Mania Rating Scale (Y-MRS) >=20 was required for inclusion, with <12 for "remission."

Results: Olanzapine-treated patients had better mean Y-MRS improvement (p<0.01) and shorter time to mania remission (p=0.047). After 3 weeks, mania remission rate was significantly higher for olanzapine (47.2%) than divalproex (34.1%) (p=0.039); among remitters, mania relapse rates did not differ statistically between treatments during the 44-week continuation: olanzapine (40.7%), divalproex (50.0%) (p=0.418). Median time to relapse was 270 and 74 days for olanzapine- and divalproex-treated patients, respectively (p=0.392). Treatment-emergent adverse events and laboratory abnormalities for olanzapine (p<.05) were somnolence, dry mouth, increased appetite, weight gain, akathisia, and liver function test (increased ALT), and for divalproex (p<.05) were nausea, nervousness, manic reaction, rectal disorder, and decreased platelets. Mean weight increase (LOCF) was olanzapine 3.4 kg vs. divalproex 1.7 kg (p=.045).

Conclusions: Compared to divalproex-, olanzapine-treated patients had significantly greater mania improvement and faster time to remission.

P04.06

Case report of 5 bipolar disorder patients (Rapid Cycling) followed for 3 years, treated with lamotrigine

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Introduction: There are a number of categories of Bipolar Disorder (BPD), one of which is Rapid or Ultra Rapid Short Cycling. Patients with a severe form of Rapid Short Cycling Disorder responded well to lamotrigine in combination with neuroleptics when followed up over a shorter period of time. The purpose of this study was to investigate the effect of the drug regimen in 5 cases that have been followed up since 1998.

Methods: Rapid Cycling patients are those who have two or more affective episodes per year. Five Rapid Cycling BPD patients aged 50–70 years have been followed since 1998 for varying periods of time. Diagnosis was made in accordance with the DSM IV criteria. When treatment was initiated all these patients were experiencing a major depressive or manic episode. The patients had previously been treated with mood stabilizers, neuroleptics and anti-depressive agents without good response. The following rating scales were used to monitor the patients and register improvement: HAMILTON-D; Mania Rating Scale (MRS) from SAD; Clinical Global Improvement (CGI); Clinical Global Severity (CGS) and Global Assessment Function (GAF) measuring Scale.

Conclusions: In this study lamotrigine showed promising efficacy in limiting depression and manic episodes in the patients with Rapid Cycling Bipolar Disorder. However, a multi center, randomized, double blind trial is warranted in order to examine the efficacy of the drug.

P04.07

The bipolar spectrum disorders: implications for new drug development

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The integral character of the bipolar spectrum disorders is undoubted, testified by such powerful common denominators as genetics and natural history. This fact raises several important questions. For example, could the non-specific sedative or "anti-psychotic" effect of an antischizophrenia drug, make it an antimania agent, in the absence of a specific mood stabilizing action? The question is all the more important given the inherent tendency of manic states to be followed by major depressive episodes and vice versa, with or without intervening periods of enthymia, tendency facilitated or prompted by the effect of the "anti-psychotic" drugs. A related question concerns the legitimacy of extending findings on drug efficacy in type I, to type II bipolar disorder, a subtype characterized by it's own, very particular features, notably higher commorbidity, chronicity and impairment, multiple episodes especially of depression and more frequent hospitalization.

The implications for future drug development would seem obvious. An antimania drug should be one with specific and good effect on acute manic symptoms, combined with long-term mood-stabilizing, prophylactic and relapse-preventive action. Despite the formidable difficulties inherent in organizing and conducting proper drug trials in patients with bipolar disorders, a suitable overall design should include: a) Short-term (4-week), 2-or 3-arm

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