

The combined approach with aripiprazole and natrium valproate in bipolar mania

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Background:

Bipolar affective disorder (BAD) is a chronic illness that is characterized by recurrent episodes of mania, depression or mixed symptoms. BAD has a prevalence of approximately 2-4% in the general population and is associated with a substantial rates of recurrence, interepisodic dysfunction, comorbidity, and premature mortality. Mania is one of the most difficult to treat manifestations of BAD and antipsychotic drugs play a major therapeutic role in this respect. Patients with BAD require combined therapeutic approach because of the cyclic disorder nature.

Many studies report the combination of mood-stabilizing agents with atypical antipsychotics. Aripiprazole is approved for the acute management and maintenance of manic and mixed episodes associated with BD. Aripiprazole acts as a serotonin 5-HT_{2A} receptor antagonist, as well as a partial agonist of the serotonin 5-HT_{1A} and dopamine D₂ receptors. It can be safely used, as it is highly tolerated and shows lower rates of the side effects typically observed with other antipsychotic drugs, including sedation, weight gain, hyperprolactinemia, and extrapyramidal syndrome.

Aim:

To explore the efficacy, tolerability and safety of the combined approach with aripiprazole and natrium valproate in bipolar mania.

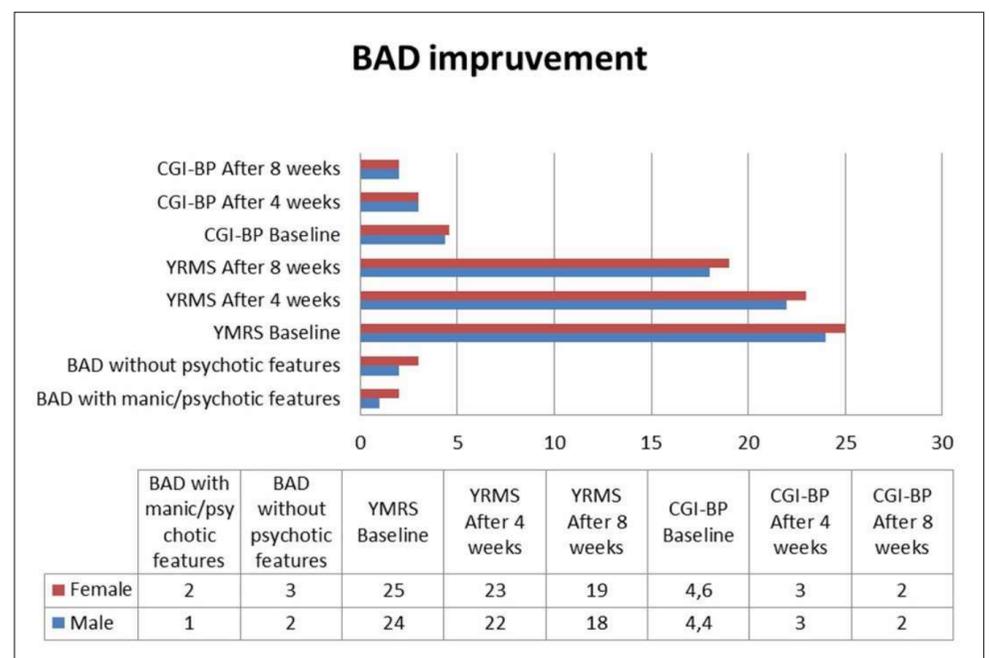
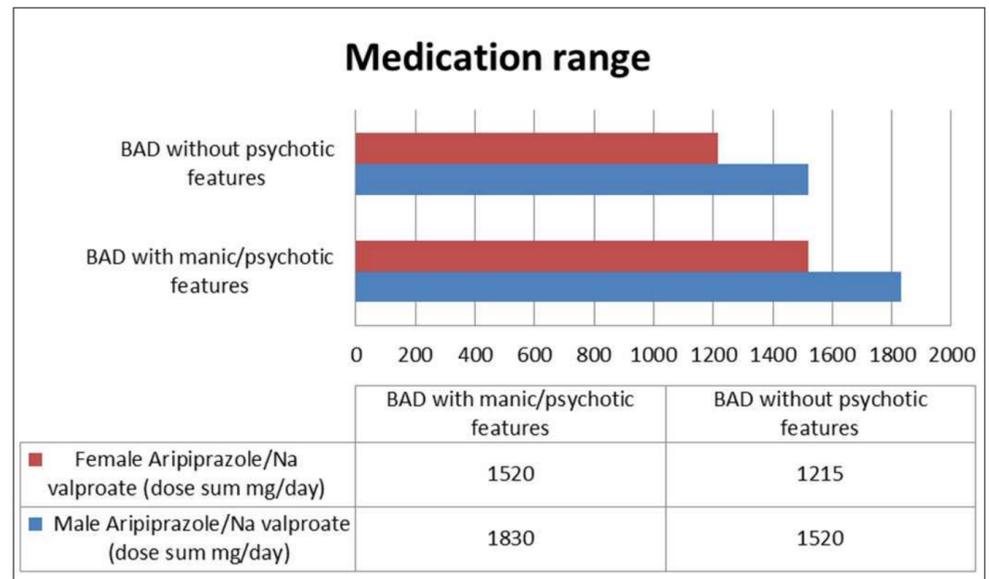
Method:

8 patients participated in this observation. Inclusion criteria were a diagnosis of BAD with manic features, with or without psychotic features according to ICD-10. Patients were treated with the combination of natrium valproate and aripiprazole. At the 8 week follow-up patients were being treated with mean doses of aripiprazole (range 15-30 mg/day) and natrium valproate (range 1200-1800 mg/day). Every patient in this group had previously been unsuccessfully treated with one typical or atypical antipsychotic drugs as combination therapy with mood stabilizers. Clinical status was evaluated at baseline and at the 4 week and 8 week, follow-up using the total Young Mania Rating Scale (YMRS), Clinical Global Impressions Bipolar (CGI-BP) mania scale.

Follow-up evaluations, using the same rating scale as at baseline, were undertaken 4 week and 8 week, from the start date of aripiprazole.

Results:

All patients (5 women and 3 men) aged between 23 and 45 years, completed 8 week of combination treatment. The results obtained indicate that aripiprazole added to natrium valproate treatment showed a beneficial effect on the general psychopathological symptomatology in a sample of BAD patients. The YMRS total score decreased significantly from baseline to 4 week and 8 week follow-up ($p < 0.05$). Significant improvements were also noted on the CGI-BP scores.



CONCLUSION:

ARIPIPRAZOLE AND NATRIUM VALPROATE COMBINATION IS AN EFFECTIVE AND WELL-TOLERATED OPTION IN ACUTE MANIA OF BAD WITH THERAPEUTIC BENEFIT FOR PATIENTS WHO ARE PARTIALLY RESPONSIVE TO OTHER DRUGS COMBINATIONS. NATRIUM VALPROATE/ARIPIPRAZOLE COMBINATION PROVIDES GREATER IMPROVEMENT IN MANIA, AND IT APPEARS TO BE SAFE WITH A LOWER RISK OF METABOLIC SYNDROME, WITHOUT INCREASED RISK OF ADVERSE EFFECTS, COMPARED WITH OTHER MEDICATIONS COMBINATION.

References:

- [1] Vieta, E., Tjoen, C., Mcquade, R.D., Carson, W.H. Jr., Marcus, R.N., Sanchez, R., Owen, R., Nameche, L. Efficacy of adjunctive aripiprazole to either valproate or lithium in bipolar mania patients partially nonresponsive to valproate/lithium monotherapy: a placebo-controlled study. *American Journal of Psychiatry*. 2008;165:1316-1325.
- [2] Scherk H, Pajonk FG, Leucht S (2007) Second-generation antipsychotic agents in the treatment of acute mania: a systematic review and meta-analysis of randomized controlled trials. *Arch Gen Psychiatry* 64: 442-455.
- [3] Marcus, R., Khan, A., Rollin, L., Morris, B., Timko, K., Carson, W., Sanchez, R. Efficacy of aripiprazole adjunctive to lithium or valproate in the long-term treatment of patients with bipolar I disorder with an inadequate response to lithium or valproate monotherapy: a multicenter, double-blind, randomized study. *Bipolar Disorders*. 2011;13:133-144.
- [4] Keck PE Jr, Marcus R, Tourkodimitris S, Ali M, Liebeskind A, et al. (2003) A placebo-controlled, double-blind study of the efficacy and safety of aripiprazole in patients with acute bipolar mania. *Am J Psychiatry* 160: 1651-1658.