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EFFICACY, SAFETY AND TOLERABILITY OF ARIPIRAZOLE

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Introduction: The simultaneous prescription of two or more antipsychotic drugs in combination is a common treatment strategy for those patients who have demonstrated a suboptimal response to clozapine; evidence suggesting potential advantages of combination treatment with clozapine plus one antipsychotic, in terms of efficacy and tolerability are still sparse. Clozapine has a unique receptor-binding profile with high affinities for dopamine D4, serotonin 5-HT2A, 5-HT2C, muscarinic M1, M4, α1-adrenoceptors and histamine H1 receptors, and relatively low affinities for D1, D2, D3, D5, 5-HT1A, 5-HT3, α2-adrenoceptors and M2 receptors. Aripiprazole is a novel atypical antipsychotic drug chemically characterized as a quinolinone derivative. Aripiprazole is a partial agonist at D2 and 5-HT1A receptors and has antagonist activity at the 5-HT2A receptor. It has a low to moderate affinity for the 5-HT2C receptor and H1 receptor. Compared with clozapine, aripiprazole has greater affinity for D2 receptors. Aripiprazole treatment was associated with a good safety and tolerability profile with minimal liability for the adverse effects that limits treatment with other agents. Therefore, aripiprazole might be a possible candidate for clozapine augmentation.

Aim: to explore the efficacy, tolerability and safety of aripiprazole add-on pharmacotherapy on clinical symptomatology in a sample of patients with schizophrenia receiving clozapine.

Method: 9 patients with a diagnosis of schizophrenia according to ICD-10 participated in this observation. Patients were treated with the combination of clozapine and aripiprazole. At the 3 month follow-up patients were being treated with mean doses of aripiprazole (range 15-20 mg/day) and clozapine (range 200-400 mg/day). Every patient in this group had previously been unsuccessfully treated with at least two typical and/or two atypical antipsychotic drugs as monotherapy. Clinical status was evaluated at baseline and at the 3 month follow-up using

CGI Scores with BPRS/PANSS Scores

Baseline - 9 patients - clozapine (range 200-400 mg/day)

CGI-Severity	BPRS Total Score	PANSS Total Score
Markedly ill	40-45	88-96
Severely ill	64-70	105-118

After a 3 months follow up of combination treatment clozapine (range 200-400 mg/day) and aripiprazole (range 15-20 mg/day) – therapeutic improvement – 6 of 9 patients

CGI-Improvement	BPRS Reduction, %	PANSS Reduction, %
Much improved	44-58	40-53
Minimally improved	23-30	19-28

Results: all patients (5 women and 4 men) aged between 23 and 58 years, completed 3 months of combination treatment. The results obtained indicate that aripiprazole added to stable clozapine treatment showed a beneficial effect on the positive and general psychopathological symptomatology in a sample of schizophrenia patients. 6 (66.66 %) of the 9 patients had responded after 3 months of combination treatment. The BPRS total score, PANSS total score decreased significantly from baseline to 3 months follow-up ($p < 0.05$). CGI-I scores is significantly lower at the endpoint.

Conclusion: aripiprazole augmentation of clozapine treatment is well-tolerated and may be of benefit for patients who are partially responsive to clozapine monotherapy. Combined application of clozapine and aripiprazole is in accordance with a neurobiological rationale

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No potential conflict of interest