Efficacy of High-Dose Aripiprazole for Treatment-Resistant Schizoaffective Disorder: A Case Report
By Omer Saatcioglu, Sevda Gumus, Kirkor Kamberyan, Medaim Yanik

ABSTRACT ~ Aripiprazole is an atypical neuroleptic with a unique mechanism of action. According to the package insert, the maximum recommended dose for aripiprazole is 30 mg/day. In clinical practice, off-label prescribing of medications, including the use of doses that exceed the manufacturer’s recommendations, is not uncommon. Most premarketing studies are designed principally to demonstrate safety, efficacy, and tolerability and often exclude many patients who are treated after a drug has been released. To report a case with treatment-resistant schizoaffective disorder in which a patient tolerated and responded to high-dose aripiprazole; an objective is to discuss the use of aripiprazole dosages at higher than those recommended in the product’s labelling. Psychopharmacology Bulletin. 2010;43(4):70–72.

INTRODUCTION
Aripiprazole is an atypical neuroleptic with a unique mechanism of action. Rather than antagonizing the D2 receptor, aripiprazole appears to be a D2 partial agonist and selective agonist. Aripiprazole is also a partial agonist at the 5-HT1A receptor, and like the other atypical antipsychotics displays an antagonist profile at the 5-HT2A receptor. Aripiprazole has moderate affinity for histamine and α-adrenergic receptors and for the serotonin transporter, and no appreciable affinity for cholinergic muscarinic receptors. Aripiprazole also acts as a 5-HT2C partial agonist, which may underlie the minimal weight gain seen in the course of therapy. D2 and D3 receptor occupancy levels are high, with average levels ranging between 71% at 2 mg/day to 96% at 40 mg/day. According to
the package insert, the maximum recommended dose for aripiprazole is 30 mg/day. In clinical practice, off-label prescribing of medications, including the use of doses that exceed the manufacturer’s recommendations, is not uncommon. Most premarketing studies are designed principally to demonstrate safety, efficacy, and tolerability and often exclude many patients who are treated after a drug has been released. To report a case with treatment-resistant schizoaffective disorder in which a patient tolerated and responded to high-dose aripiprazole; an objective is to discuss the use of aripiprazole dosages at higher than those recommended in the product’s labelling.

CASE

A 38 year-old woman was diagnosed in 2006 with schizoaffective disorder of 29 months’ duration. The patient, who had psychiatric disorder since 1998, used many psychotropic medications (olanzapine, fluanxol, lithuril, amisulpiride, fluvoxamine) for 10 years. She presented with persecutory and reference delusions of a derogatory nature that were interfering with her social and academic functioning. Past and family histories were unremarkable. The patient had sequential trials of haloperidol up to 30 mg/day for 3 weeks, but experienced no improvement. She had epilepsy during two years and used oxcarbazepine to 1200 mg/day. At this point, aripiprazole 10 mg/day was initiated then increased by dose titration until achieving a dosage of 30 mg/day by the end of the two days. After obtaining informed consent from the patient to exceed the maximum recommended dose and rapid dose titration, the dose of aripiprazole was increased further to 80 mg/day. The patient showed a complete response, with an approximately 80% reduction in psychotic and affective symptoms. An electrocardiogram (ECG) was normal. Laboratory testing indicated the absence of hyperglycemia or dyslipidemia. One week later, aripiprazole was decreased to 60 mg/day, because she had side effects as dizziness and concentration failure. Within a month, the persecutory and reference delusions completely resolved. Moreover, social functioning improved as well. Over the next 10 weeks, the patient was maintained on 60 mg/day of aripiprazole with sustained complete remission of symptoms, and no adverse effects such as extrapyramidal symptoms, akathisia, nausea, vomiting, orthostatic hypotension, seizure, or weight gain.

DISCUSSION

Schizoaffective disorder shares clinical characteristics with schizophrenia and affective disorders, with patients experiencing concurrent manic,
mixed, or depressive episodes during psychosis. Glick et al suggested that aripiprazole was efficacious and well tolerated in patients with schizoaffective disorder.4 Dosages of atypical antipsychotics higher than those recommended by the Food and Drug Administration are often used in clinical practice for refractory patients, despite the lack of evidence. The literature available on this subject is limited to small, double-blind trials; open-label trials;5 and case reports.6,7 Although certain patients may benefit from higher doses of atypical antipsychotics, the lack of evidence limits their use. High-dose aripiprazole was well tolerated and controlled this patient’s symptoms effectively. Rapid dose titration of high-dose aripiprazole may be beneficial and safe in refractory patients; however, large, double-blind, randomized clinical trials are needed.

REFERENCES