Aripiprazole Use in an Individual With Intellectual Disability and Schizoaffective Disorder

Gerard Gallucci, M.D., MHS,[1] Lawrence Mernaugh, M.A., MSW, LCSW-C[1] & Donald Dyson, M.S.W, M Ed[1]

[1]The Special Needs Clinic, Department of Psychiatry, The Johns Hopkins Bayview Medical Center

The treatment of individuals with intellectual/developmental disabilities and schizophrenia or related disorders represents a challenge for clinicians. Individuals with cognitive impairment may be especially vulnerable to the adverse effects of conventional and atypical antipsychotic drugs. We report on the successful treatment of an individual with schizoaffective disorder and intellectual disability with aripiprazole, a novel antipsychotic agent with a favorable side effect profile.
Keywords: aripiprazole, atypical antipsychotics, diabetes mellitus, intellectual/developmental disability, mental retardation, psychiatric disorder, schizoaffective disorder, schizophrenia

There are many challenges related to the treatment of individuals with intellectual/developmental disability and a psychiatric illness. The appropriateness of certain medications for this population has been questioned. More specifically, diagnostic considerations and other issues involved with the treatment of people with an intellectual/ developmental disability include the safety of different psychotropic medications, efficacy and treatment response, dosage selection and the short- and long-term side effects of these medications. Reiss and Aman[16] attempted to address some of these concerns with their International Consensus Handbook on Psychotropic Medication and Developmental Disabilities.

Antipsychotic drugs have been used to treat a variety of psychiatric conditions including the positive and negative symptoms of schizophrenia, symptoms associated with depression and mania, behavioral disturbances and hyperactivity, and certain tic and motor disorders. Baumeister *et al.*[2] note that this class of medication has become the most prescribed class of psychotropic medication for people with developmental/intellectual disabilities. Consequently, attention has focused on the appropriate use of certain antipsychotic drugs for individuals with developmental disabilities who may be particularly vulnerable to the significant and often dangerous side effects of these medications. The older agents are more frequently associated with movement disorders and other motor abnormalities such as extrapyramidal effects including dystonic reactions, akathisia, pseudo-parkinsonism as well as tardive dyskinesia. The newer agents, also known as the atypical antipsychotics, are perhaps better tolerated but can contribute to potentially serious adverse effects such as weight gain and can impact glucose, lipid and cholesterol metabolism.[1,8,12,13,19] A recent epidemiologic, retrospective cohort study suggests that people who are treated with either conventional or atypical antipsychotic drugs may be at increased risk for developing diabetes.[3]

In November 2002 the FDA approved aripiprazole, a novel antipsychotic agent for the treatment of schizophrenia. A number of Phase III trials have studied aripiprazole in patients with schizophrenia and schizoaffective disorder. Aripiprazole (7-(4-(4-(2,3-dichlorophenyl)-1-piperazinyl) butoxy)-3,4-dihydro-2(1H)-quinolinone) is a quinolinone derivative with a unique mode of action. It is believed that aripiprazole's antipsychotic action involves partial agonist activity at dopamine D2 and serotonin 5-HT1A receptors and antagonist activity at serotonin 5-HT2A receptors. The clinical efficacy and safety of aripiprazole has been demonstrated in a number of PhaseII/PhaseIII studies.[14] More specifically, these studies indicate that there is no significant weight gain between aripiprazole and placebo, and the drug did not adversely impact cholesterol or glucose metabolism. We report on the use of aripiprazole in an individual with schizoaffective disorder and intellectual disability. Issues related to the selection criteria, efficacy and safety of aripiprazole use for people with intellectual/developmental disability and

schizophrenia or other psychotic disorders are discussed.

CASE REPORT

Mr. T is a 25-year-old Hispanic male with Schizoaffective Disorder who was referred for aftercare treatment after an inpatient psychiatric admission at age 22. He was referred to an outpatient clinic that specialized in the care of adults with developmental disabilities and psychiatric illness. The patient had no history of psychiatric treatment before age 22. Six months prior to hospitalization at age 22, he was noted to laugh and cry spontaneously for no apparent reason. His personal hygiene began to deteriorate, and he demonstrated some disorganization with regard to his activities of daily living, such as putting his clothing on backwards. He began to talk to himself and was seen talking to the television on occasion. On the day of admission, he was brought to the Emergency Room by his mother after he began hitting his head and saying "Mom, I need help." Two weeks prior to admission he told his mother that he had thoughts of killing himself. While in the ER he began screaming, "Get off me" and "They're after me." He was subsequently admitted for his first of two inpatient psychiatric hospitalizations.

Family history was unremarkable for psychiatric illness. His mother had a history of diabetes. He denied any history of substance abuse and drug and alcohol toxicology screens were negative at time of admission. Other laboratory studies were unremarkable including a normal thyroxin level, normal B12 and folate levels and a non-reactive RPR. Glucose was noted to be 99. A CT scan and MRI of the head were normal. Mr. T is a high school graduate but had been in special education classes since age six. Shortly after admission to the outpatient program, the patient was referred for psychological testing. A WAIS full scale IQ was 70. Physical exam was remarkable for obesity with an admission weight of 216 lbs., height of 5'-9," and BMI calculated as 31.9.

While on the inpatient unit, Mr. T was noted to be isolative and quiet, and difficult to engage in conversation. He appeared guarded but denied any active psychotic symptoms. He appeared to talk and laugh to himself and at times seemed to be responding to auditory hallucinations.

He was treated by the author on the inpatient unit with risperidone and the dosage titrated to 7 mg/day. He appeared to tolerate this dose without any significant side effects. After a two-week hospital stay, he was referred to the intensive outpatient program and later admitted to the outpatient clinic for follow-up care.

During the next two years, Mr. T had five admissions to the intensive outpatient program and a second inpatient admission due to worsening affective and psychotic symptoms. Lithium (900 mg/day), haloperidol (4 mg/day) and benztropine (2 mg/day) were added to his medication regimen during the patient's second hospitalization (age 24) due to mood lability and intermittent violent outbursts, with some overall improvement in his symptoms. He remained on varying doses of risperidone between the ages of 22-25. Mr. T was referred to a psychosocial rehabilitation program where he was encouraged to participate in vocational training and recreational activities. He was fairly isolative and difficult to engage but made some progress in advancing in the vocational training program.

Mr. T had significant weight gain and approximately eight months after starting risperidone (age 22), he developed symptoms of diabetes with a markedly elevated glucose level of 771. He was emergently treated and started on Glucotrol with the addition of increasing dosages of NPH and Regular insulin due to poor control of blood sugars. Glucotrol was discontinued and Glucophage was started but blood sugars remained in the 200-300 range. The patient was unable to comply with strong recommendations for an appropriate diet and exercise regimen. Due to concerns about his significant weight gain to approximately 290 lbs., poor control of his diabetes, and persistent affective and psychotic symptoms, it was felt that a trial with the new antipsychotic agent, aripiprazole, was warranted. He was started on aripiprazole 15 mg/day and his weight was recorded at 290 lbs. Haloperidol and benztropine were discontinued at that time and risperidone tapered over the next 10 days and discontinued. After eight weeks of treatment with aripiprazole, he was noted to be more interactive with peers and staff at the psychosocial program. His outpatient therapist found him to be more communicative and less preoccupied. Mr. T had admitted that he previously had been experiencing auditory hallucinations and paranoid thoughts but denied any current active psychotic symptoms. His overall mood appeared improved. He stated he preferred the aripiprazole to previous medications and suggested that he felt less tired on the new medication. Blood sugars had

improved and a fasting blood glucose at time of his 8-week visit on aripiprazole was 120 and his weight was in the 275-280 range. He has remained on his oral hypoglycemic agent/insulin regimen with good glucose control. Hemoglobin A1C levels have been within normal range since starting aripiprazole. Mr. T continues to make progress in his work-training program and has moved into a supported employment position where he is performing housekeeping and maintenance at a hospital for wages. He recently moved into supported housing where he has been successful in improving his independent living skills, personal hygiene and appropriate peer interactions. He has joined and continues to participate in a men's group where he is noted to be increasingly more interactive and communicative.

CONCLUSION

The diagnosis and treatment of schizophrenia and related conditions in people with an intellectual or developmental disorder represents a challenge for clinicians. While some studies have suggested that low IQ may be a risk factor for schizophrenia,[6] it has been pointed out that misdiagnosis of psychotic symptoms is not uncommon in persons with intellectual/ developmental disabilities.[10] Consequently, care should be taken before initiating treatment with antipsychotic medication especially since both typical and atypical agents may result in significant side effects and lead to other medical problems.

As pointed out previously, the older or typical antipsychotic agents are limited by a variety of movement disorders, and individuals with cognitive impairment may be particularly vulnerable to extrapyramidal symptoms, dystonia and tardive dyskinesia.[21] While the development of the atypical antipsychotic medication represented a major advance in the treatment of schizophrenic disorders, these agents are not without their own, sometimes serious, side effects. Weight gain and the development of diabetes mellitus has been noted, and patients are often reluctant to maintain treatment with atypical antipsychotics because of the potential health risks associated with these drugs.

Some literature suggests that individuals with schizophrenia may have an increased predisposition for diabetes and the atypicals may impose an additional risk for developing this condition.[7,9,18]

Aripiprazole is a novel antipsychotic drug with partial agonist activity at dopamine D2 and serotonin 5-HT(1A) receptors and antagonist activity at serotonin 5-HT(2A) receptors. The "dopaminergic stabilization" attributed to aripiprazole and other dopamine partial agonists may account for the beneficial aspects of these drugs as well as their favorable side effect profile.[11] In a number of multicenter, randomized clinical trials, aripiprazole was shown to be effective for controlling acute exacerbations of schizophrenia and schizoaffective disorder as well as maintaining remission of symptoms. In addition, aripiprazole was well-tolerated and without significant side effects.

We selected a person with a developmental disability and schizoaffective illness to be treated with aripiprazole because of persistent symptoms and significant weight gain from his previous medication regimen. He had developed diabetes as a young adult shortly after beginning treatment with risperidone. Risperidone had been considered because of the drug's reported usefulness in treating schizophrenia and other disorders in both children and adults with developmental and intellectual disabilities.[4,15,17,20] Weight gain has been reported, however, in individuals with intellectual disability who are treated with risperidone.[5]

Despite increasing doses of risperidone, both positive and negative symptoms of his illness persisted and this individual gained approximately 75 lbs. He responded favorably to a medication switch to aripiprazole as noted in the case history. In addition to resolution of his positive symptoms, he exhibited more motivation and progressed in various aspects of his psychosocial rehabilitation.

Aripiprazole may represent a safe, efficacious drug for the treatment of schizophrenia and schizoaffective disorder in persons with an intellectual or developmental disability. Further studies are necessary to establish the role of aripiprazole for the treatment of psychotic and other illnesses in special populations.

REFERENCES

1. Ananth J, Venkatesh R, Burgoyne K, et al. Atypical antipsychotic drug use and diabetes. **Psychother Psychosom** 2002;71:244-254.

2. Baumeister A, Sevin J, King B. Neuroleptics. In: Reiss S, Aman MG (eds), **Psychotropic Medications and Developmental Disabilities:**

The International Consensus Handbook. Columbus, OH: The Ohio State University Nisonger Center, 1998.

3. Buse JB, Cavazzoni P, Hornbuckle K, et al. A retrospective cohort study of diabetes mellitus and antipsychotic treatment in the United States. **J Clin Epidemiol** 2003;56:164-170.
4. Cohen SA, Ihrig K, Lott RS, et al. Risperidone for aggression and self-injurious behavior in adults with mental retardation. **J Autism Dev Disord** 1998;28:229-233.
5. Cohen S, Glazewski R, Khan S, et al. Weight gain with risperidone among patients with mental retardation: Effect of calorie restriction. **J Clin Psychiatry** 2001;62:114-116.
6. David AS, Malmberg A, Brandt L, et al. IQ and risk for schizophrenia: A population-based cohort study. **Psychol Med** 1997;27:1311-1323.
7. Green AI, Canuso CM, Brenner MJ, et al. Detection and management of comorbidity in patients with schizophrenia. **Psychiatr Clin North Am** 2003;26:115-139.
8. Halbreich V, Kahn LS. Hormonal aspects of schizophrenia: An overview. **Psychoendocrinology** 2003;28(suppl 2):1-16.
9. Henderson DC, Ettinger ER. Schizophrenia and diabetes. **Int Rev Neurobiol** 2002;51:481-501.
10. Hurley AD. The misdiagnosis of hallucinations and delusions in persons with mental retardation: A neurodevelopmental perspective. **Semin Clin Neuropsychiatry** 1996;1:122-133.
11. Kane JM, Carson WH, Saha AR, et al. Efficacy and safety of aripiprazole and haldol versus placebo in patients with schizophrenia and schizoaffective disorder. **J Clin Psychiatry** 2002;63:763-771.
12. Lean ME, Pajonk FG. Patients on atypical antipsychotic drugs: Another high-risk group for type 2 diabetes. **Diabetes Care** 2003;26:1597.
13. Lindenmayer JP, Czobor P, Volavka J, et al. Changes in glucose and cholesterol levels in patients schizophrenia treated with typical or atypical antipsychotics. **Am J Psychiatry** 2003;160:290-296.
14. Marder SR, McQuade RD, Stock E, et al. Aripiprazole in the treatment of schizophrenia: Safety and tolerability in short-term, placebo-controlled trials. **Schizophr Res** 2003;61:123-136.
15. Purdon SE, Lit W, Labelle A, et al. Risperidone in the treatment of pervasive developmental disorders. **Can J Psychiatry** 1994;39:400-405.
16. Reiss S, Aman MG (eds). **Psychotropic Medications and Developmental Disabilities: The International Consensus Handbook** Columbus, OH: The Ohio State University Nisonger Center, 1998.
17. Simon EW, Blubaugh KM, Pippidis M. Substituting traditional antipsychotics with risperidone for individuals with mental retardation. **Ment Retard** 1996;34:359-366.
18. Subramaniam M, Chong SA, Pek E. Diabetes mellitus and impaired glucose tolerance in patients with schizophrenia. **Can J Psychiatry** 2003;48:345-347.
19. Sussman N. The implications of weight changes with antipsychotic treatment. **J Clin Psychopharmacol** 2003;23(3 suppl 1):S21-S26.
20. Williams H, Clarke R, Bouras N, et al. Use of the atypical antipsychotics olanzapine and risperidone in adults with intellectual disability. **J Intellect Disabil Res** 2003;44:164-169.
21. Wszola BA, Newell KM, Sprague RL. Risk factors for tardive dyskinesia in a large population of youths and adults. **Exp Clin Psychopharmacol** 2001;9:285-296.

Correspondence: Gerard Gallucci, M.D., MHS, The Special Needs Clinic, Department of Psychiatry, The Johns Hopkins Bayview Medical Center, 4940 Eastern Avenue, Baltimore, MD 21224; tel.: 410-550-0088; fax: 410-550-1748; email: ggallucc@jhmi.edu.