Use of Atypical Antipsychotics in Children with Mental Retardation, Autism, and Other Developmental Disabilities

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Although developmental disabilities (DD) and mental retardation (MR) always begin in childhood, the risk of having a major mental disorder with associated behavioral problems increases with age. Common behavioral presentations are aggression, self-injurious behavior, and prolonged periods of agitation that are unresponsive to cognitive or behavioral approaches. Patients with DD or MR are at increased risk for schizophrenia, bipolar disorder, and other psychotic disorders that often present as inability to self-regulate severe behavioral dangerousness to self or others. Antipsychotic medications have long been used for this population, and although the results may justify prescribing, the risk of tardive dyskinesia, acute extrapyramidal reactions, cognitive dulling, and other side effects have helped create a strong antipaiscotic lobby in sectors of the provider community. Concepts of “least effective dosing” and a continual push to lower dosages for recently stabilized patients may lead to recidivism and prolongation of illness. In children, bias to delay the use of antipsychotic medication may be especially strong, regardless of presentation. Sensitivity to the issues and careful history-taking are essential to appropriate diagnosis and psychopharmacology.

In the United States, we now have three FDA-approved atypical antipsychotic medications, with a fourth expected soon and others in development. These are clozapine, risperidone, and olanzapine, with sertindole to be released. An early definition of atypicality meant little or no risk of tardive dyskinesia and no clinically significant extrapyramidal symptoms. With time, we have realized a very small risk of tardive dyskinesia exists with atypical antipsychotic agents, but it is not of the magnitude or severity seen with earlier generation antipsychotics. We refer to atypical agents as having both serotonin and dopamine modulating activity. In fact, the dopamine hypothesis of schizophrenia may give way to a downstream dysregulation of serotonin dysfunction, which secondarily turns on dopamine overproduction. This hypothesis may partially explain the superiority of the serotonin-dopamine antagonists, now known as the atypical agents.

The atypical agents may protect against tardive dyskinesia and extrapyramidal symptoms through both their lowered affinity for the D2 dopamine receptor and their enhanced serotonin modulation. Further, no significant cognitive dulling appears to be associated with their use. In fact, positron emission tomography and single photon emission computer tomography scanning suggest a normalizing of neuronal mass, especially in the hippocampus. Anecdotal reports suggest a subtle enhancement of cognitive functioning, perhaps by diminishing psychotic thought processing without generalized central nervous system sedation. Taken together, these factors represent improvements of the atypicals, which are advantageous for the treat-
ment of psychotic and severe behavioral disorders in the DD or MR patient population. Family members, guardians, and physicians may experience relief knowing that the probability of acquiring a disfiguring and painful movement disorder or interfering with the patient's already compromised cognitive functioning are quite remote while chances of resolving positive and negative symptoms are improved.

Although studies of atypical agents in the DD and MR populations are limited, the results thus far are very promising. Clozapine was the first atypical agent released in the United States in the early 1990s, although initially synthesized in the 1960s. A 1974 European study reported on the use of clozapine for behavioral disorders associated with "idiocy and imbecility." Later studies confirmed the advantages of clozapine in treating typical antipsychotic-resistant patients in both the DD and non-DD populations. A study of eight patients with mental retardation and dual diagnoses of either schizophrenia, autism, or bipolar disorder treated with clozapine for 1 year showed improvement in areas of target behaviors and symptoms (assaultiveness, self-abuse, paranoia, hostility, delusions, and property destruction), affect regulation, thought disorders, general cognitive abilities, and movement of some patients into less restrictive settings.

Risperidone has significant calming properties without undue sedation, factors that are advantageous in a DD or MR population. Our clinic has treated children as young as 3 who present with unyielding self-abuse or aggression not responsive to a number of other medication and behavioral approaches. These treatment-resistant behaviors are common in the Pervasive Developmental Disorders (PDD), Autistic Disorders, and MR populations referred for psychiatric services, and parents suffer terribly while their children may harm themselves or their siblings. Combinations of risperidone and divalproex are often effective and may supercede the need for stimulant medication in cases of comorbid attention deficit hyperactivity disorder. Small doses of a selective serotonin uptake inhibitor, such as paroxetine, can be added when anxiety, insomnia, or mood dysphoria are concomitant.

William, a 3.5-year-old boy, was diagnosed with autism after a hospitalization for severe destructive behavior, aggression toward family members and caretakers, head banging and biting, food refusal, and hyperactivity with sleeping less than 2 hours per night. He was mute and preferred aloneness with tactile defensiveness, although he enjoyed deep muscle stimulation and brushing (sensory integration techniques). Because he had developed some language earlier that was now lost, a diagnosis of childhood disintegrative disorder was considered. After a variety of medication regimens were tried, he began taking 2 mg of risperidone twice daily. Within 1 week, he was significantly calmer and returned home. Six months later, he increased his doses to three times daily (because of breakthrough behaviors) with excellent results. He now attends specialized preschool, has improving eye gaze, and is developing pre-social skills. His earlier language of several words has returned, and he has learned several new words at school.

Tiffany, a 5-year-old adopted girl, has mild MR, fetal alcohol syndrome, and PDD. She has language skills but maintains a restricted range of interests, prefers to be alone, makes fleeting eye contact, and has extreme tactile defensiveness. She has screaming tantrums that include tearing at her skin and face with frequent head banging. Aggression toward other children and an assault toward her schoolteacher precipitated her referral. She had a history of hyperactivity, was a poor eater and sleeper, and she had previously tried methylphenidate, dexterdine, clonidine, imipramine, paroxetine, and divalproex. She had an additional behavior of wearing a spandex undergarment constantly, which soothed her, and wrapping ponytail bands tightly around her fingers when upset. Shortly after beginning a risperidone regimen of 0.5 mg twice daily, she showed improvement in all disruptive behaviors. She returned to school while taking 1 mg twice daily with minimal further inappropriate behaviors at both 2 and 4 months' follow up. No side effects were seen in either of these children.

Eric, a 17-year-old boy with moderate MR, autism, and bipolar disorder had a major behavioral problem for which multiple medication (including haloperidol, risperidone, and high-dose divalproex) and behavioral trials failed. He continued to have rapid cycles of mood oscillation with unpredictable tantrums and aggression. Olanzapine, in dosages of up to 10 mg three times daily, was started. Pacing, aggression, and bizarre bodily posturing diminished, and his mood appeared stabilized. Eye gaze is good, and he is using some sign language learned earlier. His mother agreed to a trial of clozapine if olanzapine does not maintain his improvement.

Recommendations for treating severe disruptive behavioral disorders in children with developmental disabilities or mental retardation who do not respond to behavioral interventions, non-antipsychotic medications, or typical neuroleptic agents, such as haloperidol or thioridazine, may include a trial of one or more atypical antipsychotic drugs now available. Although good risk management must include a discussion of possible adverse effects, the common experience is that these medications are at least as safe as many others we prescribe daily, and with proper monitoring, they may offer significant target symptom reduction with minimal problematic side effects while allowing the child to enhance learning, social, and communication skills, thereby building self-esteem and eventual productive citizenship.

REFERENCES