

# The role of second generation antipsychotics in autism disorder

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## KEYWORDS

Autism, antipsychotic, second generation, atypical

*EG is a 9-year old boy who is brought to clinic for evaluation; he is accompanied by his father who appears distressed. He apologizes for being late to the appointment, but he states that he had a hard time getting EG to leave the house because he would not stop playing with his Yu-gi-oh cards. When dad tried to take the cards away, EG became angry, began to cry loudly, and started to hit himself and his dad. Dad says this is common behavior for the past few years and now that he is getting older they are worried that he could hurt himself or others. He displays these behaviors both at home and at school with his teachers and therapists.*

*EG's past medical history is significant for being diagnosed with Autism Disorder at age 3. He has been undergoing different kinds of therapy since then, including applied behavior analysis, speech therapy, and occupational therapy. He was speech delayed when he was younger but can talk and communicate without problems now. He has never tried any medications.*

*Family history: Non-contributory; has one older sibling who is healthy and displays no autistic behavior. Parents are divorced, but both parents are involved in the care of EG.*

*Dad has questions about what medication options are available to help EG with his anger to prevent him from hurting himself or someone else.*

Before starting any treatment in children with developmental disorders, it is important to educate the parents or caregivers that medications are only effective in treating the associated behavioral symptoms; they are not a cure for the actual disorder and do not treat the core symptoms of autism. Associated behavioral symptoms include aggression, irritability, and self-injurious behavior. The core symptoms of autism are deficits in social skills, delayed or lack of communication skills, and stereotypical behaviors and movements. Children with autism disorder

may not present to a psychiatrist with any overt problems until school age or when they start being placed in more social settings. However, diagnosis can be made much earlier. Parents should have their child screened by their physician during their physical exams as young as 18 months of age.

Before starting any medications, providers must communicate well with parents to educate them on what symptoms they are treating and the expectations of treatment. Aggression and irritability are the targeted symptoms most commonly treated with pharmacotherapy. These symptoms are usually treated with pharmacotherapy when other modalities have been tried, the parents feel they cannot handle it on their own, or if the child poses a danger to himself or others.

Overall, antipsychotics are the most commonly used medications to treat these associated behavioral symptoms, not just in autism disorder but in all developmental disorders. In recent years, the second generation antipsychotics have received more attention in this patient population.

Risperidone (Risperdal) and aripiprazole (Abilify) are both FDA approved to treat irritability, aggression, self-injurious behaviors, and temper tantrums associated with autism. Both of these drugs currently have the most evidence supporting their use in autism disorder.

Risperidone has been shown effective in double-blind, placebo controlled trials in reducing the above behaviors not only in autistic patients, but also in patients with mental retardation.<sup>1-3</sup> The primary outcome in most of the studies was the Aberrant Behavior Checklist (ABC) – Irritability subscale, in which risperidone showed statistically significant improvement for up to 12 months (RUPPAN). Improvement in these symptoms can be seen as early as 1-2 weeks after initiation of therapy. Drowsiness (49%) and increased appetite (73%) were the most common side effects in these studies. The average weight gain was 2.7 kg with risperidone versus 0.8 kg in

the placebo group. The average risperidone dose used in clinical trials in autism is below 2 mg/day.<sup>1,2,4</sup> The same tends to be true in clinical practice. A starting dose of 0.25mg once daily is recommended to minimize sedation with titrations every 1-2 week to an average of 1-2 mg/day.

Aripiprazole also has positive data in double-blind, placebo-controlled trials using the same ABC-Irritability subscale as in the risperidone trials.<sup>5,6</sup> Efficacy was seen in doses ranging from 5mg-15mg/day. An average weight gain of 1.5 kg was seen with aripiprazole, compared to an average weight gain of 0.3 kg with placebo. This is lower than the average weight gain seen in the trials with risperidone. However, it is important to remember that some patients may still experience significant appetite increase and weight gain with aripiprazole. The most common events leading to discontinuation in aripiprazole trials were sedation, drooling, and tremor, with a discontinuation rate of 11.6%. Lower doses are also preferred with aripiprazole to minimize side effects, particularly sedation and extrapyramidal symptoms.

Other second generation antipsychotics (olanzapine, quetiapine, ziprasidone) have not consistently shown improvement in clinical trials, and therefore should not be recommended in this patient population at this time.<sup>4</sup>

Children receiving atypical antipsychotics should be monitored for weight, fasting blood glucose, and fasting lipid profile at baseline, at 3 months, and then at least yearly thereafter. Increased appetite and weight gain are the two most troublesome side effects with these medications; parents should be counseled appropriately regarding these side effects. Instructing parents to keep healthy snacks in the house is one way to limit weight gain from increased appetite. Usually, if these side effects are going to occur, they will occur during the first few months of treatment.

Parents should also be counseled on drowsiness, which is another common side effect of these medications. It is important to inform parents that patients may be drowsy the first few days, but in most children, this side effect does diminish over time. If drowsiness does not decrease and is affecting the child in school, consider decreasing the dose or changing medication.

Both risperidone and aripiprazole are available in orally disintegrating tablets and oral solutions for children who may have a hard time swallowing tablets. Cost could be an issue with these different dosage forms.

Parents should be informed of the goals of medication treatment, and made aware that medication will not treat the core symptoms of autism. It should also be emphasized that medications should be part of a larger treatment plan including different modalities of therapy, such as applied behavior analysis, speech therapy, occupational therapy, and individualized educational plans. Perhaps by treating the irritability and anger associated with autism, these other therapies can be more effective. Children on antipsychotics should be re-assessed periodically to evaluate the need for ongoing treatment. The preferred method for discontinuation is to taper the drug slowly, and assess for return of symptoms at each dose decrease.

In conclusion, second generation antipsychotics, particularly risperidone and aripiprazole, can be effective in treating children with associated behavioral symptoms of autism disorder. Low doses can be used to achieve this efficacy with minimal side effects.

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