The information in this column is not intended as a definitive treatment strategy but as a suggested approach for clinicians treating patients with similar histories. Individual cases may vary and should be evaluated carefully before treatment is provided. The patient described in this column is a composite with characteristics of several real patients.

Managing disruptive behaviour in autism-spectrum disorder with guanfacine

Lukas Propper, MD

This is a case of a 10-year-old boy with an autism-spectrum disorder (ASD), global developmental delay and chronic disruptive behaviour, including impulsivity, self-injurious behaviour (biting, hitting self with fist), and aggression toward others (kicking, punching, biting). He had chronic difficulties in both initiating and maintaining sleep, resulting in an increase of his disruptive behaviour and further contributing to the distress of his family. His disruptive behaviour was unpredictable, present in all environments, and usually escalated quickly into severe aggression. Although he presented with symptoms of attention-deficit/hyperactivity disorder (ADHD) he did not meet full criteria for ADHD, and there were no other psychiatric comorbidities present. His speech was limited, and his cognitive profile was not assessed owing to his noncompliance. Intensive behavioural interventions were implemented in both the school and home environments with limited success. Treatment attempts with several different medications failed owing to adverse effects: risperidone and aripiprazole were both stopped because of excessive weight gain, methylphenidate and lisdexamphetamine were both stopped because of increased irritability and disruptive behaviour, and atomoxetine was stopped because of headache.

The patient was started on extended-release guanfacine (guanfacine XR) at a dose of 1 mg in the evening, initially. Even 1 mg resulted in improvement to both his sleep and behaviour, particularly in the evening, and the dose was increased to 1 mg twice a day after one week. This increased dose resulted in significant improvement of his behaviour in the school and home environments. An additional dose of 1 mg was added early in the afternoon after three weeks, as the family reported a pattern of mild worsening of disruptive behaviour occurring later in the day. Once the dose was optimized at 3 mg/d, his behavioural symptoms were fully controlled without any adverse effects, and he has remained well in the subsequent six months.

Clinically referred children with ASD frequently present with disruptive behaviour.[1] Although behavioural interventions have become a predominant and effective treatment modality,[2] the use of medication is often necessary in patients with high-risk behaviours to decrease the severity of symptoms before any behavioural intervention can be undertaken. Risperidone and aripiprazole are approved for the treatment of irritability in children and adolescents with ASD and have been shown in randomized controlled trials (RCTs)[3–5] to have a positive effect on disruptive behaviour and hyperactivity, but excessive weight gain and metabolic adverse effects sometimes prevent their long-term use.

Many children with ASD exhibit high rates of ADHD symptoms,[6,7] and their disruptive behaviour is often secondary to hyperactivity and impulsivity; thus, the use of medication for ADHD may be more appropriate. However, the efficacy is less favourable and adverse effects more frequent in this population,[8] and the use of lower dosages, and sometimes redistribution into several smaller dosages, is needed because of increased vulnerability to adverse effects and fluctuation of the behavioural symptoms, even with a long-acting medication (e.g., stimulants and guanfacine XR).

Guanfacine XR is a selective α-2A adrenergic receptor agonist that has 15–20 times higher affinity for α-2A than α-2B/2C adrenergic receptors.[9] Several RCTs support the efficacy of guanfacine XR in the treatment of children with ADHD and disruptive behaviour and report only mild to moderate adverse effects that very infrequently lead to discontinuation.[10–12] Common adverse effects may include sedation, dizziness, headache, nausea and stomach pain. There is also a warning about cardiovascular adverse effects: guanfacine XR can cause hypotension, bradycardia and syncope, and patients should be instructed not to discontinue the medication abruptly owing to a risk of hypertension.[9]

Guanfacine XR has been found to be superior to placebo in two RCTs in school-age children with ASD, with significant improvement in hyperactivity in particular;[13,14] it was also reported to be effective in reducing oppositional behaviour and demonstrated a modest effect on repetitive behaviour in children with ASD and ADHD symptoms in a recent analysis of secondary outcome measures.[15]

Guanfacine XR has shown some promise as an alternative to psychostimulants, but larger RCTs are needed to further evaluate its efficacy and tolerability in children with ASD. Therefore, careful monitoring of any adverse effects is required.

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