Sulpiride for Autism Spectrum Disorder

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Autism spectrum disorder (ASD) is commonly associated with a host of challenging behaviors. Pharmacotherapy is indicated if psychosocial and educational interventions fail. Here, a case of a child with metabolic-prone essential ASD/mild intellectual disability with a severe behavioral component that responded to low-dose sulpiride is presented. A brief discussion of sulpiride's unique pharmacologic profile is also provided.

Case Report

A 9-year-old Kuwaiti boy was referred by the developmental pediatrics outpatient department for behavioral dyscontrol. He was long diagnosed with essential ASD, with mild intellectual disability. He was minimally verbal and nonepileptic and was attending special schooling. As reported by his parents, he was hyperactive, yelling and screaming, and cranky, with continuous body rocking movements and disturbed sleep (difficulty falling asleep and frequent nocturnal awakenings). This behavior was escalating lately in a crescendo manner with self-injurious behaviors (head banging and self-mutilation). He was admitted to the hospital for safety concerns. He was meticulously examined for medical and environmental causations that could be contributory to this behavioral decompensation with negative results. He was metabolically prone (45 kg) with a strong family history of type 1 diabetes mellitus. He had been trialed on aripiprazole (uptitrated to 7 mL/d) with a tangible response over 2 weeks but developed transaminitis (alanine transaminase [ALT] of 200 U/L). Abdominal ultrasound revealed a fatty liver, and viral serology and autoimmune panel results were unrevealing. Aripiprazole was discontinued, and liver function tests were normalized over 2 weeks (ALT decreased to 30 U/L). Risperidone was used in lieu, but soon at 0.75 mL, he developed oculogyric crisis, and liver function test results again began to increase. Paliperidone was suggested as a more hepatic-friendly option, but only 3-mg osmotic-controlled release oral delivery system extended-release capsules were available—a high dose to start with in this vulnerable population. Moreover, the child could not swallow the capsule whole. Neurohormonal as well as metabolic side effects of paliperidone were also detracting. Since substituted benzamides are renally cleared, sulpiride, available in solution form as Sulpiride Rosemont (200 mg/5 mL), was proposed. Informed consent was obtained from the patient's parents beforehand. He was started on 1.25 mL twice/day. Then, the dose was increased to 2.5 mL twice/day over a week. Dosing was based on the British National Formulary[1] for Tourette syndrome and titrated to effect. At this relatively low dose, behavioral dyscontrol was greatly improved according to the Clinical Global Impressions Scale-Improvement scale.[2] This result was achieved with great tolerability. No extrapyramidal side effects were noted. Liver function tests, as well as fasting serum prolactin and metabolic screen, were checked at baseline and periodically and remained within normal limits throughout. Better socialization was noticed in parallel. Twelve weeks have elapsed at the time of this writing, and the response is well sustained.

Discussion

Hepatic-friendly antipsychotics include low-dose haloperidol, paliperidone, and substituted benzamides (eg, sulpiride and amisulpride). Both haloperidol (2 randomized controlled trials) and paliperidone (1 open-label trial) have a modicum of an evidence base supporting use to address behavioral concomitants in ASD.[3,4] Literature on substituted benzamides in ASD is surprisingly scant. A literature search revealed only 1 case report[4] in which sulpiride (up to 400 mg/d) significantly reduced abnormal speech and withdrawal in a teenager with ASD. For amisulpride (1.5 mg/kg/d), 1 randomized double-blind cross-over trial with bromocriptine showed no statistically significant effect on autism global scores, although amisulpride had a more positive effect on behavioral inhibition and withdrawal symptomatology.[5] The pharmacologic portfolio of sulpiride is quite interesting.[6] At low doses, sulpiride inhibits presynaptic dopamine (DA) autoreceptors from releasing DA, which might account for its antidepressant as well as precognitive and disinhibiting (prosocial) actions and could be the case in the patient presented here. At higher doses, it selectively blocks D_2/D_3 postsynaptic receptors and exerts antipsychotic actions. Furthermore, sulpiride was shown to bind γ-hydroxybutyric acid receptors, which are thought to impact DA neurotransmission, a unique and novel mechanism of action. Large-scale studies are needed to replicate the findings presented in this report.

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