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Lumateperone for Aggression in Autism Spectrum Disorder and Intermittent Explosive Disorder

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Description

The use of lumateperone in reducing aggression in patients with Autism Spectrum Disorder (ASD) and Intermittent Explosive Disorder (IED) has not heretofore been described. Case 1 is a non-verbal 18-year-old male with autism who presented with anger and aggression, biting his hands, intermittently grunting, and screaming. The patient's hostility subsided after ten days of establishing lumateperone 42 mg nightly, in cross-titration with aripiprazole. Case 2 is a non-verbal 18-year-old male with a history of hypsarrhythmia, and Lennox-Gastaut syndrome, presented with similar aggression coincident increase in the frequency of myoclonic seizures. Management was initiated with 42 mg of lumateperone nightly. Aggression and hostility were remitted after ten days and one month, respectively, for cases 1 and 2; however, the seizures persisted in Case 2. Due to its dual action on dopamine D2 receptors and better side effect profile compared to other antipsychotics, the authors encourage a trial of lumateperone in treating aggression associated with ASD and IED. We report the case of a single 58-year-old man, and proper functioning (Functional Assessment Staging Tool (FAST) the baseline score 26), treated at the outpatient clinic of a major Tertiary Hospital with a history of MDD (treatment-resistant), suicidal ideation and with suspicion borderline traits of autism (25 points in Autism-Spectrum Quotient Test (AQ)) as well as to clinical judgment of a senior psychiatrist.

Electroconvulsive Therapy

We used the cutoff of 26 because in clinical patients the literature describes good screening properties of AQ in adults referred for an ASD assessment with a cutoff of 26 Patient showed severe depressive symptoms in his first visit to hospital, without symptoms of mania or psychotic symptoms, as per score zero in Young Mania Rating Scale (YMRS) and denied previous suicide attempt or psychiatric hospitalization, or other comorbidities. He has not received electroconvulsive therapy and denied lifetime alcohol, or illicit drug abuse and never used tobacco. At baseline, he weighed 94.40 kg and had a body mass index of 29.1. The patient was referred to esketamine treatment after failure to respond to sertraline, amitriptyline, citalopram, venlafaxine, trazodone, divalproex, pregabalin, aripiprazole, and brexpiprazole. Observations of autistic traits were made later in life, as he reported enduring difficulties in social relationships despite high academic achievements (fluent in 5 idioms, graduated from one of the top universities in Brazil).

Genetic Disorders

Esketamine treatment followed the SC protocol described with esketamine 50 mg/ml SC, with patient comfortably resting on the stretcher with basic life support equipment, with four hours fasting. The patient received esketamine SC, with an initial dose of 0.5 mg/kg (47 mg). As an adequate response was not obtained, a second infusion was performed two days after the first, using 10% more than the concentration of the first dose (60 mg). The patient used an average dose of 0.67 mg/kg SC (63.5 mg of esketamine). Sessions were held twice a week for five weeks (totaling 10 applications) and once a week, totaling 8 more applications. Safety was observed by monitoring vital signs, side effects, cognitive/psychiatric status, and physical symptoms for approximately 1 h after application. He was regularly (all esketamine applications) evaluated using the following scales: FAST, Montgomery Asberg Depression Rating Scale (MADRS), 17-item Hamilton Rating Scale for Depression (HAMD) and Columbia-Suicide Severity Rating Scale (C-SSRS). Based on baseline and after treatment, we observed a great improvement of 72% MADRS, 58% HAM-D17, 35% FAST and 100% C-SSRS reduction from baseline. Complementary qualitative evaluation of esketamine effects on his mood was collected and, as an example, he said: “What has changed is that the sense of finitude is almost non-existent. Being able to realize this brought me a little more security in everyday life, without being so scared of what might happen. It is as if the feeling of constant threat has ceased. Now I can enjoy every moment of the day with more tranquility.” Patient described the effect of esketamine on relationships with others as: “In a way, I'm still a little isolated from people. But when I need to get in touch with someone, I can be more natural. Before, I saw people as a certain threat and now I can have more empathy and compassion for other people. Contacts became more fluid.” Neurofibromatosis type 1 (NF1) is an autosomal dominant genetic disorder caused by mutations in the NF1 gene, with a prevalence of 1/4560. It is characterized by café -au-lait spots, axillary or groin freckling, and optic gliomas. Although NF1 is often considered a cancer-prone syndrome, up to 80% of

children with the disorder may also exhibit cognitive and behavioral problems. The prevalence of Autism Spectrum Disorder (ASD) in patients with NF1 ranges from 0.3% to 30%. This report describes a rare large deletion of the NF1 gene in a patient with comorbid NF1 and ASD. Foreign body ingestions are quite common and most often will uneventfully pass in stool, however, some ingestions, can lead to complications such as obstruction. If left untreated, this can lead to perforation and fistula formation. Hence, threshold for intervention should be low and diagnostic imaging can assist with treatment decisions. We present to you a case of 17-year-old male with non-verbal autism with an unusual hollow foreign body ingestion leading to small bowel obstruction. Limb girdle muscular dystrophies are a group of genetic disorders manifesting with progressive proximal muscle weakness. There are rare case reports of individuals who also have intellectual disability or developmental delay, but an association has not been clearly defined. Autosomal recessive Limb-Girdle Muscular Dystrophy-3 ("LGMDR3"), is caused by biallelic pathogenic variants in the SGCA gene. There have been no reports of neurodevelopmental disorders in individuals with this disorder to date. This case report details the presentation of a patient with LGMDR3 and autism spectrum disorder.