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Letter to the Editor

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Lumateperone monotherapy for treatment-resistant obsessive-compulsive disorder in an adolescent

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Case vignette

A 15-year-old Saudi male youngster was referred to our outpatient clinic for treatment-resistant obsessive-compulsive disorder (OCD). He had an uneventful perinatal history, and normal developmental milestones. Medical history and physical examination were unremarkable, with no tics or illicit drug use, and his electroencephalogram and magnetic resonance imaging findings were unrevealing. No family history of neuropsychiatric disorders was reported.

At the age of 13, he started to endorse blasphemous religious ideas. A couple of months later, he began to repeat his prayers because of uncertainty about proper ablution and he eventually stopped praying altogether. He started being late at school on most days with a serious academic drop. He looked blue and distressed most of the time, gave up most of the heretofore pleasurable hobbies he used to pursue, lost much of his weight, had fragmented sleep, and he felt totally drained and indrawn.

After rounds at traditional (faith) healers, parents finally sought psychiatric advice at a private clinic. Baseline laboratory investigations including thyroid function tests were within normal. A diagnosis of OCD with secondary depression was entertained. Fluvoxamine up to 300 mg/d and clonazepam 2 mg/d were prescribed more than 2 months, with only mediocre response. Parents reported bouts of agitation over these medications. He was then shifted to sertraline, and rapidly titrated to 200 mg/d over another month with clonazepam at 2 mg/d kept in place. Cognitive behavioural therapy (CBT) was introduced, but the patient attended only three sessions stating it was futile. After 3 months with inadequate response augmentation with 2 mg/d of risperidone was pursued. After 5 weeks, the patient became demoralized and harboring passive death wishes which prompted a referral to our outpatient department.

At the initial evaluation, the diagnosis of OCD with secondary depressive mood was endorsed, according to Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, Text Revision (DSM-5-TR) criteria. Yale-Brown Obsessive Compulsive Scale (CY-BOCS) was administered where the patient scored 32, that is, on the severe range. Clomipramine (CMI) was added to his previous regimen and titrated up to 100 mg over a month. The patient looked less distressed and had better sleep quality, although his bothersome ideas and washing compulsions remained adamant. He complained of oversedation and weight gain coupled with continued poor academic and social functioning. CBT (ERP) was reinstituted in our center on a weekly basis. After 3 months, a minimal improvement was objectively reported by the parents, in terms of less time spent in the bathroom in comparison to previous months. Nevertheless, the Y-COBS was readministered and yielded yet again a severe score of 30, while the patient had a significant weight gain and a triple-fold increase in serum prolactin level. Risperidone was discontinued and sertraline was increased up to 300 mg/d. Due to the prolonged unresolved symptoms, parents sought help at a private hospital in India where add-on iv CIM, lithium up to 800 mg/d (with serum level of 0.7 mmol/L), aripiprazole 15 mg/d, and buspirone 45 mg/d were trialed in succession but sorely with minimal results. ECT was also suggested but declined by parents.

At his re-evaluation in our center, patient's Y-BOCS was still in the severe range (latest read 31). At this point in time, we proposed a trial with the newest antipsychotic lumateperone, at our multi-disciplinary meeting. Parents' consent and patient's assent were obtained beforehand. Lumateperone dosed at 42 mg nighttime with dinner was commenced after a 2-week washout period of meds but clonazepam (remained at 2 mg/d). After 4 weeks, the patient started to feel better for the first time. One month later, his Y-COBS decreased down 12 (mild range) and the patient had been far less distressed, more insightful for the irrationality of his ideas, less involved in washing compulsions, back to school, and to socializing with his peers. His CGI-improvement

read 2 ('much improved') at weeks 6, 8, and 12 since lumateperone was started. In his latest follow-up visit before writing this report, after yet another 6 months, the patient has exponentially improved, reporting only some residual mild OC symptoms with minimal impact on his life. Trial was achieved with high tolerability. PRL level normalized and significant weight loss was noticed. Failure to multiple previous trials on psychotropic agents would conceivably defy a placebo response.

Discussion

A substantial minority of patients with OCD are treatment-resistant to standard serotonin reuptake inhibitors (SRIs), that is SSRIs and clomipramine, which might be largely ascribed to clinical and neurobiological heterogeneity.

Lumateperone (Caplyta)

Lumateperone (Caplyta) is a butyrophenone FDA-approved for adult schizophrenia and bipolar depression. It possesses a potent antagonistic activity at 5-HT2A receptors and also binds to dopamine (DA; D1 and D2) receptors with partial agonism at presynaptic D2 receptors and postsynaptic low antagonism. It uniquely acts as an indirect modulator of glutamatergic phosphoprotein with D1-dependent augmentation of both NMDA and AMPA activity via the mTOR pathway and also has intrinsic SSRI activity.[1]

A fundamental serotonergic dysfunction is typically underpinning the neurobiology of OCD.[2] DA blockade seems critical to facilitate 5HT transmission in the cortico-striato-pallido-thalamo-cortical neurocircuity in OCD informing the widespread practice of antipsychotic augmentative strategies.[3] Moreover, Glutamate and GABA are highly expressed in neurocircuity underlying OCD giving kudos to glutamergic modulators in refractory cases of OCD.[4]

Lumateperone's inherent serotonergic, dopalytic, and glutamergic activities, sounds at least theoretically, mechanistically attractive and might dynamically explain the outcome in this report. We failed to locate similar reports of lumateperone efficacy for OCD even in adult literature. Lumateperone is user-friendly, dosed at 42 mg/d, and has a benign cardio-metabolic and hormonal profile which is a major consideration when choosing an antipsychotic notably in the CAP population who are at a heightened risk by virtue of age.[5]

Our case remains one of the earliest to report on the efficacy and safety of lumateperone in OCD especially in the CAP population. There is currently an ongoing trial testing the safety of lumateperone in the pediatric population (with diagnoses of schizophrenia and schizoaffective disorders).

This, albeit off-label use, might open new treatment venues for such complicated clinical scenarios. Large, rigorous, and well-conducted studies are awaited to replicate these interesting findings.

Author contribution. All authors have materially participated in the manuscript preparation.

Disclosure. The authors declare none.

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