

## Add-on Atomoxetine Mitigated Different Symptom Domains in a Case of Early-Onset Schizophrenia

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### To The Editor

Early-onset schizophrenia (EOS), with an onset before age of 13, is notorious to be of poor prognosis, male preponderance, insidious onset, heavy genetic load, negative and cognitive domains presentation, subtle neurologic signs, gross impairment and generally poor antipsychotic response [1]. Despite initial enthusiasm about the potential of Atypical Antipsychotics (AAPs) to help with negative and cognitive domains, in stark contradistinction to conventional neuroleptics, clinical experience with these agents called this conjecture into question [2]. Significant cognitive impairment is commonplace affecting up to 75% of patients and is a prime driver of the significant disabilities in social, occupational and economic functioning [3]. Negative symptoms affect individuals' ability to cope with everyday activities and have a negative impact on their quality of life and continues to remain a major clinical hurdle [4]. Atomoxetine (ATX), is a non-stimulant, FDA-approved for Attention-Deficit/Hyperactivity Disorder (ADHD) and selectively inhibits norepinephrine reuptake (NRI) [5]. Here, we are reporting a pharmacologically-challenging case of EOS where add-on ATX was very impressive, helped with negative and cognitive domains, and curbed binge-eating-like episodes that occurred more as part of disorganized symptom cluster (DSC) rather than bona fide comorbid eating disorder and strikingly counteracted weight gain induced by AAPs. This was achieved with high tolerability and no significant drug-drug interactions.

A 15-year-old Kuwaiti male youngster was brought in to hospital by his parents for disorganized behaviours coupled with scholastic failure. This dated circa 2 years back with incipient onset of social withdrawal, neglected grooming and hygiene, fitful sleep, vague and digressive speech, and scholastic underachievement. School reported recent hostile and quarrelsome behaviours, dishevelled appearance and academic failure. At home, he began to demonstrate pervasive suspiciousness, giggling, binge-eating-like episodes with no rationale, and at times muttering under breath. It ran a progressively deteriorating course and reached a nadir when the patient, in jactitation, gripped a knife to 'protect' himself from those 'stealing' his thoughts as he reported. The patient has a schizophrenic paternal uncle. He has unremarkable developmental trajectories, apart from notable 'clumsiness' as parents reported. Hospitalization for safety concerns was suggested, but declined by parents. Full work-up for a 'first-episode psychosis' was contemplated including baseline laboratory investigations, TFT, B12, Prolactin, Toxicology screen, ECG, EEG, and MRI brain, all with negative yield. The patient has failed adequate sequential trials on Aripiprazole, Olanzapine, and Quetiapine monotherapy, despite ensured compliance. Enormous weight gain was recorded. Clozapine was proposed but again declined by parents in spite of psychoeducation. We decided to embark on Risperidone trial at 4 mg/d. Clonazepam 1 mg/d was added to help with agitation and insomnia. Lamotrigine augmentation, 6 weeks later on, was then pursued at 100 mg/d for associated parathymia. Tangible

improvement was noticed chiefly in the positive domain. Contrariwise, binge-eating, which was more bothersome to parents, together with negative and cognitive domains were very much impairing both socially and academically. Atomoxetine, after another 6 weeks, was suggested and parents' consent obtained. At 40 mg/d, over 4 weeks now, binge-eating dramatically diminished. Simultaneously noted was better interpersonal socialization. Negative symptomatology improvement clinically was objectified on Scale for Assessment of Negative Symptoms (SANS) in comparison to baseline records. Digital Symbol Substitution Test (DSST) was employed to assess cognitive domains and the results were very impressive, again when contrasted with pre-treatment scores. Response was well-sustained at 4, 8, and 12 weeks with great tolerability and no pharmacokinetic drug interactions of significance. Strikingly, the patient experienced significant weight loss with ATX, which was so advantageous given previous AAPs-induced weight gain. He is now being engaged in social skills training facility.

We assume that boosting nor-adrenergic (NE) drive in the prefrontal cortex (PFC) by atomoxetine accounts for its pro-cognitive effects akin to its mechanism in ADHD. Having said so, a pilot study of adjunctive ATX to AAP for cognitive deficits was negative, however [6]. NRI by atomoxetine with subsequent disinhibition of dopaminergic projections to the dorsolateral PFC hence corrects the hypofrontality that is thought to underlie the negative symptoms. Moreover, decreased NE in chronic schizophrenics is well-documented in the literature and psychotropics acting primarily to increase NE (e.g. milnacipran, mirtazapine) were reported to mitigate negative symptoms [7,8]. We postulate that ATX ameliorated negative symptoms in this case through a similar mechanism and also, possibly, by reducing extra-pyramidal burden, a finding reported in idiopathic Parkinson disease [9]. Binge-eating markedly diminished, ascribed to anorexogenic effects of ATX and goes in tandem with numerous reports of utility of ATX in binge-eating disorder [10]. Given the propensity of AAPs to expectedly invoke weight gain and subsequently metabolic syndrome, ATX, possibly by virtue of its anorexogenic effect, might counteract this, as is the case with reboxetine in anecdotal reports [11,12].

We opine that cognitive enhancers, like atomoxetine, remain a viable option to tackle residual negative and cognitive domains in schizophrenia that adversely impact functioning, and possibly a novel strategy to counteract metabolic syndrome that plagued treatment

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with AAPs, now increasingly and oftentimes indiscriminately used in paediatric population, a definitely top priority in youngsters with EOS.

## Disclosures

Authors declare no conflicts of interest.

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