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'Mirtazapine-Galantamine Combo' Tackles Behavioral Facets in Autism

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To The Editor

Autism Spectrum Disorders (ASD) are associated with a host of challenging behaviors that constitute a focus of clinical attention and a target for psychopharmacologic interventions [1]. Only Risperidone and Aripiprazole are FDA-approved to address these behavioral facets once psychological and educational approaches (e.g. Applied Behavioral Analysis, Sensory Integration) are ineffective, inaccessible, or, unaffordable [2]. Moreover, no single drug is currently approved to alter core symptoms of ASD. These behaviors include, inter alia, ADHD-like symptoms, tics and stereotypies, auto- and hetero-aggression, irritability and mood and anxiety symptoms, disturbed eating and sleeping patterns, and sexually-inappropriate behaviors [1].

Unfortunately, the use of these atypical antipsychotics is fraught with a multitude of cardio-metabolic and neurologic syndromes [3]. This calls for novel psychotropic agents that are both effective and tolerable.

Mirtazapine is atypical antidepressant with unique mechanism of action, namely; Noradrenergic-Specific Serotonergic Antidepressant (NaSSA); blocking α2 auto&hetero-receptors, thus increasing norepinephrine, also blocking 5HT2&3 receptors, as well as H1 receptors.

Galantamine is anti-dementia specific acetylcholinestrase inhibitor (AchE-i) and allosteric ligand at nicotinic acetylcholine receptors (nAchR).

Here, we are reporting on a case of an adolescent with ASD, where 'Mirtazapine-Galantamine cocktail' brought about a significant improvement in the behavioral domains and strikingly, hit some of the core social features. This was achieved with great tolerability.

A 14-year-old Kuwaiti youngster, eldest of five sibs, a product of elective Caesarean Section, emanating from a consanguineous monogamous family, attending special schooling, long diagnosed as ASD/ID (Intellectual Disability)/Epilepsy, maintained on Valproate for seizure control, was escorted by his parents for escalating behavioral dyscontrol, notably irritability, aggression, hyperactivity, fitful sleep and socially flouting over sexualized behaviors. Medical and environmental causation of this behavioral decompensation were meticulously ruled out. He couldn't tolerate a trial on Risperidone where he developed recurrent torticollis and oculogyric crisis. He failed a 6-week trial on 15 mg/d Aripiprazole. Clonidine was also tried at 300 µg/d but prematurely aborted for severe hypotension (80/50) and symptomatic bradycardia (50/min). Atomoxetine, for hyperactivity was instituted, uptitrated to 40 mg/d over 8 weeks, but, without clinically meaningful response. Ecitalopram at 10 mg/d, for 4 weeks, was introduced for aggression, but to no avail. We suggested a trial with Mirtazapine as data from the literature support its use for sexually-inappropriate behaviors in ASD, and also to help with sleep and irritability. We went to 45 mg/d over 4 weeks. Sleep improved markedly, irritability diminished significantly and most importantly, sexual behaviors were greatly tamed. Both frequency and severity of aggression became obviously less. This was well-sustained at follow-ups W-6, 8, and 12. We, then, opined to embark on a trial of Galantamine, as burgeoning evidence from literature favors its use for both core and behavioral symptom sets of ASD. We dosed it at 8 mg/d for 4 weeks, then up to 16 mg/d (in 2 divided doses). Strikingly, hyperactivity noticeably decreased, but, most importantly, better eye contact, vocalizations, gestures and social relatedness were observed. This was plateaued at follow-ups W-6, 8, and 12. No pharmacokinetic drug interactions reported with this combination. No side effects, of significance, were noted. These findings were objectified on Aberrant Behavior Checklist (ABCL) and Krug's Autism Behavior Checklist (ABC). Medications Chart is portrayed in table (1).

Drug	Comment
Risperidone	Extrapyramidal Side Effects
Aripiprazole	Ineffective
Clonidine	Hypotension and bradycardia
Atomoxetine	Ineffective
Ecitalopram	Ineffective
Mirtazapine	Improved sleep, irritability, sexually-inappropriate behaviors and aggression
Galanatmine	Improved behavioral facets and socialization

Table 1: Medication Chart

These promising results concords with those demonstrated in a naturalistic open-label study of mirtazapine in ASD where almost a third of subjects showed improvement across different domains including aggression, self-injury, irritability, hyperactivity, anxiety, depression, and, insomnia [4].

Anti-libidinal properties of mirtazapine helped sexually-inappropriate behaviors in ASD [5-6].

Cholinergic stimulation of central serotonergic subsystem with galantamine may enhance language and communication in autistic adults as shown in three cases [7]. A prospective open-label trial of galantamine in ASD showed it was well-tolerated and beneficial for interfering behaviors, particularly aggression, behavioral dyscontrol

and inattention [8]. Recently, an RCT showed galantamine was effective and safe augmentative strategy for alleviating some of autism-related symptoms [9].

Such data accrue to open new venues of psychopharmacologic interventions in ASD that are both effective and well-tolerated.

Disclosures

Authors declare no conflicts of interests or financial affiliations with psychopharmaceutical companies or industry-sponsored research.

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