



Case Report
Volume 11 Issue 1 - January 2023
DOI: 10.19080/GJIDD.2023.11.555804

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Case Series Reporting the Use of Cariprazine in the Treatment of Autism Spectrum Disorder Patients



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Submission: December 19, 2022; Published: January 10, 2023

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Abstract

Autism Spectrum Disorder (ASD) is a lifelong complex developmental condition involving persistent changes in social communication, restricted interests, and repetitive behavior that presents in levels of impaired functioning [1,2]. Management of the mood instability, anger, and aggression of this unique population can often be challenging for providers [3]. This case series includes the use of Cariprazine in the management of 12 individuals with a confirmed diagnosis of autism spectrum disorder. The cases presented represent each level of ASD from the minimally verbal low functioning individual through the patient that is verbal and high functioning. All patients had been previously treated with multiple antipsychotics and traditional mood stabilizers and did not demonstrate improvement in mood, aggression, or agitation. Initiation of Cariprazine in these patients demonstrated decreased mood lability, aggression, and agitation. Nonverbal patients were noted to be more socially interactive with caregivers. High-functioning patients were noted to have improved social skills and improved autonomous lifestyles.

Keywords: Antipsychotic; Anger; Aggression; Autism spectrum disorder; Intellectual disability; Cariprazine; Mood lability

Introduction

ASD is noted to have varied presentations and can be challenging to treat. Various medications are used to treat the behaviors associated with ASD, however, risperidone [4] and aripiprazole [5] are the only medications that are FDA-approved for treatment at this time. Metabolic parameters add an additional level of complexity in managing ASD patients, as there is often an increase in appetite with commonly used medications, and the ASD patients have preferred foods or a history of using food as a reward for good behaviors. This combination can result in significant weight gain negatively impacting their metabolic profile. Implementation of strict diet and exercise programs can pose behavioral challenges in the ASD population. Early interventions with various lines of therapy are also important in the management of ASD patients. The addition of Cariprazine has demonstrated decreased behaviors with no notable increases in weight, metabolic parameters (Total cholesterol, triglycerides, HbA1C), or prolactin levels [6].

Case Reports

Case 1

The first case is a 17-year-old Caucasian male diagnosed with level three ASD and a history of seizure disorder and precocious puberty. He was noted to attend an alternative school that focused on the development of individuals with ASD. He had a history of being nonverbal until using sign language at the age of 9 years old, however, communication had been minimal in recent years. He presented with agitation and aggression toward himself and his family members. He was noted to become violent and destructive on a daily basis. He was treated with gabapentin, ziprasidone, lamotrigine, clonazepam, and fluvoxamine. Several adjustments to his medications failed to decrease agitation, his behaviors continued to worsen, and triglycerides, total cholesterol, and weight steadily increased.

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At the age of 20 years old, Cariprazine was initiated at 1.5mg daily. Decreased aggression and irritability were noted at his two-week follow-up visit. After one month, his father reported the return of basic sign language that he had been taught (to signal simple gestures including being hungry, having to use the restroom, and gestures of hello, goodbye, and thank you]. Dad also reported that he was less oppositional about walking on the treadmill with his father or going outside to walk. His weight did not increase, and triglycerides are noted to be slightly lower [which the father relates to the family diet and notes planned improvements) the patient's father was actively working on eating habits for the entire family. The patient remains stable on Cariprazine for more than five years.

Case 2

The second case is an 18-year-old Caucasian female diagnosed with level three ASD and a history of borderline diabetes and chronic bilateral leg edema. It was exceptionally challenging to maintain the safety of her mother and younger siblings due to her increased physical aggression. She was estimated to be 61 inches in height and over 220lbs at her last weight check. Obtaining the patient's vitals was difficult and frequently triggered agitation and aggression with the office staff. Neuroleptics were trialed without improvement in aggressive events. Valproic acid and oxcarbazepine were used in conjunction with trials of risperidone, aripiprazole, olanzapine, quetiapine, ziprasidone, perphenazine, and lurasidone. She was hospitalized multiple times for increased aggression. She was discharged from inpatient care with chlorpromazine 250mg twice daily added to her medication profile. The patient continued to demonstrate aggression and continued weight gain.

Cariprazine 1.5mg was initiated with the goal of cross-tapering and discontinuing chlorpromazine. After her 2-week follow-up appointment, the mother reported no increase in anger, and chlorpromazine was successfully weaned. The mother reported her appetite was increased previous to starting Cariprazine which was identified as a trigger for anger when she dd not get her preferred food. She was noted to have less aggressive behavior with school staff. The dose was noted to have been increased to 3mg daily to fully target aggression. She has not had an inpatient admission for aggression or physically assaulted her family members since treatment was started. Her mother consented to the use of Cariprazine with the knowledge that Cariprazine is not currently approved for ASD or for patients under the age of 18.

Case 3

The third case is that of a 16-year-old African American male diagnosed with level 2 ASD which was complicated by epilepsy. He was noted to have VSN stimulator in place for seizure control. He presented with mood lability, physical aggression with his younger sibling and mother, depression, and frequent intrusive thoughts of suicide. He was previously treated with neuroleptic

medications including oxcarbazepine, topiramate, and Depakote which did not demonstrate improvement. Risperdal was of minimal benefit to mood and the patient was noted to have gained weight, demonstrated an increased prolactin level, and developed gynecomastia. Lithium, olanzapine, ziprasidone, quetiapine, clonazepam and lurasidone failed to control symptoms. Aripiprazole was also attempted, and the patient was noted to have significant weight gain with a height of 62 inches and weight of 232lbs.

Cariprazine was initiated at 1.5mg daily at the age of 13 years old after collaboration with his pediatric neurologist. Aggression was noted to be decreased at a two-week follow-up and intrusive thoughts of death were reported to be decreased. This patient has remained stable on Cariprazine for greater than two years, there has been no increase in seizure activity with the use of Cariprazine, (VSN stimulator was removed) and after following a ketogenic diet for the last year (suggested by neurology), he is now 67 in tall and weighs 157lbs. His mood remains stable. His mother consented to the use of Cariprazine with the knowledge that Cariprazine is not currently approved for ASD or for patients under the age of 18.

Case 4

The fourth case is that of a 25-year-old Caucasian male diagnosed with level two ASD. He was noted to be minimally verbal and demonstrated various stimming behaviors including tapping plastic spoons. The patient was noted to have an increase in agitation and mood swings targeted toward his mother. He was previously treated with lamotrigine, oxcarbazepine, carbamazepine, lithium, risperidone, aripiprazole, olanzapine, lurasidone, and quetiapine. Several stimulants and non-stimulants including guanfacine/clonidine had also been attempted, however, anger and aggression continued to be a concern.

Cariprazine was initiated at 1.5mg daily at the age of 21 years old. It is noted that this patient did not have any metabolic implications from previous treatment lines. Decreased irritation and anger were noted at two weeks. At the four-week point, his mother reported that he was more socially interactive and responded to questions with logical thoughts and was using full sentences. His mother reported a "more calm" disposition. He has remained stable with Cariprazine for greater than five years and is currently looking for a job. His weight/metabolic parameters remain within normal range with current height of 68.5 in and weight 145lbs.

Case 5

The fifth case is a 26-year-old Caucasian male who was previously diagnosed with level one AS. He is noted to have a history of mood swings and irritability. He would also have periods of mania-like behaviors where he would perseverate on the implications of bible verses and have a heightened state

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and/or paranoia about "going to hell" if he did not meet the requirements, he believed the Bible demanded from him. This resulted in agitation and threats of self-harm and the patient required multiple admissions. He has been noted to have failed treatment with risperidone, lithium, valproic acid, and multiple SSRIs in the past.

The patient was noted to be seen after the inpatient initiation of aripiprazole. He was noted to have severe drug-induced parkinsonian movements which required discontinuation. Cariprazine 1.5mg was initiated while aripiprazole was weaned and discontinued. At the two-week follow-up appointment, there is noted to be continued stability and no return of religious preoccupation, paranoia, or thoughts of self-harm/death. The patient was noted to require a Cariprazine increase to 3mg to target continued mood lability and has remained stable for greater than 4 years. He is noted to have attended a community college and completed a certificate program in accounting. He was also able to move into his own apartment and requires minimal support and financial oversight from his parents. His mother also reports that he is more comfortable and interactive when he is interacting with family and friends as well as the family business where he must engage with the public.

Case 6

The sixth case is a 20-year-old Caucasian male who was diagnosed with level three ASD and had a history of DMDD. He was noted to be attending mainstream high school with an IEP for learning and emotional support. He was noted to experience increased anger and physical aggression both at home and school. The mother reported he previously had poor reactions to neuroleptic medications. He was treated with quetiapine which caused tardive dyskinesia, risperidone, aripiprazole, and olanzapine which caused sedation, divalproex sodium, and stimulants including Adderall and Vyvanse that resulted in increased aggression. Non-stimulants, guanfacine and clonidine were not effective for his impulsive "meltdowns".

Cariprazine 1.5mg was initiated at the age of 17 years old. At his two-week follow up both of his parents agreed that his anger and irritable mood had decreased. He denied sedation during the day and was attending school without any altercations or negative reports. At a four-week follow-up assessment, he reported he felt that he was able to regulate his anger and not react. The patient did not have any metabolic concerns. After the initiation of Cariprazine, his mood remained stable and he was able to control his anger, however, he reported feeling angry more often, therefore, an increase to 3mg daily was needed. He graduated from high school, attained a driver's license, and has maintained two part-time employment opportunities at a local grocery store as well as with a landscaping business. The patient and his mother consented to the use of Cariprazine with the knowledge that Cariprazine is not currently approved for ASD or for patients under the age of 18.

Discussion

ASD is noted to have a varied presentation and can range from level one through level three. With limited treatment options, Cariprazine was initiated in patients with each subset of ASD. While the specific behaviors varied in each case presented, there was a noted improvement/resolution of problematic behaviors including anger, aggression, self-harm, mania-like behaviors, and hyper-religiosity with paranoia. Of other significance is the family/ guardian reports of improved social skills and communication, most notably the level three male who is now living in his own apartment [with minimal support], finished a college degree, and is employed. It is also noted that there were no significant weight or metabolic shifts with the utilization of Cariprazine, which is consistent with the long-term data that has been published in relation to Cariprazine. Each case presented is noted to be a patient presentation that had failed FDA-approved treatment with risperidone or aripiprazole. Treating the ASD patient has various levels of difficulty and limited options for treatment. The use of Cariprazine in ASD patients is noted to demonstrate decreased behaviors with stable weight or metabolic parameters. Early attention to metabolic shifts in the ASD population is necessary to avoid comorbid disease states in ASD patients.

Declaration of Patient Consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient[s]/g has/have given his/her/their consent for his/her/their clinical information to be reported in the case series. The patients/guardians understand that their names and initials will not be published, and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Conflicts of Interest

Tina Matthews-Hayes has received speaker fees from AbbVie, Neurocrine, and Otsuka pharmaceuticals; served on advisory boards or as a consultant for AbbVie, Biogen, and Neurocrine. She has also been a paid consultant for Psychiatry Times and Psych Congress Bipolar disease state CME, sponsored by Intra-Cellular Therapies, Inc. She is a paid consultant fees from Abbvie for the development of and continued content development of the website nppsychnavigator.com.

Acknowledgement

This case series is done independently and without collaboration with any pharmaceutical support.

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DOI: 10.19080/GJIDD.2023.11.555804

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