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Aripiprazole induced compulsive eating in adolescent: Is this the effect of aripiprazole on Serotonin receptors?

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Summary

Objective: *To present a case of new onset Aripiprazole induced compulsive eating in an adolescent male.*

Method: *We describe a case history of an adolescent male treated with Aripiprazole who developed compulsive eating behavior.*

Result: *The compulsive eating behavior stopped once the Aripiprazole was discontinued.*

Conclusion: *We argue that the compulsive eating behavior in the adolescent male was induced by Aripiprazole and the effect of Aripiprazole on eating behavior may be due to the effect of Aripiprazole on serotonin receptors.*

Keywords: Aripiprazole, Compulsive Eating, Serotonin.

Introduction

Aripiprazole is a dihydroquinolinone antipsychotic agent. In Canada, aripiprazole is used to treat bipolar 1 disorder in adults and adolescents of 13 years of age and older. It is used to treat Schizophrenia in adults and adolescents of 15 years and older. It is also used to treat depression in adults when used in combination with other drugs [1].

USFDA (United States Food and Drug Administration) has approved aripiprazole for treatment of schizophrenia in adults; acute treatment of manic or mixed episodes associated with bipolar I; maintenance treatment of manic or mixed episodes associated with bipolar I disorder; use as an adjunct to antidepressant treatment in adults with Major depressive Disorder; in the adolescent age group it is approved for treatment of schizophrenia (age 13-17 years), acute treatment of manic or mixed episodes associated with bipolar I disorder for age group 10-17 years. It is also approved for treatment of irritability associated with autism spectrum disorder in pediatric patient's age 6-17 years and treatment of Tourette's disorder in pediatric patient's ages 6-18 years [2].

On November 2, 2015, Health Canada issued a summary of safety review for aripiprazole and long-acting preparation of aripiprazole–Abilify Maintena. It was related to the risk of certain impulse control behaviors: Uncontrollable gambling and hyper sexuality with use of aripiprazole. At the time of review, Health Canada has received five reports of pathological gambling, and hypersexuality having suspected links with aripiprazole, however, upon review of those cases, no conclusion was made regarding the role of the drug in relation to the impulse control behavior due to limited information. After reviewing scientific and medical literature, 14 of the 18 international case reports of pathological gambling, the behavior resolved or improved from the treatment with aripiprazole was stopped or the dosage was reduced. Out of the five of the six cases of hypersexuality reported in the literature, there was improvement in the behavior after the treatment with aripiprazole was stopped or the dose was reduced [1].

On May 03, 2016, The U.S. Food and Drug Administration (FDA) also issued safety warning that compulsive or uncontrollable urges to gamble, binge eat, shop, and have sex have been reported with the use of Aripiprazole. It was based on the search report of the FDA Adverse Event Reporting System (FAERS) database and the medical literature since the approval of Aripiprazole in USA on November 2002 to January 2016. There were 184 case reports including 167 FAERS cases and 17 medical literature cases that indicated an association between aripiprazole and impulse-control problems.

Of the reported events, pathological gambling was most common. It was reported in 164 out of 184 events. The other impulse control problem reported were compulsive sexual behavior (9 of 184), compulsive buying (4 of 184), compulsive eating (3 of 184) and 4 of 184 were had multiple impulse control problem (USFDA).

Mahapatra et al. reviewed 22 case of aripiprazole induced impulse control published in medical literature. Of the 22 case reviewed, only one case reported compulsive eating in 62 years old female [3].

We report a rare event of an aripiprazole induced new onset compulsive eating behavior in an adolescent. 10-year-old Hispanic male was referred for psychiatric assessment by the teacher because he was disruptive in the class and impatient for his turn. As per the teacher's report, he was over talkative in the class and to make odd noises in the class. He was not sitting in the classroom and was always moving about in the classroom. He was not focused and was easily distracted. The patient used to burp on others face. He did not follow-up instructions and was not listening to the teachers. He was not doing his homework, was not performing well in studies in the class and was in danger of failing.

The mother reported that the patient had history of being delinquent and disrespectful at home and not listening to his mother. The patient was hyperactive at home and always moving around or fidgety. He has history of throwing things in home and school. Usually, he forgets to bring books to home after school. He has a history of losing pencils and other stuff in the class.

The patient had a past history of head banging. There was no history of substance use or any other legal or social problems. No history of seizures or head injury. There was family history of depressive episodes in mother. There was no history of psychosis in the family.

On examination, the patient looked his stated age and was appropriately groomed. He was hyperactive and was moving around in the room. It was difficult to stop him from moving around. He was interrupting his mother while she was being interviewed. His mood was euthymic. There were no delusion or hallucinations observed during the mental status examination. His thought process was linear and goal directed. His general knowledge and mathematical ability was age appropriate. The patient's insight was poor.

The patient was diagnosed as Attention deficit hyperactivity disorder (ADHD), predominantly hyperactivity / impulsive presentation. We treated the patient with methylphenidate 5 mg daily in the morning, on school-days only. The patient was followed up regularly every month. Over the subsequent follow-ups, the patient remained talkative, but there was improvement in his overall behavior. He was more cooperative and less hyperactive. Complaints from the school got reduced. He was less disruptive at home. He has been compliant with medications, and no side effects were reported. His sleep and appetite remained normal. Over the next couple of months, his academic performance improved drastically. He was awarded "The student of the month" twice for two consecutive months.

Over the further follow-ups the patient started showing some mood symptoms. He was laughing for no reason. He was defiant impulsive and demanding. The patient was speaking loudly and appeared to be in a rush. His mood remained irritable. The mother reported that he was cursing and arguing with her for no appropriate reasons. He also hit the driver while going to school. The patient was showing psychomotor agitation and was angry for no appropriate reason.

To control the new onset mood symptoms patient was treated with Aripiprazole, 5 mg daily. During the follow up, it was observed that the patient's ADHD symptoms remained stable. His performance in the class improved. His behavior with the family members improved. However, the patient complained of eating more and gained 5 Kg, over the period of 3 months. The patient reported that he was not able to control his eating, and he was eating excessively. He was eating till he was uncomfortable and was eating even when he was not actually hungry. He felt bad about eating but was not able to control himself. The mother reported that he used to eat everything in the refrigerator so that nothing was left for rest of the family to eat. He used to drink the entire nutritional supplement which was prescribed to his mother. The frequency of uncontrolled eating was almost daily. There was no history of compensatory behavior in the form of purging or increased exercise. Considering it as Aripiprazole induced behavioral change, we discontinued Aripiprazole and followed up the patient after 2 weeks. Over the subsequent follow up, the patient reported reduction in his eating behavior. He reported that he was able to control his eating. The amount he used to eat previously was reduced. He was not eating up to the level of getting uncomfortable. His weight remained stable. His eating behavior remained stable. No binge eating behavior reported is subsequent follow up visits.

Discussion

Compulsive behavior is not so commonly induced with aripiprazole. The compulsive eating is rarer and compulsive eating in adolescents is rarest of rare. Health Canada safety found an increased risk of two types of impulsive behaviors with the use of aripiprazole: pathological gambling and hypersexuality. No case of compulsive eating was reported to Health Canada. As per USFDA, out of 184 cases reported, only 3 had compulsive eating disorder [4].

The role of Serotonin (5 HT) in relation of eating behavior has been documented in various studies. It has been shown that, manipulation that increased 5-HT neurotransmission reduces eating behavior, whereas those that reduce 5-HT activity precipitate compulsive or binge eating behavior [5]. Studies have shown that activation of 5-HT1A and 5-HT2B in the arcuate nucleus of the hypothalamus increase food intake and activation of 5-HT4 in nucleus accumbens inhibits the physiological drive to eat [6, 7].

Though both impulsive and compulsive behavior have been linked with a 5-HT but some of the theorist have postulated that impulsivity and compulsivity traits occupy apposite poles of the continuum of 5-HT [8, 9]. In other words, low 5-HT uptake was related with impulsive behavior whereas high 5-HT group showed more perfectionism and compulsivity [10]. Studies have also postulated the role of 5-HT_7 receptors relation with obsessive-compulsive

disorder. It has been shown in animal models that inactivation of 5 HT_7 receptors leads to decreased repetitive behavior suggesting a link of 5-HT_7 with compulsive behavior [11].

Aripiprazole is a high affinity for D2-D3 dopamine and 5-HT_7 receptors [12]. Aripiprazole has also been shown to have partial agonist properties at D3, 5-HT_{1A}, 5-HT_{2A} and 5-HT_{2C} serotonin receptors. Aripiprazole was also found to be in antagonist at 5-HT_6 receptors a weak partial agonist at 5-HT_7 receptors. Studies have also shown that Aripiprazole has an inverse agonist property at 5-HT_{2b} receptors [13]. The current evidences of a complex pharmacodynamic profile of Aripiprazole on 5HT receptors suggest that the role of Aripiprazole on 5-HT receptors may have a more significant role on compulsive behaviors like eating than the dopamine D3 which may have more effect on the impulsive and addictive behaviors such as gambling or more likely the complex interplay between serotonin and dopamine. However, currently it is very difficult to specify which specific receptor, or the neurochemical may have a correlation with which specific behavior. More studies are needed to confirm this, and we hope that we will have an answer to this question in the future.

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