Key Words: aripiprazole, adverse effect, hypertension

Aripiprazole-induced Asymptomatic Hypertension: A Case Report

by Hilal Seven, Medine Giynaş Ayhan, Ayşe Kürkcü, Süleyman Özbek, İbrahim Eren

ABSTRACT *~ Aripiprazole is a second generation antipsychotic widely prescribed for the treatment of psychiatric diseases. It is generally known that antipsychotics have hypotensive effects. In this case report, however, we present the case of a medically healthy patient with schizophrenia who developed hypertension (HT) after the initiation of aripiprazole. The patient's blood pressure returned to normal after discontinuation of aripiprazole, suggesting that aripiprazole may have led to asymptomatic acute HT.* Psychopharmacology Bulletin. *2017;47(2):53–56.*

Introduction

Aripiprazole is a second-generation antipsychotic used safely in the treatment of schizophrenia, bipolar disorder and other psychiatric diseases because of milder metabolic side effects compared to other antipsychotics. Aripiprazole acts as a strong partial agonist of D2 and 5-HT1A receptors. Common side effects include headaches, sleeplessness, agitation and anxiety.[1] It has been reported that one of the most frequent cardiovascular side effect of second-generation antipsychotics is postural hypotension.[2] However, there is little information on the development of acute hypertension (HT) due to antipsychotics. Here, a case of acute HT induced by aripiprazole is reported and the possible mechanisms of HT are discussed.

Case

A 56 year-old woman with a 25-year history of schizophrenia was admitted to our clinic due to an acute exacerbation of her psychiatric disorder. Upon admission, loss of appetite, irritability, paranoid delusions and self-talking were present. Medical history and physical examination (including blood pressure) revealed no somatic disorder. No history of drug and alcohol abuse was reported. The patient had been treated for 2 years with olanzapine 10 mg/day and risperidone 37.5 mg/15 days and recovered partially. During the follow up period, olanzapine

Drs. Seven, Giynaş Ayhan, Kürkçü, Özbek, Eren, MD, Konya Training and Research Hospital, Department of Psychiatry, Konya, Turkey.

To whom correspondence should be addressed: Dr. Medine Giynaş Ayhan, MD, Konya Eğitim ve Araştirma Hastanesi, Psikiyatri Kliniği, 42250, Selçuklu-Konya, Turkey. E-mail: drmedineayhan@gmail.com

and risperidone were discontinued because of the adverse effects of sedation and weight gain. The patient underwent no treatment for 3 months until the current admission. The vital signs and blood tests were within normal limits in admission to the hospital. Aripiprazole 5 mg/day was then started, which was increased to 15 mg/day. About 9 days after the first intake of aripiprazole, blood pressure of 180/100 mmHg was measured indicating arterial HT. The patient had no symptoms like palpitation, headache or confusion. Physical examination (temperature, pulse), laboratory studies (complete blood count, liver and kidney function, serum electrolytes, lipids, coagulation) and electrocardiograms were within normal limits. She had no endocrine or reno-vascular disease that could explain the etiology of HT. Two days later aripiprazole was discontinued and the patient's HT resolved within 24 hours without treatment. At a subsequent follow up, the blood pressure was in the normal range.

Discussion

In the case report presented here, HT after the initiation of aripiprazole and recovery after aripiprazole discontinuation was observed. The case had no other medication or systemic disease that could explain the mechanism of HT. Based on these clinical features; it was thought that the patient developed asymptomatic HT due to aripiprazole.

It is well-known that second-generation antipsychotics may cause arrhythmia, prolonged QTc interval and orthostatic hypotension in patients who have no cardiovascular disease.[2] However, case reports suggest that HT may develop with the use of aripiprazole.[3–6] Borras et al. reported that a patient with schizophrenia who used aripiprazole 30 mg/day developed HT (220/110 mmHg) and tachycardia, and that the blood pressure returned to normal after discontinuation of aripiprazole.[3] Supporting this, another study reported that the blood pressure increased (200/110 mmHg) in a patient who was taking venlafaxine 150 mg/day and aripiprazole 5 mg/day and that the blood pressure decreased to normal 48 hours after stopping aripiprazole.[4] Additionally, Bat-Pitault and Derlome reported the development of HT in an adolescent patient taking aripiprazole.[5] Moreover, it was reported that a patient with depression using duloxetine 90 mg/day and aripiprazole 5 mg/day developed HT (220/110 mmHg) and headache. The blood pressure of this patient didn't respond to antihypertensive drugs and the HT resolved only after reducing the dose of aripiprazole to 2.5 mg/day.[6] In another case report, it was presented that the blood pressure increased after adding aripiprazole to the therapy; a decrease was seen after the discontinuation of aripiprazole.[7]

For the majority of the case reports mentioned above, it was thought that a history of HT or cardiovascular disease[4,7] and use of additional drugs[4,6] might have contributed to the increase in blood pressure. However, in the current case, as corroborated in the reports by Borras[3] and Pitault and Delorme's,[5] the patient had been using only aripiprazole and had no history of HT or cardiovascular disease. Moreover, other etiologic factors that may contribute to HT could not be found and it was observed that blood pressure resolved after stopping aripiprazole treatment.

It may be necessary to review the receptors that aripiprazole acts on to understand the mechanism of hypertension induced by aripiprazole. It is known that 5-HT 2A and a-1 adrenergic receptors play important roles in the development of hypertension.[8] Aripiprazole may cause an increase in blood pressure by binding with high affinity to the a-1A adrenergic receptors. It is also thought that aripiprazole causes HT by acting an as agonist for on 5-HT 2A receptors; however, this is controversial since some articles suggest that aripiprazole acts as an antagonist for 5-HT 2A receptors.[1] While one study suggested that use of aripiprazole resulted in higher blood pressure compared to placebo,[9] there are other studies that report that no relationship between the development of blood pressure abnormality and the use of aripiprazole.[10] Although individual differences may be important, these conflicting results need to be clarified with long term follow-up studies.

In this case report, we presented a case that developed asymptomatic HT with the use of aripiprazole, which resolved after the discontinuation aripiprazole. We think that this rare side effect seen in clinical practice should not be neglected and that blood pressure needs to be monitored closely regardless of whether the patient has a cardiovascular disease or not. ✤

Acknowledgements

The authors did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of Interest

None.

References

1. Di Sciascio G, Riva MA. Aripiprazole: from pharmacological profile to clinical use. *Neuropsychiatr Dis Treat*. 2015;11:2635–2647.
2. Pacher P, Kecskemeti V. Cardiovascular side effects of new antidepressants and antipsychotics: new drugs, old concerns? *Curr Pharm Des*. 2004;10:2463–2475.

3. Borras L, Constant EL, Eytan A, Huguelet P. Hypertension and aripiprazole. *Am J Psychiatry.* 2005;162:2392.
4. Pitchot W, Ansseau M. Aripiprazole, hypertension, and confusion. *J Neuropsychiatry Clin Neurosci.* 2010;22:123.
5. Bat-Pitault F, Delorme R. Aripiprazole and hypertension in adolescents. *J Child Adolesc Psychopharmacol.* 2009;19:601–602.
6. Hsiao YL, Chen SJ, Shen TW, Chang CH, Chen ST. Aripiprazole augmentation induced hypertension in major depressive disorder: a case report. *Prog Neuropsychopharmacol Biol Psychiatry.* 2011;35:305–306.
7. Yasui-Furukori N, Fujii A. Worsened hypertension control induced by aripiprazole. *Neuropsychiatr Dis Treat*. 2013;9:505–507.
8. Martin C, Brodde O-E, Insel PA. Peripheral adrenergic receptors in hypertension. *Hypertension.* 1990;16:107–120.
9. Keck PE Jr, Calabrese JR, McIntyre RS, McQuade RD, Carson WH, Eudicone JM, et al. Aripiprazole Study Group. Aripiprazole monotherapy for maintenance therapy in bipolar I disorder: a 100-week, double-blind study versus placebo. *J Clin Psychiatry.* 2007;68:1480–1491.
10. Findling RL, Robb A, Nyilas M, et al. A multiple-center, randomized, doubleblind, placebo-controlled study of oral aripiprazole for treatment of adolescents with schizophrenia. *Am J Psychiatry.* 2008;165:1432–1441.