
Competing interests: none declared.
Conflict of interests: none declared.

All authors contributed to conception and design, manuscript preparation, read and approved the final manuscript.

All authors abide by the Association for Medical Ethics (AME) ethical rules of disclosure.
Hypertension Induced by aripiprazole: A case report

Sayar GH, Özten E, Gül IG, Eryılmaz G, Erkmen H

Gökben Hızlı Sayar  Uskudar University  ghizli@uskudar.edu.tr
Eylem Özten  Uskudar University  eozten@yahoo.com
Işıl Göğcegöz Gül  Uskudar University  isilggul@gmail.com
Gül Eryılmaz  Uskudar University  geryilmaz@npistanbul.com
Hüsnü Erkmen  Uskudar University  husnuerkmen@yahoo.com

ABSTRACT

Introduction: Hypotension is a known effect of atypical antipsychotics. However, there is little information on acute hypertension resulting from antipsychotic drugs. Aripiprazole is a potent partial dopamine D2 agonist, a serotonin 5-HT1A agonist and a 5-HT2A antagonist. It also displays high affinity for the α-1B, -2A, -2C and β1, -2 adrenergic receptors. Many studies underline the role of α-1A adrenergic receptors in malignant hypertension.

Method: Here we present a case of a 38-years old male patient with psychotic depression.

Discussion: Aripiprazole was initiated at 10 mg/d and 36 hours after the first dose the patient complained of headache and palpitation. His physical examination revealed that he developed a hypertensive crisis with arterial hypertension (170/110 mmHg) and tachycardia (118 beats/minute). His blood pressure returned to normal a week after the interruption of aripiprazole.
Conclusion: Although the mechanism underlying the rise in blood pressure remains unclear, careful monitoring of blood pressure variations when administering aripiprazole to patients previously treated for high blood pressure is necessary.

Keywords: aripiprazole, blood pressure, hypertension

INTRODUCTION

Aripiprazole was approved by the FDA in the USA in 2002 and licensed in the European Union in 2004 for the treatment of schizophrenia. Aripiprazole, by showing a partial agonistic effect on dopamine D2 receptors, is noteworthy as the first treatment among antipsychotic medications. Also, it has been shown to be a partial agonist with high affinity to dopamine D3 and serotonin 5-HT1A receptors, antagonist with high affinity to 5-HT2A and 5-HT2B receptors, weak partial agonist with moderate affinity to the serotonin 5-HT2C receptors, and weak partial agonist with high affinity to 5-HT 7 receptor\textsuperscript{1,2,3}.

Aripiprazole is pharmacokinetically metabolized in the liver through N-dealcalization, hydroxylation or dehydrogenation by cytochrome P450 (CYP) 3A4 and CYP 2D6 enzyme systems\textsuperscript{4}. Today, with its efficacy and positive side effect profile, aripiprazole is widely used in the treatment of schizophrenia and bipolar disorder. It is also emphasized as a good augmentation therapy option in treatment-resistant depression with psychotic features\textsuperscript{5,6}.

Cardiovascular side effects of aripiprazole are rarely seen, however, asymptomatic postural hypotension has been reported in elderly patients\textsuperscript{7}. Although there is no history of cardiovascular disease, many cases of orthostatic hypotension, arrhythmias and prolonged QTC interval associated with new generation antipsychotics have been reported\textsuperscript{8}. In general, orthostatic hypotension is related to antipsychotics, however, in the literature, there are case reports of hypertensive attack related to the use of aripiprazole\textsuperscript{9,10,11}. In this case report, we are aiming to review the possible relation between aripiprazole and hypertension in a case of aripiprazole-induced hypertension, without hypertension history.

CASE

A thirty-eight years old, Caucasian, male patient, without any systemic disease or cigarette smoking suffered from depression for 6 months. His mother has hypertension,
otherwise no further features in his family history. During the examinations conducted by the occupational physician in the past, high blood pressure was not detected. Four years ago, he has a history of major depressive episode, remission was achieved with sertraline, and after follow-ups the treatment was finalized. Six months ago, due to a stressor in his workplace, he had depressed mood, anhedonia, changes in sleep and appetite, feelings of guilt and worthlessness. He had reference delusions as he is monitored at work and people are talking about him. His thyroid function tests, vitamin B12, folic acid, hemogram, blood chemistry was normal. His Hamilton Depression Rating Scale 17 Item (HAMD-17) score was 27. His body mass index was 26, blood pressure was 120/70 mmHg.

The patient, who was diagnosed as major depression with psychotic features, was given a treatment of sertraline 50 mg/day and aripiprazole 10 mg/day. In his follow-up after a month, his depressive and psychotic symptoms were decreased. His HAMD-17 score became 14. However, the patient complained of frequent throbbing occipital and parietal headaches during daytime. His blood pressure was measured as 170/110 mmHg and heart rate was 118 bpm, rhythmic. His neurological examination was normal. Plasma levels for both medicines were requested and the results were within therapeutic range (sertraline 27 ng/ml with a normal range of 10-50 ng/ml and aripiprazole 140 ng/ml with a normal range of 50-350 ng/ml). His electrocardiogram was normal. He had no extrapyramidal side effects.

Aripiprazole dosage was rearranged as 5 mg/day and blood pressure follow-up was requested. During the next one-week period, his blood pressure was in the range of 130-140/100-110 mmHg and heart rate was 88 bpm. High blood pressure was considered to be related to aripiprazole. Aripiprazole was replaced with risperidone 1 mg/day. During the following week, his blood pressure was normal. After six weeks, his blood pressure was 110/70 mmHg, and HAMD-17 score was 11. His affect was euthymic and had not any psychotic symptoms.

**DISCUSSION**

In a review of the cases of hypertensive attack developed with the use of aripiprazole; Borras et al., reported a case of a 56 years old patient who is diagnosed with paranoid schizophrenia and followed up since 30 years. The patient had tachycardia and hypertensive attack (blood pressure: 220/110mmHg) 26 hours after the aripiprazole dosage was increased from 15 mg/day to 30 mg/day. After aripiprazole was stopped, the patient’s blood pressure returned to normal. Adrenergic hyperactivity is reported to be the cause of
hypertension. Having hypertension due to aripiprazole overdose in this case but not in another case\textsuperscript{10} is reported to be related to personal sensitivity.

In another case, it was reported that a 55 years old patient with major depressive disorder and diabetes mellitus, on a treatment of duloxetine 90 mg/day was given aripiprazole 2.5 mg/day and 10 days after the dosage was increased to 5mg/day, the patient’s blood pressure was measured as 220/110 mmHg. After the aripiprazole dosage was decreased to 2.5 mg/day the blood pressure became normal. Authors concluded aripiprazole and duloxetine interaction might have been the cause of high blood pressure\textsuperscript{11}. In a 24-month follow-up study in which pimozide and aripiprazole were compared in terms of cardiovascular side effects, it was shown that aripiprazole did not cause any significant changes in ECG. Hypertension reported in one of 25 patients using aripiprazole and in that case blood pressure was normalized after reducing the dose of aripiprazole\textsuperscript{12}. In another case of an 80 years-old patient who was taking venlafaxine 150mg/day, confusion and hypertension was reported after adding aripiprazole 5mg/day to the treatment. In this case, it was reported that aripiprazole augmentation, patient’s cardiovascular disease history and venlafaxine treatment all might have contributed to hypertensive tendency\textsuperscript{13}. In a 51 years old female patient with schizoaffective disorder and a history of hypertension; confusion, headache, and high blood pressure (198/100 mmHg) was observed 48 hours after the intake of aripiprazole. The blood pressure of a 62 years old patient with psychotic disorder and major depressive disorder increased up to 200-210/90-110 mmHg within 72 hours after the intake of aripiprazole\textsuperscript{14}.

In our case, high blood pressure measured a month after sertraline 50 mg/day and aripiprazole 10 mg/day was started, however the patient reported as from first week as “headache and pressure in ears.” Hypertension was detected although the patient doesn’t have a history of cardiovascular disease. As it was also observed in other cases that the blood pressure decreased with the decrease of daily aripiprazole dose so a relation between aripiprazole and blood pressure may be considered. And after aripiprazole was stopped, blood pressure became normal.

**CONCLUSION:**

In this case the hypertensive state recovered after switching to other antipsychotics, and this suggests that aripiprazole may lead to hypertension. Comprehensive prospective studies on the cardiovascular effects of aripiprazole are needed. Understanding the
mechanism leading to hypertensive crisis is important due to the increasing use of atypical antipsychotics.

REFERENCES


