

# Aripiprazole-Induced Diplopia: A Case Report

Abdullah Atli<sup>1</sup>, Yavuz Selvi<sup>2</sup>, Aydın Yıldız<sup>3</sup>, Mehmet Cemal Kaya<sup>1</sup>

## ÖZET:

Aripiprazole bağlı diplopi: Bir olgu sunumu

Diplopi çift görme olarak tanımlanan ve yaşam kalitesini bozan bir durumdur. Akut diplopi bazı genel tıbbi ilaçlar ve psikotrop ilaç kullanımında görülmektedir. Aripiprazol D2 ve 5-HT1A reseptörlerine parsiyel agonist ve 5-HT2A reseptörlerine antagonist aktivite gösteren atipik antipsikotik ajandır. Bu yazıda şizofreniform bozukluk tanısıyla takip edilen 24 yaşındaki bir hastada, oral aripiprazol kullanımını takiben ortaya çıkan, diplopi olgusu bildirilmektedir. Klinisyenler aripiprazol tedavisiyle diplopi ortaya çıkabileceğini akılda tutmalıdırlar.

**Anahtar sözcükler:** Aripiprazol, diplopi, yan etki

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## ABSTRACT:

Aripiprazole-induced diplopia: a case report

Diplopia is a condition that involves seeing double and impairs quality of life. Acute diplopia can be seen with some general medical drugs and psychotropic drugs. Aripiprazole is a new atypical antipsychotic agent; it has partial agonist activity at D2 and 5-HT1A receptors and antagonist activity at 5-HT2A receptors. This paper reports development of diplopia, a rare adverse effect of psychotropic drugs, in a 24 year old patient with schizophreniform disorder following use of oral aripiprazole. Clinicians should keep in mind that diplopia may occur with aripiprazole treatment.

**Keywords:** aripiprazole, diplopia, adverse effect

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<sup>1</sup>Assist. Prof., Dicle University School of Medicine, Department of Psychiatry, Diyarbakir - Turkey  
<sup>2</sup>Assoc. Prof., Selcuk University School of Medicine, Department of Psychiatry, Konya - Turkey  
<sup>3</sup>M.D., Balıklıgöl State Hospital Department of Ophthalmology, Sanliurfa - Turkey

Address reprint requests to:  
Dr. Abdullah Atli,  
Dicle University School of Medicine,  
Department of Psychiatry, 21280,  
Diyarbakir - Turkey

E-mail address:  
abdullahatli@yandex.com.tr

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## INTRODUCTION

Eye movements are controlled by extraocular muscles that are innervated from oculomotor nerves and the supranuclear centrum. Diplopia can occur as these structures damage, thus both eyes cannot look in the same direction (1).

Aripiprazole is an atypical antipsychotic agent; its mechanism of action consists of partial agonist activity at D2 and 5-HT1A receptors and antagonist activity at 5-HT2A receptors. Aripiprazole is commonly used for the treatment of many psychiatric disorders, such as schizophrenia (2), bipolar disorder (3), depression (4) and obsessive-compulsive disorders (5). It has been reported that, when

compared to other atypical antipsychotics, aripiprazole is safe and has better efficacy. Aripiprazole has been reported to have fewer adverse effects, such as extrapyramidal syndromes, elevated prolactin levels, prolonged QTc and sedation (6). The other side effects as insomnia, somnolence, headache, nausea, vomiting can also be observed (7).

Aripiprazole can be associated with some rare side effects, such as supraventricular tachycardia (8), Pisa syndrome (9) and parkinsonism (10). At the same time in the literature, aripiprazole is rarely reported to cause ocular side effects (11). Here, we present a case of aripiprazole-related diplopia in a patient with schizophreniform disorder.

## CASE

Ms. N, a 24-year-old single woman, was brought to our outpatient clinic by her mother and brother. She had psychotic symptoms with social isolation, mutism, occasional violence toward her family, irritability, persecution delusions, and auditory hallucinations for three months. Neither she nor her family had past psychiatric or neurological history. Physical and neurological examination was normal and there was no personal history of alcohol-substance abuse or use of drugs for any illness. We diagnosed schizophreniform disorder and we started on 15 milligram/day aripiprazole. At the end of first week of treatment the patient had developed diplopia with feelings of discomfort. The patient was evaluated by an ophthalmologist. On ophthalmic examination the patient's bilateral anterior and posterior segments were seen to be normal, her bilateral visual acuity was normal (20/20) and there was no limitation of extraocular muscle movement in any directions of view. The visual field examination did not reveal any signs that explain the double vision. Her secondary neurological examination was found to be normal. Consequently we suspected that the diplopia was related to the newly started aripiprazole treatment. Aripiprazole was discontinued and we started a new atypical antipsychotic agent. After we stopped aripiprazole, her complaint of diplopia disappeared within the first week.

## DISCUSSION

Aripiprazole is a new antipsychotic agent that is a dihydroquinolone derivative and its chemical structure is different than other antipsychotic agents. The efficacy of aripiprazole is mediated through a combination of partial agonist activity at D2 and 5-HT<sub>1A</sub> receptors and antagonist activity at 5-HT<sub>2A</sub> receptors. Aripiprazole exhibits high affinity for dopamine D2 and D3, serotonin 5-HT<sub>1A</sub> and 5-HT<sub>2A</sub> receptors, moderate affinity for dopamine D4, serotonin 5-HT<sub>2C</sub> and 5-HT<sub>7</sub>, alpha<sub>1</sub>-adrenergic and histamine H1 receptors,

and moderate affinity for the serotonin reuptake site (6). Aripiprazole has no appreciable affinity for cholinergic muscarinic receptors. Headache, insomnia, nausea, vomiting, light headiness, somnolence, constipation, increased appetite and dyspepsia are common adverse effects of aripiprazole (12). Also hiccup (13), tardive dystonia (14), paroxysmal supraventricular tachycardia (8), Pisa syndrome (9) and myopia (11) are rare side effects that have been reported as case reports in the literature.

Diplopia usually occurs after third nerve palsy, fourth nerve palsy, sixth nerve palsy, orbital disorder, cavernous sinus syndrome, superior orbital fissure syndrome, post-traumatic conditions, internuclear ophthalmoplegia, vertebrobasilar artery insufficiency and other central nervous system lesions (15).

In this case, neurological as well as ophthalmologic causes were considered. Our patient was examined by a neurologist and an ophthalmologist. In the ophthalmological examination, the bilateral anterior and posterior segments were seen to be normal and bilateral visual acuity was normal (20/20). The initial and secondary neurological examinations were normal and magnetic resonance imaging was normal. The routine blood chemistry analyses were also normal.

The development of acute diplopia has been seen with some general medical drugs, such as hydrochlorothiazide (16), sulfonamide (17) and fluoroquinolones (18). Diplopia has also been reported following treatment with some psychotropic drugs like topiramate, lamotrigine and oxcarbamazepine (19), and there have been case reports of citalopram and sertraline related diplopia (20,21). Acute myopia and diplopia secondary to aripiprazole use has been previously reported by Selvi et al. (22). Diplopia in these cases may be explained by ciliary spasm, ciliary body effusion, peripheral uveal effusion, the effect of ocular serotonergic interneuronal fibers or anticholinergic activity. In the present case diplopia cannot be attributed to anticholinergic mechanisms since aripiprazole lacks previously

shown anticholinergic activity (23). Additionally, the patient did not demonstrate any other anticholinergic symptoms. There was not sufficient evidence of other mechanisms to explain the cause of diplopia. Another cause of drug-induced diplopia is inflammation and edema in the tendons of the extraocular muscles. In these cases tendon inflammation and edema have decreased and diplopia has resolved after discontinuation of the drug (18). Diplopia was resolved after discontinuation of aripiprazole treatment in our case. As a result inflammation and edema in the tendons of the extraocular muscles may have been

a cause of aripiprazole induced diplopia in our case. A point to note is that an oculogyric crisis may occur in patients using antipsychotics. An oculogyric crisis may result in double vision with limitation of the visual field. In this case there were no additional extrapyramidal system symptoms and a limitation of extraocular muscle movements was not detected; for these reasons an oculogyric crisis was excluded.

Here, we report a case of aripiprazole-related acute diplopia. Clinicians should keep in mind that diplopia as a rare adverse event might occur during oral aripiprazole treatment.

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