

Case Report

Aripiprazole-induced Hyperprolactinemia in a Young Female with Delusional Disorder

Sam Padamadan Joseph

ABSTRACT

Hyperprolactinemia is a common adverse effect of antipsychotic medication. Switching over to aripiprazole or adjunctive aripiprazole has been advocated for optimal management of antipsychotic-induced hyperprolactinemia. Adjunctive treatment with aripiprazole has been shown to normalize prolactin levels without affecting already achieved improvements in psychotic symptoms. However, here, we present the case of a 36 year old female with delusional disorder who developed symptomatic hyperprolactinemia while on aripiprazole treatment. Dopamine acts as a tonic inhibitor of prolactin secretion through the tubero-infundibular dopaminergic system. Aripiprazole being a partial agonist has a lower intrinsic activity at the D2 receptor than dopamine, allowing it to act as both, a functional agonist and antagonist, depending on the surrounding levels of dopamine. Hence, in the absence of a competing D2 antagonist and the presence of dopamine (the natural agonist), aripiprazole could act as a functional antagonist and thus elevate prolactin levels.

Key words: Aripiprazole, dopamine partial agonist, hyperprolactinemia

INTRODUCTION

Hyperprolactinemia is a common adverse effect of antipsychotic medication.^[1] First generation antipsychotics along with amisulpride, risperidone, paliperidone, and zotepine have been consistently reported to be associated with the high rates of hyperprolactinemia and termed as “prolactin-raising,” whereas clozapine, olanzapine, quetiapine, ziprasidone, and aripiprazole, which have a more favorable profile, have been termed as “prolactin-sparing.”^[1-3] Switching over to aripiprazole or adjunctive aripiprazole, has been advocated for the optimal management

of antipsychotic-induced hyperprolactinemia.^[4,5] Adjunctive treatment with aripiprazole has been shown to normalize prolactin levels without affecting improvements in the psychotic symptoms that had already been achieved with the previous antipsychotic treatment.^[5] However, a literature search shows the case reports of paradoxical hyperprolactinemic symptoms such as galactorrhea associated with aripiprazole use.^[6] Saraf *et al.* in a case report of a female, who developed hyperprolactinemia, while on aripiprazole, postulated that aripiprazole could have dopamine antagonistic properties at higher doses as the partial D2 agonistic

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How to cite this article: Joseph SP. Aripiprazole-induced hyperprolactinemia in a young female with delusional disorder. *Indian J Psychol Med* 2016; 38:260-2.

Access this article online	
Website: www.ijpm.info	Quick Response Code 
DOI: 10.4103/0253-7176.183082	

Department of Psychiatry, Chalmeda Anand Rao Institute of Medical Sciences, Karimnagar, Telangana, India

Address for correspondence: Dr. Sam Padamadan Joseph
Department of Psychiatry, Chalmeda Anand Rao Institute of Medical Sciences, Karimnagar, Telangana, India.
E-mail: drsampj@gmail.com

activity could be dose-related.^[7] Recent research has also shown that the beneficial effect of aripiprazole on other antipsychotic-induced hyperprolactinemia is seen at lower doses and plateaus off at higher doses.^[8] However, here, we present the case of a female with the delusional disorder who developed symptomatic hyperprolactinemia even while on a low dose (10 mg/day) of aripiprazole.

CASE REPORT

A 36-year-old married female was presented to the psychiatry outpatient services with 2 years of delusion of infidelity and significant sociooccupational dysfunction in the absence of any impairment in sleep or appetite. Vitals were stable, body mass index (BMI) was calculated to be 26 and systemic examinations revealed no abnormality. Baseline prolactin level was 14 ng/ml.

In view of the high BMI and poor insight, she was started on aripiprazole. It was expected that the favorable side effect profile of aripiprazole with relatively less weight gain and extrapyramidal symptoms would ensure compliance. Aripiprazole was started at an initial dose of 5 mg at night and was increased to 10 mg and later 15 mg after 4 days each and 15 mg was continued as maintenance. However, 3 weeks later, she was presented with galactorrhea and a missed menstrual period. Her psychotic symptoms had subsided. There was no weight gain or extrapyramidal symptoms. A urine pregnancy test was done to rule out pregnancy. Serum prolactin level was found to be 96 ng/ml. Neuroimaging was done to rule out a prolactinoma. The possibility of aripiprazole-induced hyperprolactinemia was considered and aripiprazole was stopped. As she was otherwise asymptomatic, no other medication was started and she was sent home. At follow-up, 1-month later, galactorrhea had subsided, she had menstruated, and repeat prolactin levels were 18 ng/ml. Her psychotic symptoms continued to be in remission, and she returned home medication-free.

Three months later, she presented with the relapse of psychotic symptoms. Aripiprazole was restarted as previously, but was maintained at 10 mg owing to the previous history of hyperprolactinemia. She reported back within a month with the complaints of galactorrhea and amenorrhea at which time her psychotic symptoms were in complete remission. Serum prolactin levels were repeated and found to be elevated (84 ng/ml). Again, aripiprazole was stopped and patient returned home. Serum prolactin levels were normalized (19 ng/ml) and hyperprolactinemia symptoms were subsided within 1-month.

The patient and her spouse have provided consent for publishing this case report.

DISCUSSION

Peptides, steroids, and neurotransmitters regulate the synthesis and release of the hormone prolactin from the lactotrophs of the anterior pituitary.^[2] The most important hypothalamic prolactin-inhibiting factor is dopamine.^[2,4] Dopamine acts as a tonic inhibitor of prolactin secretion through the tuberoinfundibular and the tuberohypophysial dopaminergic systems.^[9] The binding of dopamine to the D2 receptors on the membrane of the lactotroph cells inhibits the prolactin gene transcription, synthesis and release of prolactin, and lactotroph proliferation.^[9] On the other hand, D2 receptor blockade by antipsychotics counteracts the tonic inhibitory effect of dopamine on prolactin secretion, thus elevating serum prolactin levels.^[10] The degree of hyperprolactinemia caused correlates with the penetrability of the blood-brain barrier and the strength of the dopamine blockade.^[1,4,11] The quicker the drug dissociation from the receptor, the lesser is the increase in plasma prolactin.^[2]

Aripiprazole is a partial agonist at the D2 receptor. The functional activity of a partial agonist at the specific receptor depends on the presence or absence of other full agonists and antagonists in the surrounding milieu. If there is no full agonist, partial agonists show functional agonist activity. They bind to the receptor to produce the physiological response seen, when the receptor is activated. However, if a full agonist is simultaneously present, the partial agonist shows functional antagonist activity. It competes with the full agonist for receptor occupancy and when bound, the response is lesser than that seen with the full agonist alone. Aripiprazole has a lower intrinsic activity at the D2 receptor than dopamine, allowing it to act as both, a functional agonist and antagonist, depending on the surrounding levels of dopamine.^[12] In the presence of a prolactin-raising antipsychotic, adjunctive aripiprazole competes with it to possibly act as an agonist in the tuberoinfundibular pathway, thus bringing down the elevated prolactin levels. However, as a stand-alone treatment, the functional activity of aripiprazole in this pathway would be dependent solely on the dopamine levels. Hence, it is possible that in the absence of a competing D2 antagonist and the presence of dopamine (the natural agonist), aripiprazole could act as a functional antagonist at lower doses also, and thus, elevate prolactin levels.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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