USE OF ARIPIPRAZOLE IN HYPERPROLACTINEMIA

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ABSTRACT

Two female patients in their 20s and 30s presented with symptoms which required them to be on antipsychotic medications. They were on different antipsychotic medications including paliperidone, risperidone, haloperidol and olanzapine. Both patients had symptoms such as galactorrhea and menstrual disturbances due to hyperprolactinemia (PRL level >100 mcg/L). MRIs of brain suggested pituitary tumor in both patients. We started aripiprazole as an adjunct with other antipsychotic medications. After starting aripiprazole, the PRL level decreased over a period of two to three weeks. This effect of aripiprazole could be due to its acting as partial agonist on D2 receptor. In both cases, antipsychotic medications and pathological brain lesions were two possible causes for hyperprolactinemia.

INTRODUCTION

Hyperprolactinemia is the most common pituitary hormone hypersecretion syndrome in both males and females. Prolactin (PRL)-secreting pituitary adenomas (prolactinomas) are the most common cause of PRL levels >100 mcg/L. Other common etiologies are drug induced, pituitary stalk compression, hypothyroidism, renal failure or physiological hypersecretion (e.g. pregnancy, lactation, chest wall stimulation or stress). Symptoms of hyperprolactinemia in women are amenorrhea, galactorrhea, and infertility; while symptoms in men are diminished libido or visual loss.[1]

Blockade of the dopamine receptors in the tuberoinfundibular tract results in the increased secretion of prolactin, which can result in breast enlargement, galactorrhea, amenorrhea, and inhibited orgasm in women and impotence in men.[2] Because of the dopamine blocking property of certain antipsychotic medications, they are known for causing hyperprolactinemia.

Aripiprazole exhibits a novel mechanism of action, combining partial agonist activity at dopamine [2] (D2), dopamine (D3), and serotonin 1A (5–HT1A) receptors with antagonist activity at serotonin 2A (5-HT2A) and D2 receptors. Aripiprazole treatment was not associated with increases in prolactin levels during short- or long-term studies (in fact, prolactin levels were shown to be slightly decreased by aripiprazole).[3]

A single Caucasian woman in her early 30s with a long history of Schizoaffective disorder, who was on paliperidone 6mg QD in community and had developed galactorrhea and abnormal menstrual cycle was admitted to DPC.

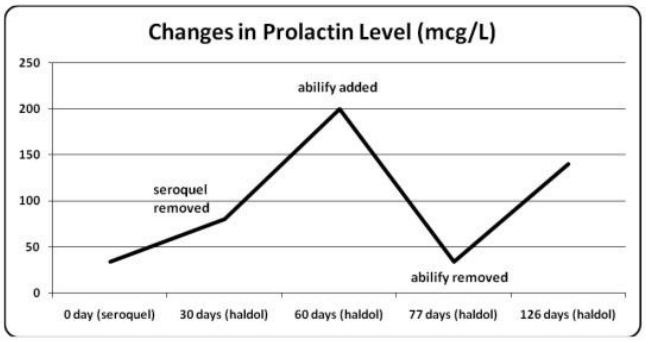
Pallperidone was discontinued in community due to hyperprolactinemia.

Due to her symptoms, she was in need of antipsychotic medications. At the time of admission, her PRL level was 34.8 mcg/L, and within one month, it increased to 200 mcg/L. Various antipsychotic medications including quetiapine, thioridaazine, and haloperidol were tried during this period. She requested that she would like to continue taking haloperidol 10mg daily despite the hyperprolactinemia because haloperidol was helping her commanding auditory hallucinations and mood symptoms. MRI of brain showed suspected microadenoma in adenohypophysis.

We recommended starting aripiprazole as an adjunct to haloperidol in an effort to reduce PRL level and treat psychotic symptoms. Aripiprazole 10mg QD was started and was increased to 15mg QD in a few days. Seventeen days after starting aripiprazole, PRL level was 34 mcg/L. She was discharged on aripiprazole 15mg and haldol 10mg but was readmitted in six weeks. She had stopped taking aripiprazole in community but continued haloperidol. Upon readmission, we checked her PRL level, which was 138 mcg/L.

Case Report 1

Days	Prolactin level (mcg/L)	Medications
0 (at admission)	34	Seroquel
30 days after admission	80	Quetiapine (started tapering off) and Haloperidol (started)
30 days after starting haldol	200	Haloperidol (decided to start aripiprazole as an adjunct to haldol)
17 days after starting aripiprazole	34	Haloperidol + Aripiprazole (pt was discharged)
7 weeks after discharge	138 (upon readmission)	Haloperidol (pt stopped taking aripiprazole in community)

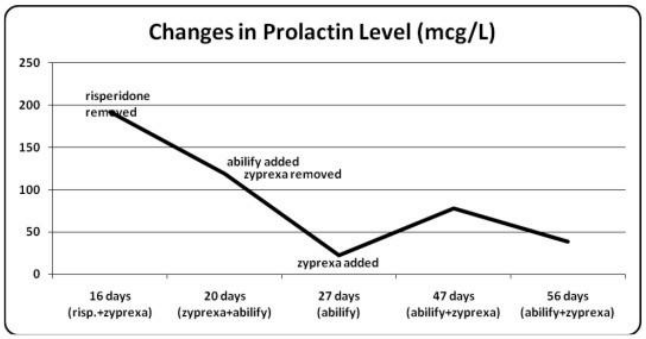


Case Report 2

20 y/o single, college student, Caucasian female was admitted from DBH after having spent more than one month at the facility due to mania with psychotic features. She was on olanzapine 20mg qhs, valproic acid 250mg qid + 500mg qhs, and risperidone 2mg bid; these medications were continued at DPC upon admission. After two weeks, she reported amenorrhea and galactorrhea with breast pain. Prolactin level was measured, which was found to be 192 mcg/L. MRI of brain with contrast was done, which suggested a 3 x 5 mm nodular enhancement of the pituitary stalk with differential diagnosis including pituitary tumor.

It was decided to taper off risperidone and olanzapine and start aripiprazole 10mg. Within four days of stopping risperidal, her PRL level dropped to 118.9 mcg/L. Seven days after starting aripiprazole, her PRL level decreased to 22.8 mcg/L. She however became more manic with delusional symptoms and olanzapine was needed to be restarted to reach 10mg bid. Her PRL level increased to 78 mcg/L after 20 days of starting olanzapine. PRL level was rechecked again after nine days when it had decreased to 39.1 mcg/L.

Days	Prolactin level (mcg/L)	Medications
0	Unknown	Zyprexa 20 mg QHS, Risperidal 2mg PO BID
16	192	Risperidone d/c
4 days after stopping risperidal	118.9	Aripiprazole 10 mg PO QD was started Olanzapine was discontinued
7 days later		MRI showed 3X5 nodule in pituitary stalk
7 days after starting Aripiprazole	22.8	Aripiprazole 10mg Qd Olanzapine was restarted
20 days after starting zyprexa	78	Aripiprazole 10mg , Olanzapine 20mg qhs
9 days later	39.1	Aripiprazole 10mg , Olanzapine 20mg qhs



DISCUSSION

In the first case report, the patient's prolactin level increased in the community when she was taking paliperidone. At the time of admission, she was started on quetiapine and then finally switched to haloperidol 10mg Qd. PRL level kept increasing (up to 200 mcg/L) with different antipsychotic medications and aripiprazole was started as an adjunct. She continued taking haloperidol + aripiprazole and her PRL level dropped to 34 mcg/L. Her symptoms of hyperprolactinemia were resolved. She stopped taking aripiprazole in the community and at readmission her prolactin level was 138 mcg/L. There appeared to be a relationship between the addition of aripiprazole and the reduction of elevated prolactin level. This was in accordance with an article in the American Journal of Psychiatry: "adjunctive aripiprazole treatment reversed hyperprolactinemia in both sexes, resulting in reinstatement of menstruation in female patients, with no significant effects on psychopathology and extrapyramidal symptoms. Aripiprazole has higher affinity to dopamine D2 receptors than haloperidol, which is the likely cause of this observation" (2007).[4]

In the second case, the patient was on risperidone, olanzapine and valproic acid when she developed hyperprolactinemia (PRL level-192 mcg/L). Risperidone was discontinued and her PRL level dropped to 118 mcg/L in four days. Her MRI also showed a 3x5mm nodule in pituitary stalk. We decided to start aripiprazole and taper off zyprexa. In seven days, her PRL level returned to normal (22.8mcg/L). It was not clear in this case whether stopping olanzapine or starting aripiprazole was the cause of the drop in PRL level. We had to restart olanzapine and her PRL level increased to 78 mcg/L in 20 days. Upon rechecking after nine days, PRL level came down to 39.1 mcg/L. From this observation, it is possible that olanzapine was causing PRL to increase while aripiprazole was causing it to decrease. This effect of aripiprazole could be due to its partial agonist activity towards D2 receptors.

CONCLUSION

In both cases, antipsychotics including haloperidol, risperidone, palliperodone, and olanzapine appeared to be associated with the rise in prolactin level. Adding aripiprazole as an adjunct appeared to help reduce prolactin levels in both patients, with reversal of hyperprolactinemia symptoms. MRI showed pathological lesions related to the pituitary gland, which could be a contributing factor in raising prolactin levels. More studies need to be done to find appropriate guidelines to use aripiprazole as an adjunct to treat hyperprolactinemia caused by antipsychotic use or by pathological lesions.

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