

# Decrease in Serum Prolactin Levels After Long-acting Injectable Aripiprazole Treatment: a Case Report

Orkun Aydin<sup>1</sup>\*, Pinar Unal-Aydin<sup>1</sup>\*

## ABSTRACT:

Decrease in serum prolactin levels after long-acting injectable aripiprazole treatment: a case report

Hyperprolactinemia is a severe problem which involves galactorrhea, amenorrhea, sexual dysfunction, and lowered bone mineral density. It can be a long-lasting problem belongs to the atypical antipsychotics that impairs treatment adherence and quality of life in patients with schizophrenia. The paliperidone palmitate may cause hyperprolactinemia and there are different approaches in management of this adverse event. Adding oral aripiprazole was shown to be useful in the treatment of hyperprolactinemia due to paliperidone palmitate. Now the new drug long-acting Injectable (LAI) aripiprazole may become a possible new agent in treatment of schizophrenia patients with paliperidone palmitate induced hyperprolactinemia.

**Keywords:** aripiprazole LAI, paliperidone palmitate, hyperprolactinemia, amenorrhea, galactorrhea

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<sup>1</sup>International University of Sarajevo, Faculty of Arts and Social Sciences, Department of Psychology, Bosnia and Herzegovina

### Corresponding Author:

Orkun Aydin  
International University of Sarajevo, Faculty of Arts and Social Sciences, Department of Psychology, Bosnia and Herzegovina

### E-mail address:

drorkunaydin@hotmail.com

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## INTRODUCTION

The atypical antipsychotics which are associated with a substantially lower liability for extrapyramidal side effects and reduced risk of tardive dyskinesia provide major advance in the pharmacotherapy of schizophrenia when compared with the typical agents (1). In contrast they are found to be related with some important adverse effects including hyperprolactinemia (which may result with gynecomastia, galactorrhea, amenorrhea, sexual dysfunction, and lowered bone mineral density), weight gain, higher risk for diabetes mellitus and prolongation of the corrected QT interval. These adverse effects may provoke the treatment non-adherence in schizophrenia patients (2). The paliperidone palmitate, one of the effective atypical antipsychotic in schizophrenia, has D2 and 5HT2A receptor antagonism effects that is similar to risperidone.

Although, the risperidone has a high affinity for 5-HT2A receptor, it increases prolactin levels like typical antipsychotics. Additionally hyperprolactinemia was also reported after paliperidone palmitate injection<sup>3</sup>. On the other hand, previous studies indicated that aripiprazole has potent partial agonist activity at D2 and 5-HT1A receptors and antagonist activity at 5-HT2A receptors (4). Since its pharmacological profile differs from other atypical agents, it is considered that aripiprazole causes lesser extrapyramidal symptoms, glucose intolerance, weight gain, and hyperprolactinemia side effects (5). In this context, there were many reports regarding the utility of aripiprazole in elevated serum prolactin levels in schizophrenia patients (6). Now aripiprazole once monthly was recently manufactured as a long-acting injection (LAI), in the form of a suspension of lyophilized aripiprazole reconstituted with an aqueous diluent, for intramuscular

administration (7). However, currently, there is not any evidence in the form of case reports of aripiprazole LAI reporting that it diminishes serum prolactin levels. Here, we present a patient who developed hyperprolactinemia due to paliperidone palmitate use and its treatment with the aripiprazole LAI.

## CASE PRESENTATION

A 37-year-old woman, who has been receiving paliperidone palmitate 100 mg/month, presented to our psychiatry outpatient clinic. According to her family, she was hospitalized with the diagnosis of schizophrenia 2 years ago. During her hospitalization she had been using risperidone 6 mg/day and after her psychotic symptoms improved she was discharged from the clinic with the same treatment regimen. After 2 months from discharge she discontinued oral risperidone and then her psychiatrist started paliperidone palmitate 100 mg/month immediately. Her psychotic symptoms did not occur again while she has been undergoing injectable treatment. When we first met with the patient, she had still been receiving her monthly injections of paliperidone palmitate and her PANSS score was 37. She was only suffering from galactorrhea and amenorrhea for 4 months. There were no specific disorders and other medication information in her self-history. In blood tests we detected hyperprolactinemia (97 ng/ml), solely. The other serum hormone levels were normal and regarding to the cranial MRI, there were no pathologies arising from the brain specifically, pituitary gland. In addition, there were no organic pathologies identified after the consultation with obstetrics and gynecology department. Use of the Naranjo Adverse Drug Reactions Probability Scale<sup>8</sup> with a score of 6 indicated a “probable” relationship between the hyperprolactinemia and paliperidone palmitate. Firstly, we diminished the paliperidone palmitate dosage to 75 mg/month and added aripiprazole 5 mg/day. The first follow-up examination was 15 days after the injection with lowered dosage but our patient had not taken oral aripiprazole treatment properly. Galactorrhea and amenorrhea had still been continuing and the serum prolactin level was 82 ng/ml. In order not to have any digestive tract problems such as constipation, diarrhea, vomiting, and gastro-oesophageal reflux, she refused to take oral treatment. After 1 month from the first follow-up examination, although serum prolactin level

decreased to 73 ng/ml, galactorrhea and amenorrhea have remained. Furthermore, her PANSS score increased to 58. Because of not receiving oral treatment, high serum prolactin level and possibility for exacerbation of the psychotic symptoms, we decided to switch treatment to aripiprazole LAI 400 mg/month and hospitalized the patient for requirement of oral aripiprazole treatment at the initiation. We intended to continue aripiprazole with 20 mg/daily for 14 days after the first injection. After one month, prolactin level decreased to 45 ng/ml and we discharged her with the PANSS score 42. After 2 injections of the aripiprazole LAI, prolactin level decreased to 28 ng/ml and she started to menstruate with no sign of galactorrhea. The prolactin level was 14 ng/ml after 7 months from the initiation of the aripiprazole LAI. During the follow-up visits she did not have any psychotic symptoms or hyperprolactinemia.

## DISCUSSION

In our case hyperprolactinemia occurred due to paliperidone palmitate injection and we reported the decrease in prolactin levels after switching the treatment to the aripiprazole LAI. In the literature, some reports stated that oral aripiprazole addition lowers prolactin levels in hyperprolactinemia cases with the use of both oral and injectable paliperidone (9). If the patient provides benefit from the antipsychotic treatment, it is suggested that adding oral aripiprazole to the treatment may be better option (10). In our case, we added oral aripiprazole according to the literature but weak oral treatment adherence caused sustained hyperprolactinemia, despite we had lowered the paliperidone palmitate dosage from 100 mg to 75 mg/mont. In order to avoid recurrence, her medication was switched to the aripiprazole LAI. According to prescribing information, in conjunction with first dose of LAI, the patient should take 14 consecutive days of concurrent oral aripiprazole but additionally there is not any information including switching from paliperidone palmitate, hence we waited for the injection cycle and hospitalized the patient for oral treatment adherence. The serum prolactin levels remained between normal ranges for 7 months with aripiprazole LAI. Hyperprolactinemia impaired treatment compliance of our patient therefore specifically young female patients should be monitored closely regarding these adverse events. To the best of our

knowledge, this is the first case report of aripiprazole LAI that showed the effect on hyperprolactinemia caused by paliperidone palmitate. This case showed that aripiprazole LAI could maintain lower serum prolactin levels in paliperidone palmitate-induced hyperprolactinemia just

like its oral form. It can be said that if clinicians detect impaired treatment compliance and have to use injectable treatment regimens, they should consider aripiprazole LAI switching rather than adding oral aripiprazole to the paliperidone palmitate in hyperprolactinemia cases.

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