

# Severe hyperprolactinemia during lurasidone treatment in a 16-year old girl with schizophrenia – a case report

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## Abstract

**Background:** Increase of serum prolactin is a common adverse effect to antipsychotic medication, potentially leading to galactorrhea, menstrual cycle disturbances or sexual adverse effects. Lurasidone is commonly associated with a low risk of prolactin change.

**Objective:** To describe a case of severe hyperprolactinemia in a 16-year old female with schizophrenia.

**Method:** Case report.

**Results:** We saw a severe and sustained prolactin increase during treatment with lurasidone.

**Conclusions:** Although lurasidone is usually considered not to increase prolactin, some patients may experience this adverse effect. As related subjective consequences may be falsely attributed to the disease or as direct effects of the antipsychotic agent, serum prolactin measurements should be made prior to and during antipsychotic treatment regardless of medication choice.

**Keywords:** Prolactin; schizophrenia; adverse effects; antipsychotics; case report

## Introduction

Few antipsychotics are approved for use in children and adolescents with mental disorders. The European Medicines Agency (EMA) has approved the use of Lurasidone for patients aged 13-17 years [www.ema.europa.eu]. As other second-generation antipsychotics (SGA), lurasidone has an antagonistic effect on a wide range of receptors, including dopamine, serotonin and adrenaline receptors, but shows weaker binding to histamine and muscarine-receptors. The antipsychotic effect is primarily mediated by the blocking of dopamine D2 receptors.(1)

Increased prolactin levels - hyperprolactinemia - is a relatively common adverse effect to antipsychotic treatment. A Bayesian meta-analysis found odds ratios ranging from 10 to 40 for clinically significant hyperprolactinemia.(2) Dopamine is excreted by tubuloinfundibular neurons in the anterior pituitary gland and regulates the production of prolactin through its effect on D2 receptors in lactotrophic cells. Blocking of these receptors leads to decreased inhibitory effect by dopamine and thus an increased production and secretion of prolactin, which, in turn,

may lead to gynecomastia and galactorrhea, and decreased levels of gonadal hormones that may cause subjective adverse effects such as amenorrhea, loss of libido, erectile and ejaculatory/orgasmic dysfunction. In youths, these manifestations may cause significant distress and may lead to treatment discontinuation, especially as both patients and treating physicians may find these subjects difficult to address. Finally, prolonged hyperprolactinemia could potentially lead to disturbance of pubertal development and growth disruption.(3)

While several antipsychotic agents have been associated with hyperprolactinemia, SGAs with lower D2-affinity have weaker effects on prolactin levels. Lurasidone is usually associated with moderate effects on prolactin levels.(4) Here we present a case of a 16-year old girl (V) treated with lurasidone who experienced abrupt and extensive prolactin increase.

## Case Report

At age 14 years and 9 months (14, 9), V had her first contact with the Child and Adolescent Mental Health Services (CAMHS), Capital Region of Denmark. She was diagnosed with schizophrenia due to extensive

hallucinatory experiences. She was treated first with aripiprazole, then with paliperidone, both with insufficient effect, before lurasidone was considered. Sertraline was added due to depressive symptoms.

A few days after starting on paliperidone-lurasidone crossover (age 16, 2 months), prolactin level was severely elevated (4240 10<sup>-3</sup> International Units per liter (mIU/L), normal range 60 – 400 mIU/L), at this point considered an adverse effect to paliperidone. Prolactin levels had been normal during treatment with aripiprazole but unfortunately, prolactin was not measured during paliperidone treatment. A normal magnetic resonance imaging (MRI) of cerebrum was present from a few months earlier.

During titration of lurasidone to a maximum of 111 milligrams (mg) per day, prolactin levels continued to increase. V experienced breast tension and galactorrhea. A new MRI was performed but was also normal showing no signs of prolactinoma. Seven measurements of prolactin were made during five months of treatment, of which all except one (156 mIU/L, which may have been erroneous) were in the range of 4240 to 6140 mIU/L. She was admitted to an inpatient clinic for cross-over to clozapine. After cessation of lurasidone, prolactin levels normalized.

## Discussion

Increased serum prolactin is associated with sexual disturbances, gynecomastia, galactorrhea, menstrual disturbances and decreased bone mineral density.(3) In youths, these adverse effects may cause poor treatment adherence and there is concern that they may lead to cardiovascular disease and disturbed pubertal development. Antipsychotics usually associated with prolactin increase include risperidone and paliperidone, but lurasidone is usually not associated with prolactin increase. One case report from 2020 describes normalization of prolactin levels and associated adverse effects (galactorrhea and breast tenderness) in a 40-year old female after switching from risperidone to lurasidone. (5) In the present case lurasidone is shown to cause severe and sustained prolactin elevation. This contradictory observation may reflect that genetic variations may affect the susceptibility for antipsychotic-mediated hyperprolactinemia.

Until recent changes in national guidelines, prolactin was not measured routinely in adolescents treated with antipsychotics in Denmark, unless typical adverse effects were present. However, subjective adverse effects may be absent, attributed to the underlying disease, or seen as non-specific adverse effects to the antipsychotic itself. Routine prolactin measurements should be made before and during antipsychotic treatment. Interventions that may reduce prolactin levels include decreasing dose

or switching to a different antipsychotic, adding aripiprazole, or treating with bromocriptine or cabergoline. (6)

## Informed consent

Informed permission has been attained from parents and assent from the patient.

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## Disclosures

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