Case Report

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Galactorrhea and hyperprolactinemia during vortioxetine use: case report
Vortioksetin kullanımını sırasında galaktore ve hiperprolaktinemi: olgu sunumu

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Abstract

Background: Hyperprolactinemia is one of the most common endocrine disorders of the hypothalamic-pituitary axis. Hyperprolactinemia and galactorrhea are rarely seen as adverse effects of antidepressant drugs.

Case presentation: Thirty-three years old women, between 2011 and 2017, three depressive episodes were observed. Initially, fluoxetine was used, no galactorrhea was detected. Secondly, she was given escitalopram and visited the clinic with amenorrhea and galactorrhea. Her serum prolactin levels were 50.88 ng/mL and MRI findings were normal. Escitalopram was discontinued and prescribed cabergoline and then prolactin levels were 16.56 ng/mL in the third month. During the vortioxetine treatment, she developed galactorrhea and prolactin level was 43.65 ng/mL. Vortioxetine was discontinued and it was measured at 20.14 ng/mL after 4 weeks of drug-free observation.

Conclusion: Vortioxetine is a multimodal agent that modulates a select population of 5-HT receptors. To literature, there was no case presentation of galactorrhea observed during the use of vortioxetine. Galactorrhea associated with SSRIs are limited to case presentations. Antidepressants are thought to cause galactorrhea through tubero-infundibular dopaminergic neurons or postsynaptic serotonergic neurons in the hypothalamus. When galactorrhea was observed during antidepressant drug use, prolactin levels and MRI should be investigated, and termination/replacement of antidepressant treatment is recommended if necessary.

Keywords: Vortioxetine; Galactorrhea; Hyperprolactinemia; Antidepressants; Depression.

Öz

Giriş: Hiperprolaktinemi, hipotalamik-pitüiter eksenin en sık görülen endokrin bozukluklarından biridir. Hiperprolaktinemi ve galaktore nadiren antidepresan ilacların istenmeyen etkileri olarak görülmektedir.

Olgu sunumu: 33 yaşındaki kadın hastaya 2011–2017 yılları arasında, üç depresif epizotun ayakta takip edildiği, ilk epizotda fluoksetin kullanılmış, galaktore görülmemiştir. İkinci epizotda essitalopram kullanımı sırasında amenore ve galaktore gelişmiştir. Kadın doğum polikliniğinde prolaktin düzeyi 50.88 ng/mL, MRI bulguları normal bulunmuştur. Essitalopram kullanımı sonlandırılmış ve uygulanan cabergolin tedavisiyle prolaktin düzeyleri normale dönmüştür (3. ayda 16.56 ng/mL). Üçüncü epizotda Vortioksetin kullanımı sırasında galaktore yanması üzerine ölçülen prolaktin düzeyi 43.65 ng/mL tespit edilmiştir. Vortioksetin kesilmiştir, ilaçsız geçen 4 hafta sonra prolaktin: 20.14 ng/mL bulunmuştur.

Sonuç: Vortioksetin multimodal bir ajan olup serotonin geri alm inhibitoryidir. Literatürde gözlem konulan galaktore, SSRI’lerle ilişkili galaktore makaleleri olgu sunumları ile birlikte değerlendirildi. Antidepresanın tuberin hipotalamik nöronları, hipotalamustaki postsinaptik serotonerjik nöronlar yoluya galaktoreye neden olduğu düşünülmektedir. Antidepresan ilac kullanımını sırasında galaktore gözlemlendiğinde; prolaktin düzeyleri ölçülmeli, etiyolojik nedenlerin ayırt edilmesi için MRI araştırılması; lüzumlu halinde antidepresan tedavinin sonlandırılması/değiştirilmesi önerilir.

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Huseyin Murat Ozkan: Galactorrhea and hyperprolactinemia during vortioxetine use

Anahtar Kelimeler: Vortioksetin; Galaktore; Hyperprolaktinemi; Antidepresanlar; Depresyon.

Introduction

Hyperprolactinemia is described as increased secretion of the prolactin hormone above normal physiological levels by the lactotroph cell off hypophysis. It is one of the most common endocrine disorders of the hypothalamic-pituitary axis. In addition to physiological and pathological causes of the condition, several drugs can cause significant increases in serum prolactin levels [1, 2]. Hyperprolactinemia is reported as a side effect of treatment with different types of antidepressants including tricyclic antidepressants selective serotonin reuptake inhibitors (SSRIs), and selective noradrenaline reuptake inhibitors SNRIs [1, 3]. The medications that can cause hyperprolactinaemia include antipsychotics, antidepressants, antihypertensive agents, and drugs which increase bowel motility. Often the medication-induced hyperprolactinemia is symptomatic, causing galactorrhea menstrual disturbances, or erectile dysfunction [2]. Antidepressants with serotonergic activity, including SSRIs, monoamine oxidase inhibitors (MAO-Is), and some tricyclics can cause modest and generally asymptomatic hyperprolactinemia [2].

Patients and methods

Our case is a 33-years old, divorced female with a university license degree education. She visited a psychiatry clinic in June 2011 because of marital problems, unhappiness, crying, and anger. She was diagnosed with a mixed anxiety and depressive disorder, according to DSM IV-R diagnostic criteria.

She was prescribed fluoxetine 20 mg/day. After 3 months of treatment, she felt better and self-discontinued her medication. In January 2012 she was amicably divorced and presented again to the psychiatry clinic with complaints of crying, anhedonia, fatigue, and hopelessness. She was given escitalopram 10 mg/day for 3 months, then increased to 20 mg/day. By late August 2012, while she was still being treated with antidepressants, she visited a gynecology and obstetrics clinic with amenorrhea, painful breasts, and galactorrhea. Her serum prolactin levels were 50.88 (reference range 4.79–23.3 ng/mL) and magnetic resonance imaging (MRI) [Siemens, Magnetom Avonto Tm (32×8) 1.5 T, Germany] findings were normal. The concentration of serum prolactin was detected by electrochemiluminescence immunoassay diagnostic kit by using Cobas 6000 analyzer (Roche Diagnostics, Germany). Escitalopram was discontinued and she was prescribed cabergoline 0.5 mg/week, beginning in October 2012.

After 1 month of treatment with cabergoline, her prolactin level was <0.60 ng/mL and her complaints of galactorrhea were resolved. Two months later (November 2012) her prolactin level was 16.56 ng/mL (Table 1) and magnetic resonance imaging findings were normal. Her third visit was at the end of November 2016 where she exhibited a lack of concentration and interest, decreased daily performance, anhedonia, and crying. She was diagnosed with the major depressive disorder (MDD) and began taking vortioxetine 10 mg/day, initially for 4 days 5 mg/day. At the end of the first month, her vortioxetine dosage was increased to 20 mg/day.

Results

At the beginning of the fourth month, she developed galactorrhea and breast pain. Amenorrhea was not reported. Her prolactin level was 43.65 ng/mL (Table 1). Vortioxetine was discontinued in March 2017. After a 1-month drug-free period, her prolactin level was 20.14 ng/mL and her galactorrhea and breast pain were resolved (Table 1).

Table 1: Prolactin levels; with and without antidepressant (AD) treatment.

| Depression episode | Antidepressant (AD) | Galactorrhea | MRI       | Prolactin levels (ng/mL) | Prolactin levels (ng/mL) |
|--------------------|---------------------|--------------|-----------|--------------------------|--------------------------|
|                    |                     |              | With AD treatment | Without AD treatment    |                          |
| First-2011         | Fluoxetine          | Negative     |            |                          |                          |
| Second-2012        | Escitalopram        | Positive     | Normal     | 50.88                    | 16.56                    |
| Third-2016         | Vortioxetine        | Positive     |            | 43.65                    | 20.14                    |
Discussion

Besides typical antipsychotics, some atypical antipsychotic drugs can induce hyperprolactinemia such as risperidone, molindone, olanzapine, and quetiapine. Typical antipsychotics cause increased secretion of prolactin by strongly antagonizing D2 receptors. Usually, prolactin levels are less than 100 ng/mL with psychotropic medications, and usually, fall to normal levels within 48–96 h of discontinuing antipsychotic therapy [4]. Antidepressant drugs are thought to cause galactorrhea through tuberoinfundibular dopaminergic neurons or postsynaptic serotonergic neurons in the hypothalamus [5–7]. Antidepressant drugs can cause modest but generally asymptomatic hyperprolactinemia [2]. There are a small number of well-documented case reports of symptomatic hyperprolactinemia from SSRIs [1, 5–8]. The most common pharmacological compounds currently used for the treatment of MDD inhibit the reuptake of 5-HT (SSRIs) or 5-HT and NA (SNRIs) from presynaptic terminals, thereby effectively enhancing 5-HT or 5-HT/NA neurotransmission. Vortioxetine is a multimodal agent that modulates a select population of 5-HT receptors with serotonin transporter (SERT) inhibition. In vitro studies indicate that vortioxetine is a 5-HT3 and 5-HT7 receptor antagonist, 5-HT1B/D receptor partial agonist, 5-HT1A receptor agonist, and SERT inhibitor [9].

Conclusion

Vortioxetine is a new antidepressant, and as far as we know, is not associated with galactorrhea and hyperprolactinemia [9]. We followed our patient between 2011 and 2017, over three depressive episodes. Her complaints of galactorrhea led us to measure prolactin levels. Interestingly, galactorrhea and hyperprolactinemia are sometimes seen with escitalopram and vortioxetine treatment, but not with fluoxetine. There are published articles about escitalopram induced hyperprolactinemia and galactorrhea, but we know of no published articles describing hyperprolactinemia and galactorrhea as side effects of vortioxetine. There is no evidence of vortioxetine-induced hyperprolactinemia, it is thought that serotonin somehow increases prolactin secretion, either directly or indirectly.

When galactorrhea was observed during antidepressant drug use; prolactin levels and MRI should be investigated, and termination/replacement of antidepressant treatment is recommended if necessary.

Ethical considerations: Informed consent was obtained from the patient.

Conflict of interest statement: The author declares that there is no conflict of interest regarding the publication of this article.

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