



## CASE REPORT

# Hyperprolactinemia and galactorrhea with duloxetine in neuropathic pain management

*Nöropatik ağrı tedavisinde duloksetin ile ortaya çıkan hiperprolaktinemi ve galaktore*

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## Summary

Duloxetine is a serotonin-norepinephrine reuptake inhibitor that is widely used in chronic pain treatment in various diseases. Hyperprolactinemia and galactorrhea are rare side effects of this medication. Here, we reported a 34-year-old female with multiple sclerosis who used duloxetine for pain management and mood disorder and experienced galactorrhea.

Keywords: Duloxetine; galactorrhea; hyperprolactinemia; mood disorder; neuropathic pain.

## Özet

Duloksetin çeşitli hastalıklarda kronik ağrı tedavisinde sık olarak kullanılan serotonin-noradrenalin geri alım inhibitörüdür. Hiperprolaktinemi ve galaktore bu tedavinin nadir görülen bir yan etkisidir. Burada, multipl skleroz tanısı olan 34 yaşında bir kadın hastada ağrı ve duyu durumu bozukluğu nedeni ile duloksetin kullanımı ve medikal tedaviye bağlı gelişen galaktore olgusunu sunmaktayız.

Anahtar sözcükler: Duloksetin; galaktore; hiperprolaktinemi; duygudurum bozukluğu; nöropatik ağrı.

## Introduction

Hyperprolactinemia is one of the most common cause of acquired hypogonadotropic hypogonadism and defined as elevated serum prolactin levels above the upper limits of normal range, with a prevalence of 1–1.5%.<sup>[1,2]</sup> Galactorrhea was seen alone in approximately 30% and with amenorrhea in 75% of patients.<sup>[1]</sup>

Hyperprolactinemia may be seen in the course of systemic disorders such as renal failure, hypothyroidism, hypothalamic disease, pituitary disease, and also commonly with drugs, especially antipsychotic agents.<sup>[1]</sup> The other drugs such as selective serotonin reuptake inhibitors and serotonin and noradrenalin reuptake inhibitors may cause the elevation of prolactin levels but it is not common.<sup>[1,2]</sup> The exact mechanism underlying this condition was not fully elucidate, but in neuroendocrine system, prolactin, dopamine, serotonin, and noradrenaline interact in several ways.<sup>[1–3]</sup>

Duloxetine is a serotonin-norepinephrine reuptake inhibitor that is widely used in chronic pain treatment in various diseases. Hyperprolactinemia and galactorrhea are rare side effects of this medication, reported only in few case reports.

## Case Report

Our patient was a 34-year-old female, diagnosed with multiple sclerosis, on interferon beta 1b and gabapentin treatment. She used duloxetine (60 mg/d) for neuropathic and muscle pain and concomitant depressive symptoms for 3 months. In routine control, she complained of milk like breast discharge that continued for 1 month. We considered this discharge as galactorrhea and measured the serum prolactin level. The serum prolactin level was 93 ng/ml (normal limits; 5.18–26.53 ng/ml). First, we changed the duloxetine to escitalopram (10 mg/d) to eliminate the drug effect. Escitalopram also can rarely cause hyperprolactinemia, but we

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**Table 1.** Review of case reports of duloxetine treatment and galactorrhoea in literature

Case report	Dosage	Patient demographics	Indication	Symptom	Medical history	Evaluation	Prolactine level	Management	Outcome
Korkmaz et al. <sup>[8]</sup>	–	44 F	Depression	Milk-like breast discharge, pain and tenderness	Past usage of various antidepressant treatment	Normal pituitary gland magnetic resonance imaging Normal metabolic and biochemical blood tests	38.8 ng/ml	Switch to essitrolapram and initiation of cabergolin 0.5 mg/twice a week	At the end of first month prolactin level was normal then cabergolin treatment stopped
Belli et al. <sup>[9]</sup>	60 mg	46 F	Depression	Milk-like breast discharge, pain, discomforting feeling of limbs at rest	–	Normal pituitary gland magnetic resonance imaging Normal metabolic and biochemical blood tests	37.9 ng/mL.	Switch to bupropion	Galactorrhoea and restless legs symptoms improved after 2 weeks and normal prolactin level after six week
Demirci et al. <sup>[6]</sup>	30 mg 60 mg	28 F	Migraine	Milk like breast discharged	–	Normal pituitary gland magnetic resonance imaging Normal metabolic and biochemical blood tests	8.05 ng/mL (N)	Cessation of duloxetine	Galactorrhoea stoped on the third day
Ashton et al. <sup>[10]</sup>		40 F	Dysthymic disorder	Milk like breast discharge	Past usage of various antidepressant galactorrhoea with venlafaxin	Normal pituitary gland magnetic resonance imaging Normal metabolic and biochemical blood tests	28.2 ng/ml	Switch to bupropion and modofinil	Breast discharge discontinued and prolactin level decreased to normal level

did not prefer to cease all antidepressant treatment because of additional depressive disorder. Galactorrhea stopped within days after cessation of duloxetine and also prolactin level decreased (39.78 ng/l) without additional treatment. At the same time, we started to investigate endocrinologic causes of hyperprolactinemia. Metabolic tests and pituitary gland magnetic resonance imaging revealed normal results. Cabergoline treatment was initiated (0.25 mg twice in a week) by endocrinologist and the dosage was decreased in 3 months interval and prolactin level stayed within normal range. We thought that possible cause of the hyperprolactinemia in our case was antidepressant treatment.

## Discussion

Duloxetine is widely used in neurology practice with diagnose of various pain disorders such as neuropathic pain, headache, and fibromyalgia.<sup>[4,5]</sup> Hyperprolactinemia and galactorrhea are very rare side effects of these drugs (Table 1). Galactorrhea may occur in even with normal prolactin level.<sup>[6]</sup>

In a French pharmacovigilance cohort, in 11,863 patients who used serotonin reuptake inhibitors, hyperprolactinemia was reported as a side effect in 187 (1.6%).<sup>[2]</sup> In this cohort, fluvoxamine, citalopram, fluoxetine, and paroxetine had higher ratios among them. Although there were several reports, they mentioned that duloxetine was not associated with an increased risk of hyperprolactinemia (1/225).<sup>[2]</sup>

Antipsychotics are the most known drugs that are related to elevated prolactin levels and in the course of treatment, reaching up to 70% of the patients.<sup>[7]</sup> Antipsychotic drugs showed their effect through dopamine receptor blockage. Dopamine is the main inhibitory factor for prolactin and this blockage causes elevation of the hormone levels.<sup>[7]</sup> How do serotonin reuptake inhibitors cause hyperprolactinemia? It is known that serotonin is related to prolactin release.<sup>[3]</sup> Several mechanisms proposed for this relation; one is through central 5-HT<sub>1C/2</sub> receptors and the other is stimulation of GABAergic neurons situated near the tuberoinfundibular dopamine cells which have 5-HT<sub>1A</sub> receptors on, and may increase prolactin levels through inhibition of inhibitory effect of dopamine in prolactin metabolism.<sup>[3]</sup>

In drug-induced hyperprolactinemia, serum prolactin levels are usually below 100 ng/mL. The prolactin levels decrease in a few days after discontinuation of the related drug.<sup>[1]</sup> If hyperprolactinemia persists or drug discontinuation is not appropriate, then the pituitary imaging can be performed to rule out adenoma.<sup>[1]</sup> In symptomatic patients, dose reduction or switch to another drug is recommended, if it's not possible, then low-dose dopamine agonist is added to current treatment.<sup>[1]</sup> Asymptomatic and mild elevation (<50 ng/ml) of prolactin may be followed without any treatment alteration.<sup>[1]</sup>

## Conclusion

While using these drugs, we have to consider hyperprolactinemia in patients with any of the symptoms such as menstrual dysregulation, sexual dysfunction, and breast discharge. Routine follow-up of prolactin level is not recommended, but in our opinion, the symptoms may be reviewed in routine controls not to overlook this condition.

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