Klinik Psikofarmakoloji Bülteni-Bulletin of Clinical Psychopharmacology

ISSN: 1017-7833 (Print) 1302-9657 (Online) Journal homepage: https://www.tandfonline.com/loi/tbcp20

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**To cite this article:** Assoc. Prof. Aslihan Polat, Hatice Turan & Assist. Prof. Ugur Cakir (2014) Late-Onset Normoprolactinemic Galactorrhea Associated with Fluoxetine Use: a Case Report, Klinik Psikofarmakoloji Bülteni-Bulletin of Clinical Psychopharmacology, 24:3, 265-267, DOI: 10.5455/bcp.20140701043755

**To link to this article:** https://doi.org/10.5455/bcp.20140701043755

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# Late-Onset Normoprolactinemic Galactorrhea Associated with Fluoxetine Use: a Case Report

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**ÖZET:**

Fluoksetin kullanımı ile ilişkili geç başlangıçlı normoprolaktinemik galaktore olgusu

Serotonerjik antidepresanların endokrin yan etkilerinden nadiren söz edilmektedir. Mekanizması bilinmemekle birlikte galaktore oldukça rahtsız edici olabilir. Fluoksetine bağlı galaktore nadiren bildirilmiştir. Bu makalede 35 yaşında fluoksetine bağlı geç başlangıçlı normoprolaktinemik galaktore geliştiren bir olguyu sunmaktayız.

**Anahtar sözcükler:** fluoksetin, galaktore, prolaktin, SSGİ, normoprolaktinemi

**Klinik Psikofarmakoloji Bulteni 2014;24(3):265-7**

**ABSTRACT:**

Late-onset normoprolactinemic galactorrhea associated with fluoxetine use: a case report

Endocrine side effects of serotonergic antidepressants (SSRIs) are seldom mentioned and although its mechanism is unknown, the development of galactorrhea may be very disturbing. Fluoxetine-induced galactorrhea has been relatively rarely reported. We present a case of a 35-year-old woman who developed late onset normoprolactinemic galactorrhea associated with fluoxetine use.

**Keywords:** fluoxetine, galactorrhea, prolactin, SSRI, normoprolactinemia

**Bulletin of Clinical Psychopharmacology 2014;24(3):265-7**

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**Date of submission:**
January 30, 2014

**Date of acceptance:**
July 01, 2014

**Declaration of interest:**
A.P., H.T., U.C.: The authors reported no conflict of interest related to this article.

## INTRODUCTION

Galactorrhea may be associated with various medical conditions or can be caused by several pharmacological agents, a mechanism which needs to be differentiated from other neuroendocrinological disorders[1]. There are a significant number of studies reporting that all selective serotonin reuptake inhibitors (SSRI) are associated with galactorrhea and/or prolactin abnormalities (hyperprolactinaemia), but the number of reported cases is limited[2-6,8,9]. Endocrine side effects of fluoxetine are uncommon and galactorrhea is rarely mentioned[10]. A detailed search of medical literature in English and Turkish revealed just eight cases of fluoxetine-induced galactorrhea[4,7,9,10,11]. We present a case, which developed galactorrhea following treatment with fluoxetine.

## CASE

A 35-year old woman with major depressive disorder, according to the DSM-IV was started on treatment of fluoxetine 20 mg/day. After 3 weeks of treatment, her complaints started to decline. During her subsequent follow-up, she showed significant improvement with minimal side effects. By the 9$^{th}$ month of treatment with fluoxetine 20 mg, she reported milk discharge from both nipples. Upon physical examination, bilateral breast secretion was expressed without any tenderness. After consulting a gynecologist, hormonal testing in addition to routine systemic evaluation was ordered. There were no abnormalities in the results of laboratory tests such as TSH, fT3, fT4, FSH or LH. Serum prolactin level was within the normal range (8 ng/mL) and B-HCG was

**Table 1: Previously reported cases with galactorrhea secondary to fluoxetine treatment**

| Study | Drug | Dosage | Time Onset | Age/sex | Current Medication | Prolactin Level |
|---|---|---|---|---|---|---|
| Arya-Taylor (4) | Fluoxetine | 20mg/day | 3 days | 15/ F | - | 933 m u/ L |
| Peterson MC (7) | Fluoxetine | 20mg/day | ? | 71/F | Conjugated estrogen | 37.4 ng/ml |
| Canan et al. (9) | Fluoxetine | 20mg/day | 21 days | 29/ F | - | 18.18 ng/ml |
| Mondal et al. (10) | Fluoxetine | 40mg/day | 6 months | 31/ F | | 122 ng/ml |
| Mondal et al. (10) | Fluoxetine | 20mg/day | 1 month | 22/ F | - | 138 ng/ml |
| Egberts et al (16) | Fluoxetine | 20mg/day | 14 days | 17/F | Fluconazole | Normal |
| Egberts et al (16) | Fluoxetine | 20mg/day | 1 month | 31/F | Oxazepam | ? |
| Egberts et al (16) | Fluoxetine | 20mg/day | 3 months | 64/F | - | ? |

negative. Cranial MRI also showed no pathological lesions in the hypothalamic/ pituitary area. Because of the temporal relationship between the drug administration and onset of galactorrhea and due to the lack of any other underlying medical condition, we stopped fluoxetine treatment. Ten days after drug cessation, the galactorrhea disappeared. The patient refused to use any other antidepressants, so we decided to provide supportive psychotherapy and follow-up; however, after a few months her depressive symptoms relapsed. She decided to try fluoxetine again because she had a history of prior positive response. We started 20 mg/day of fluoxetine after obtaining informed consent concerning the possibility of galactorrhea. Three months later, she reported galactorrhea again. All the medical and laboratory examinations, which were repeated, revealed no underlying pathology. Serum prolactin level was again within the normal range (8.3 ng/mL). Therefore, fluoxetine was stopped for the second time followed by the resolution of galactorrhea on the fifth day. An objective causality assessment using Naranjo Adverse Drug Probability Scale suggested that fluoxetine was the definite cause of the galactorrhea (score was 10 out of 13)[12]. After a two-week wash-out period without any antidepressant, a small dose of sertraline was administered and increased slowly. She is now on sertraline 100 mg/day treatment with no reemergence of galactorrhea or hyperprolactinaemia for almost a year.

## DISCUSSION

Although the occurrence of galactorrhea induced with fluoxetine use is very rare, several cases have been reported in the literature[4,7,9-11]. To our knowledge, this is the third reported case with normoprolactinemic galactorrhea secondary to fluoxetine treatment as shown in the table (Table 1). In our case, there was a relatively later onset galactorrhea in both trials with fluoxetine (9 months and 3 months respectively). This case is also important in the context of practical implications. Although all of the SSRIs share the same mechanism of actions, therapeutic and side effect profiles, each patient reacts differently to a particular SSRI. No two SSRIs have identical secondary pharmacological characteristics[10]. Although there are several case reports about the endocrinological side effects of sertraline such as galactorrhea[2,5,8], we observed no significant adverse effects in our case during a one-year follow-up. With the exception of fluoxetine, all SSRIs commonly cause hyperprolactinaemia through presynaptic mechanisms indirectly via 5-hydroxytryptamine-mediated inhibition of tuberoinfundibular dopaminergic neurons[10]. Hypothetically serotonin regulates prolactin release either by increasing the oxytocin level via direct stimulation of vasoactive intestinal protein or indirectly through stimulation of GABAergic neurons[10,13]. However, according to some researchers approximately 30% of the patients presenting with galactorrhea may have normal serum prolactin levels[14]. There are some other cases reporting normoprolactinemic galactorrhea

associated with SSRI use, and only one case with late onset associated with venlafaxine[15]; however, the exact mechanism still remains unknown[5,9,11,16,17]. Normoprolactinemic galactorrhea may be related to an effect on thyroid releasing hormone (TRH). TRH sensitivity may be another factor that plays a role in the emergence of galactorrhea[18]. Alternatively, euprolactinemic galactorrhea is hypothesized to be caused by indirect inhibition of tuberoinfundibular dopaminergic neurons[19]. It is also possible that the prolactin levels of our patient, although in the reference range, were higher than this patient's normal and thus capable of producing pathology. In fact, in most of the reported cases with hyperprolactinaemia secondary to SSRIs, prolactin levels were just slightly above the upper limit[7,17]. The increasing number of case reports on SSRI-related neuroendocrine side effects might be signifying a possible endocrine-disrupting effect of SSRIs. Trenque, using data from the spontaneous-reporting French Pharmacovigilance Data in his study, reported that treatment with serotonin reuptake inhibitors (SRIs) was associated with an increased risk of hyperprolactinaemia. He also suggests that the risk of hyperprolactinaemia should be mentioned in the labeling of SRI compounds[20]. Therefore, larger studies about the effect of SSRIs on the hypothalamic- pituitary axis are needed in order to draw attention to the need of well-designed studies about endocrine side effects of SRIs.

## References:


1. Pena KS, Rosenfeld JA. Evaluation and treatment of galactorrhea. Am Fam Physician 2001;63(9):1763-70.
2. Bronzo MR, Stahl SM. Galactorrhea induced by sertraline. Am J Psychiatry 1993;150(8):1269-70.
3. Bonin B, Vandel P, Vandel S. Fluvoxamine and galactorrhea. A case report. Therapie 1994;49(2):149-51.
4. Arya DK, Taylor WS. Lactation associated with fluoxetine treatment. Aust N Z J Psychiatry 1995;29(4):697.
5. Lesaca T. Sertraline and galactorrhea. J Clin Psycopharmacol 1996;16(4):333-4. [CrossRef]
6. Gonzalez E, Minguez L, Sanguino RM. Galactorrhea after paroxetine treatment. Pharmacopsychiatry 2000;33(3):118. [CrossRef]
7. Peterson MC. Reversible galactorrhea and prolactin elevation related to fluoxetine use. Mayo Clin Proc 2001;76(2):215-6. [CrossRef]
8. Ghosal M, Mukhopadhyay S, Sanyal D. A case of paroxetine-induced galactorrhoea. German Journal of Psychiatry 2005;8:23-4.
9. Canan F, Aydınoglu U, Sinani G. Transient normoprolactinemic galactorrhea induced by fluoxetine. Journal of Clinical and Experimental Investigations 2013;4(1):105-6.
10. Mondal S, Saha I, Das S. A new logical insight and putative mechanism behind fluoxetine induced amenorrhea, hyperprolactinaemia and galactorrhea in a case series. Ther Adv Psychopharmacol 2013;3(6):322-34. [CrossRef]
11. Egberts AC, Meyboom RH, De Koning FH, Bakker A, Leufkens HG. Non-puerperal lactation associated with antidepressant drug use. Br J Clin Pharmacol 1997;44(3):277-81. [CrossRef]
12. Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, et al. A method for estimating the probability of adverse drug reactions. Clin Pharmacol Ther 1981;30(2):239-45. [CrossRef]
13. Mahasuar R, Majhi P, Ravan JR. Euprolactinemic galactorrhea associated with use of imipramine and escitalopram in a postmenopausal woman. Gen Hosp Psychiatry 2010;32(3):341.
14. Kaye TB. Hyperprolactinaemia. Causes, consequences, and treatment options. Postgrad Med 1996;99(5):265-8.
15. Berilgen, MS. Late-onset galactorrhea and menometrorrhagia with venlafaxine use in a migraine patient. J Clin Psycopharmacol 2010;30(6):753-754. [CrossRef]
16. Egberts ACG, Meyboom RHB, De Koning FHP, Bakker A, Leufkens HG. Non – puerperal lactation associated with antidepressant drug use. Br J Pharmacol 1997;44(3):277-81. [CrossRef]
17. Aggarwal A, Kumar R, Sharma RC, Sharma DD. Escitalopram induced galactorrhoea: A case report. Prog Neuropsychopharmacol Biol Psychiatry 2010;34(3):557-558. [CrossRef]
18. Ataya KM, Subramanian MG, Lawson DM, Gala RR. Euprolactinemic galactorrhea. Response of bioassay able prolactin to thyrotropin releasing hormone. J Reprod Med 1996;41(3):156-60.
19. Nebhinani N. Sertraline – induced galactorrhea: a case report and review of cases reported with other SSRIs. Gen Hosp Psychiatry 2012;35(5):576.
20. Trenque T, Herlem E, Aurichi P, Drame M. Serotonin reuptake inhibitors and hyperprolactinaemia. A case/non - case study in the French Pharmacovigilance Database. Drug Saf 2011;34(12):1161-66. [CrossRef]