

# Rising Trend of Use of Antidepressants Induced Non-Puerperal Lactation: A Case Report

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## ABSTRACT

Non puerperal lactation or galactorrhea is a well known side effect of antipsychotic drugs but has been infrequently described with the use of antidepressants. In past few decades, there have been emerging trend of isolated case reports of selective serotonin reuptake inhibitors induced non puerperal lactation. We report a case of non puerperal lactation following usage of second generation tricyclic antidepressant, nortriptyline and resolution on withdrawing the drug. Literature review has been done for antidepressant induced galactorrhea to understand the current trends, putative mechanism as different from one implicated for antipsychotics and its clinical utility.

**Keywords:** Galactorrhea, Nortriptyline, Tricyclic antidepressants

## CASE REPORT

A 21-year-old young unmarried female patient with no past medical or psychiatric history presented with complaint of daily occurring vague, dull aching mild to moderate intensity headache lasting for whole day since 4 months duration, with no associated history of nausea, vomiting, photophobia, phonophobia or any discharge from eye, ear or nose was reported. No specific aggravating or relieving factors were found. No past history suggestive of head injury, visual impairment, recurrent sinusitis, significant stressors or other co-morbid physical or psychiatric illness was apparent. Severity of headache on visual analog scale was recorded to be 6 to 7. Patient was on, on and off self medicating with analgesics. Diagnosis of tension type headache was made and she was started on nortriptyline 25mg once daily and stress relieving exercises (deep breathing). Improvement was reported by the patient within 10 days in headache and intensity on visual analogue scale decreased to 3. But after 2 weeks, she developed complaint of heaviness and milky discharge from both the nipples. There was no associated history of recent chest wall surgery, sexual contact, menstrual irregularities, blood stained or foul smelling discharge per vagina, fever, skin rash, visual blurring or headache. Patient was not on any other herbal/ over the counter medications or oral contraceptive pills and had no prior or family history suggestive of any endocrinopathies. Physical examination was inconclusive except bilateral galactorrhea. Biochemical investigations (urine pregnancy test, haemogram, liver function, renal function, thyroid function test, serum prolactin level) and radiological investigations (mammogram, ultrasound pelvis and MRI brain) were non contributory. Since, symptoms had developed after initiation of nortriptyline so, it was stopped. Within a week galactorrhea stopped. Due to this alarming side effect, patient being a young unmarried female of reproductive age group refused to take psychotropics further and was continued on deep breathing exercises alone. For next two months patient did not report of headache or recurrence of galactorrhea and subsequently was lost to follow-up.

## DISCUSSION

Non-puerperal lactation or galactorrhea refers to non purulent milky discharge from the breast. Literature suggests prolactin release can be mediated via postsynaptic 5- Hydroxytryptamine (5-HT)

receptors directly in the hypothalamus [1], or tubuloinfundibular dopaminergic neurons inhibition via 5-HT mediated receptors indirectly [2]. Non lactation or galactorrhea can be a very disturbing complaint and can be detrimental for future compliance. It first requires ruling out the possible causes through detailed history, physical examination and relevant investigations. Physiological causes include pregnancy, breast feeding, breast stimulation, sexual intercourse, stress, exercise. Pathological causes may include causes related to central nervous system (Tumours, seizure, irradiation, Empty sella syndrome) or systemic diseases (Hypothyroidism, cirrhosis, chronic renal failure, polycystic ovary, Cushing's syndrome) or local causes (Herpes-zoster infection, chest wall surgery) [3]. Once ruled out, then attention should also be drawn towards iatrogenic agents. Possible psychotropics which can be putative agents include antipsychotics commonly and few of the antidepressants infrequently [4].

Most of the physicians are cautious regarding antipsychotic induced galactorrhea which is a common entity, however in past three decades there have been trend of emerging isolated case reports of galactorrhea due to antidepressant usage. Metanalysis by Egberts et al., shows that serotonergic antidepressants are associated with an approximately eight times higher risk of non-puerperal lactation compared with other antidepressants [5]. This effect is probably mediated by an indirect inhibition effect of serotonin on the dopaminergic transmission, caused by either presynaptic inhibition of dopamine discharge by serotonergic receptors or the direct stimulation of hypothalamic post synaptic serotonergic receptors leading to hyperprolactinaemia [6]. Literature review suggests that nearly 95% of the case reports are due to SSRIs, mainly paroxetine, fluoxetine, sertraline, fluvoxamine, escitalopram [5,7] Single case reports for amitriptyline, amoxapine and duloxetine are also available [5,8]. This data breaks the usual myth of tricyclic antidepressants being considered to have all side effects more frequent than SSRIs. However, against the usual mechanism hypothesized of hyperprolactinaemia, few of the case reports have documented euprolactinaemic galactorrhea [9-11] which calls for searching for some other mechanisms. In this case, all possible physiological and pathological causes were ruled out and the temporal association with onset and offset of symptoms with the use and stoppage of nortriptyline points towards drug

induced aetiology. Scoring on the Naranjo Adverse Drug Reaction (ADR) scale [12] was four suggestive of “possible” drug induced ADR. Unlike all previous reported cases with serotonergic antidepressants, this was the first case of a norepinephrine antidepressant, a secondary tricyclic antidepressant causing non-puerperal lactation [5,7,11]. In all previous cases, underlying diagnosis was depressive or anxiety disorder which can have inherent changes in hypothalmo-gonadal-axis predisposing the patient towards such possible ADR on therapeutic dosage of antidepressants [5,7,11,13,14]. However, this was a case of tension type headache with no co-morbid psychiatric disorder, developing this side effect at suboptimal (analgesic) dose of an antidepressant. To the best of our knowledge, this is the first case report from India of a second generation tricyclic antidepressant, nortriptyline induced non-puerperal lactation. Nortriptyline and desipramine are considered relatively devoid of the typical side effects associated with other tricyclic antidepressants and because of their higher affinity for norepinephrine transporter are often being used in somatic pain syndromes also besides use as antidepressants [15]. Such reports raise an alarm for not just psychiatrists but also the physicians and surgeons using this drug so frequently to be cautious for monitoring of such side effects especially in young reproductive age group.

## CONCLUSION

Antidepressants will continue to find their place in prescription pattern of all health professionals for a range of somatic and mental health conditions, but side effects like galactorrhea can be detrimental for future compliance. This calls for preparedness to be watchful for such side effects while using in young adults.

## REFERENCES

- [1] Nicholas L, Dawkins K, Golden R. Psychoneuroendocrinology of depression. Prolactin. *Psychiatr Clin North Am.* 1998;21:341–58.
- [2] Arya D. Extrapyramidal symptoms with selective serotonin reuptake inhibitors. *Br J Psychiatr.* 1994;165:728–33.
- [3] Pena KS, Rosenfeld JA. Evaluation and treatment of galactorrhea. *American Family Physician.* 2001;63(9):11763–70.
- [4] Daria La Torre DL, Falorni A. Pharmacological causes of hyperprolactinaemia. *Therapeutics and Clinical Risk Management.* 2007;3(5):929–51.
- [5] Egberts ACG, Meyboom RHB, Koning FHPD, Bakker A, Leufkens HGM. Non-puerperal lactation associated with antidepressant drug use. *J Clin Pharmacol.* 1997;44: 277–81.
- [6] Haddad PM, Wieck A. Antidepressant-induced hyperprolactinaemia. *J Psychopharmacol.* 2000;14(Suppl 3):A28.
- [7] Nebhinani N, Sertraline-induced galactorrhea: Case report and review of cases reported with other SSRIs. *Gen Hosp Psychiatry.* 2013;35(5):576.e3-5.
- [8] Belli H, Akbudak M, Ural C. Duloxetine related galactorrhea and restless legs syndrome: a case report. *Psychiatria Danubina.* 2013;25(3):266–67.
- [9] Gulsun M, Algul A, Semiz UB, Ates MA, Doruk A, Ebrinc S, et al. A case with euprolactinaemic galactorrhea induced by escitalopram. *Int J Psychiatry Med.* 2007;37:275–78.
- [10] Chakraborty S, Sanyal D, Bhattacharyya R, Dutta A. A case of paroxetine-induced galactorrhea with normal serum prolactin level. *Indian J Pharmacol.* 2010;42:322-23.
- [11] Mondal S, Saha I, Das S, Ganguly A, Das D, Tripathi SK. A new logical insight and putative mechanism behind fluoxetine-induced amenorrhea, hyperprolactinaemia and galactorrhea in a case series. *Therapeutic Advances in Psychopharmacology.* 2013;3(6):322-34.
- [12] Naranjo CA. A method for estimating the probability of adverse drug reactions. *Clin Pharmacol Ther.* 1981;30:239-45.
- [13] Lambert G, Johansson M, Agren H, Friberg P. Reduced brain norepinephrine and dopamine release in treatment-refractory depressive illness: evidence in support of the catecholamine hypothesis of mood disorders. *Arch Gen Psychiatry.* 2000;57:787–93.
- [14] Turner RA, Altemus M, Yip DN, Kupferman E, Fletcher D, Bostrom A, et al. Effects of emotion on oxytocin, prolactin, and ACTH in women. *Stress.* 2002;5(4): 269–76.
- [15] Gillman PK. Tricyclic antidepressant pharmacology and therapeutic drug interactions updated. *British Journal of Pharmacology.* 2007;151:737–48.

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