

# A study of association of menstrual irregularities and galactorrhoea in women taking antipsychotic, antidepressant and antiepileptic drugs

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## Abstract

**Introduction:** Most antipsychotic and antidepressant drugs like Duloxetine, Olanzapine and Risperidone etc. are known to cause hyperprolactinemia by acting on Dopamine D2 receptors in the hypothalamus and pituitary gland. Antiepileptic drugs like Valproic acid act on GABA receptors and are known to induce PCOS-like symptoms. Out of various symptoms of hyperprolactinemia – delayed menstrual cycle and galactorrhoea are significant in women patients. **Aims and Objectives:** To study the association of delayed menses and galactorrhoea in women taking antipsychotic, antidepressant and antiepileptic drugs in 120 women attending tertiary health care center. **Methodology:** In a random study where woman from 18 yrs. to 40 yrs. age group on antipsychotic, antidepressant and antiepileptic drugs are studied having complaints of delayed menstrual cycles. Patients were examined for galactorrhoea which was present in significant number of them. Serum Prolactin levels done in all patients, which were found to be raised in significant number of patients. **Result:** There is a clear association between certain antipsychotic, antidepressant and antiepileptic drugs causing menstrual irregularities and galactorrhoea. Hence should be prescribed with caution.

**Keywords:** Menstrual irregularities, Galactorrhoea, antipsychotic drugs, antiepileptic drugs, antidepressant drugs.

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## INTRODUCTION

Prolactin a polypeptide hormone is produced by lactotroph cells of the anterior pituitary<sup>1</sup>. Prolactin receptors are found in brain, mammary gland also in the liver, kidneys, ovaries, uterus, prostate and testis<sup>1,2</sup>. In women after puberty serum Prolactin levels are twice that in men. Dopamine is the predominant inhibitor of the Prolactin secretion. Dopamine binds to the D2 dopamine receptors on the membrane of lactotroph cells inhibiting Prolactin gene transcription and proliferation of

lactotrophs<sup>3,4</sup>. Hyperprolactinemia may be seen in chronic renal failure, primary hypothyroidism and patients presenting with prolactinoma<sup>5</sup>. The signs and symptoms of hyper prolactinemia are galactorrhoea, gynecomastia, infertility, menstrual irregularities (Oligomenorrhoea, amenorrhoea) sexual dysfunction and decreased bone mineral density<sup>6</sup>. Normal ranges are generally quoted at around 10 – 28microgram/ml for women and 5-10 microgram/ml for men. Levels above 250 microgram/ml are associated with pituitary adenomas and the levels due to medication like antipsychotic and antiepileptic drugs etc. are in range between 25 to 100microgram/ml. There are other categories of drugs like Ranitidine, Cimetidine, Beta- blockers, Verapamil, O.C. pills, Metopromide etc. which also can cause hyperprolactinemia<sup>4,9</sup>.

## MATERIALS AND METHODS

120 patients already on antipsychotic, antidepressant and antiepileptic drugs for more than 6 months of treatment coming to a gynecologist for chief complaints of menstrual irregularities like secondary amenorrhoea

ranging from 1/2 months to 4 months were included. Age group included was 18 yrs to 40 yrs as patients below 18 and more than 40 can have physiological reasons for delayed menses. All women were examined clinically for galactorrhoea and a sample for serum Prolactin levels was studied.

**RESULT**

All most all patients had galactorrhoea statically significant. Almost all had raised Prolactin levels in range of 25 to 100 microgram/ml.

**Table 1:** Distribution of patients according to age

Age group	Frequency	Percentage
>25	45	37.5
25-35	52	43.3
35-45	19	15.8
>45	4	3.3
<b>Total</b>	<b>120</b>	<b>100</b>

**Table 2:** Distribution of patients according to Rx

Rx	Frequency	Percentage
<6 months	23	19.2
6 months to 1 year	85	70.8
>1 year	12	10.0
<b>Total</b>	<b>120</b>	<b>100</b>

**Table 3:** Distribution of patients according to Period of Ammenohera

Ammenohera	Frequency	Percentage
0-3 months	105	87.5
3-6 months	11	9.2
>6 months	4	3.3
<b>Total</b>	<b>120</b>	<b>100</b>

**Table 4:** Distribution of patients according to Galactorrhoea

Galactorrhoea	Frequency	Percentage
Present	107	89.2
Absent	13	10.8
<b>Total</b>	<b>120</b>	<b>100</b>

**Table 5:** Relationship between drugs and galactorrhea

	Galactorrhea		Total
	Present	Absent	
Anti Psychotic	68	8	76
Anti Anxitey	39	5	44
<b>Total</b>	<b>107</b>	<b>13</b>	<b>120</b>

**P<0.01; Highly Significant**

**DISCUSSION**

In our study 30.6% patients on antipsychotic, 47.5 % on antidepressants and 15% antiepileptic, 100 % had menstrual irregularities (delayed cycles from 1/2 months to 4 months amenorrhoea) and > 85 % had

galactorrhoea. This shows significant association between the women taking these 3 category drugs having menstrual irregularities and hyperprolactinemia which can cause infertility, reduce sexual libido, and bone density can also be reduced. Also some studies suggest breast cancer in women. In one study patients treated with antipsychotic drugs 23.2 % of women and 31% of men had osteopenia associated with raised Prolactin levels. Hyperprolactinemia is one of the most common side effect associated with antipsychotic, occurs in 40 – 50 % of subjects though very high levels are less common, especially with drugs like Risperidone, Sulpride or Amisulpride<sup>12</sup>. Similar result is seen in our study.

Antidepressant also cause hyperprolactinemia, Duloxetine having commonly used drug in our study definitely shows strong association with menstrual abnormality and galactorrhoea. A study by Ashton and Longdon shows similar association<sup>14</sup>. This article suggests Mirtazapine is the only safest antidepressant shown not to elevate Prolactin levels<sup>15</sup>.

Another antipsychotic Olanzapine used in our study showed early dose related increase in S. Prolactin levels, for a transient period as per study by A.M.Crowford.(Schizophrenia research)<sup>16</sup>. Our study also shows strong association between drug therapy and galactorrhea, menstrual irregularities and hyperprolactinemia. Last category of antiepileptic drugs 15% women on Valporic acid also showed delayed menstrual cycles. There was no galactorrhoea and Prolactin levels were normal. Valporate is highly effective antiepileptic drug used to treat epilepsy, bipolar disorder and migraine. Valporate induces features of (PCOS) polycystic ovary syndrome in approximate 7% of women, where delayed menstrual cycles is one of significant symptoms. Thus detailed menstrual cycle history should be taken and appropriate antipsychotic/antidepressant or antiepileptic drugs should be prescribed to prevent undesirable side effects of delayed menstrual cycles, galactorrhoea- leading to breast cancer in future or leading to osteopenia.

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