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Antipsychotics in a Tertiary
Institution in South-South
Nigeria

HATASO

Galactorrhea among Female Mentally Ill Patients Using Antipsychotics in a Tertiary Institution in South-South Nigeria

Omamurhomu E Olose^{1*}, Donald C Chukwujekwu², Cecilia O Busari³

¹Department of Psychiatry, University of Calabar, Cross River State, Calabar, Nigeria.

²Department of Psychiatry, University of Port Harcourt, Port Harcourt, Nigeria.

³Department of Clinical Services, Federal Neuropsychiatric Hospital, Calabar, Nigeria.

*Correspondence: oloseoe@yahoo.com

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Abstract

Objective was to determine the prevalence of galactorrhea among respondents, to determine the correlation between the dose of antipsychotic and the presence of galactorrhea, to determine the relationship between the duration of drug use and the prolactin level, to determine the relationship between class of antipsychotic and galactorrhea, and to determine the predictors of galactorrhea among the respondents. This is a cross-sectional study. From 81 consenting patients taking prescribed antipsychotic medications and all of whom have met the inclusion criteria, a sociodemographic interview schedule was administered. Next, the venous blood sample was collected for the estimation of the serum prolactin level. The prevalence of galactorrhea was 50.6%, there was a correlation between galactorrhea and chlorpromazine equivalent dose of antipsychotics ($r = 0.356$, $p = 0.001$), there is an association between galactorrhea and the use of typical antipsychotics, there was also an association between the duration of antipsychotic use and galactorrhea, and the greatest predictor of galactorrhea was found to be the duration of antipsychotic medication usage. Galactorrhea can result from the use of atypical or typical antipsychotics, and the duration of antipsychotic use was the greatest predictor of galactorrhea.

Keywords: Galactorrhea; Mentally ill; Antipsychotics.

1. INTRODUCTION

Galactorrhea is the secretion of breast milk in nonbreastfeeding subjects. Although it has been reported in both males and females, it has been shown to be commoner among females. Galactorrhea is a common clinical disorder and can also be described as nonlactational milk production, which is usually defined as milk production 12 months after pregnancy and discontinuation of breastfeeding [1].

It may arise from a variety of etiologies, including the use of antipsychotic agents. Hormonal dysregulation is a recognized cause of galactorrhea. This includes hyperprolactinemia and thyroid diseases associated with increased thyroid-stimulating hormone (TSH) levels or thyrotropin-releasing hormone [2]. It may be caused by serious underlying benign conditions; therefore, it should be properly investigated [3]. Galactorrhea also occurs in males as well as newborn infants and adolescents irrespective of gender [4].

Primary hypothyroidism has the propensity to cause hyperprolactinemia and galactorrhea. This is because increased levels of the thyroid-releasing hormone increase the secretion of prolactin and TSH. Galactorrhea may be due to a prolactin-secreting pituitary adenoma (prolactinoma). Perhaps because of later recognition, the frequency of microadenomas is much lower in men. Due to the pressure effect on the pituitary stalk and the resultant reduction of the action of dopamine, which is a prolactin inhibitor, nonfunctioning pituitary mass lesions also can increase prolactin levels.

Thorough evaluation of galactorrhea includes taking a detailed food and drug history (methyldopa, opioids, antipsychotics, serotonin reuptake inhibitors, as well as licorice [5]) and eliciting likely behavioral triggers (stress, breast, and chest wall stimulation), evaluation for the presence of pregnancy, pituitary adenomas (with prolactin overproduction or pituitary stalk compression), and hypothyroidism. More often than not, adenomas of the anterior pituitary are prolactinomas. Overproduction of prolactin leads to menstrual irregularities and infertility, which may be a diagnostic clue. Galactorrhea may also result from hormonal imbalances resulting from the use of birth control pills. Galactorrhea and hyperprolactinemia may result from the use of medications [6-9], most commonly antipsychotics, gastrointestinal promotility agents, and verapamil.

Galactorrhea is also a side effect associated with the use of the second-generation H₂ receptor antagonist cimetidine (Tagamet). By blocking dopamine receptors that are responsible for the control of prolactin release, galactorrhea can

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also be caused by antipsychotics that cause hyperprolactinemia. Risperidone is very notorious for causing this complication. Case reports have also suggested that the use of proton-pump inhibitors may be associated with the occurrence of galactorrhea.

Galactorrhea also may be caused by the ingestion of certain drugs, including phenothiazines, other antipsychotics (presumably because of a dopamine receptor blockade), certain antihypertensives (especially α -methyldopa), and opioids.

Galactorrhea has been reported to occur in 5%-32% of women. Differences in galactorrhea definition may be responsible for most of the reported differences in galactorrhea incidence values [1]. Galactorrhea has been reported in a 16-year old girl with normal prolactin levels (euprolactinemic) [10].

Galactorrhea has been reported to occur in nulliparous and postmenopausal women [11] with variable incidence rates of up to 90% of women with hyperprolactinemia [12]. The marked variability is likely a result of the difference in how the milk is expressed and how galactorrhea is defined. One case report suggests the occurrence of galactorrhea resulting from visual and auditory cues from an unrelated newborn, the so-called emotionally induced galactorrhea (pseudolactation) [13].

Studies on the relationship between antipsychotics usage and galactorrhea are scarce in this environment. This research, therefore, aims to elucidate the nature of the relationship between antipsychotics use and galactorrhea among female mentally ill patients taking antipsychotics in a tertiary hospital in south-south Nigeria.

2. AIM AND OBJECTIVES

2.1. Aim

To determine the relationship between galactorrhea and antipsychotic use among female mentally ill patients.

2.2. Objectives

- (1) To determine the prevalence of galactorrhea among respondents
- (2) To determine the correlation between the dose of antipsychotic and the presence of galactorrhea.
- (3) To determine the relationship between the duration of drug use and prolactin level.
- (4) To determine the relationship between the class of antipsychotics and galactorrhea.
- (5) To determine the predictors of galactorrhea among the respondents.

3. METHOD(S)

3.1. Study Location

This study was conducted in Madonna University Teaching Hospital Elele, Rivers State, South-South Nigeria.

3.2. Ethical Issues

Approval to proceed with the study was obtained from the management of Madonna University Teaching Hospital, Elele, Rivers State, South-South Nigeria. The study was conducted without coercion to participate. The consent to participate was obtained from each respondent. The confidentiality of the participants was maintained during and after the study. Discontinuation from the study at any stage did not negatively impact on the level of patient care. Costs of the laboratory investigations were borne by members of the research team.

3.3. Determination of Sample Size

The minimum required sample size was calculated using the following formula [14].

$$n = z^2 pq/d^2$$

where

n = sample size

z = confidence interval is 1.96

p = prevalence from previous study.

q = 100- p (the proportion of those without galactorrhea)

d = degree of accuracy required, usually set at 0.05(5%) level.

From the earlier formula, a minimum sample size of 81 was obtained.

3.4. Study Population

Female patients diagnosed with mental illness who are attending

Out-patient clinic of the department of psychiatry, Madonna University Teaching Hospital, Elele, Nigeria.

➤ **INCLUSION CRITERIA:**

- (1) Female patients who have been diagnosed to be mentally ill and are on the antipsychotic drug for at least 4 weeks
- (2) Patients should be between 18 and 65 years old
- (3) Patients who are able to communicate verbally
- (4) Must give informed consent

➤ **EXCLUSION CRITERIA:**

- (1) Patients that are breastfeeding
- (2) Patients that are pregnant
- (3) Patients who are too debilitating to participate in the study.
- (4) Medical conditions related to hyperprolactinemia (hypothyroidism, cirrhosis of the liver, chronic kidney failure, prolactinoma)
- (5) Taking medications relating to hyperprolactinemia (verapamil, antipsychotics, α -methyl dopa, opioids, cimetidine, hormonal contraceptives, and selective serotonin reuptake inhibitors).

3.5. Procedure

Data collection took place from June 2018 to February 2019. First, all female patients diagnosed with any psychotic illness by the attending physician at the emergency and crisis intervention unit of the hospital were identified. Next, the nature of the study is carefully explained to both the caregivers and the patients. Thereafter, informed consent was sought to enable them to take part in the study. A sociodemographic questionnaire is also given to the patient or any accompanying caregiver or relative to collect information about age, educational status, occupation, and marital status.

A venous blood sample was obtained for serum prolactin level estimation. The entire blood samples were processed by one laboratory scientist. Participants were grouped according to the class of antipsychotics (atypical or typical) that they used before the assessment. The attending clinician determined the antipsychotics prescribed for each patient.

3.6. Statistical Analysis

Version 22 of the statistical package for social sciences (SPSS) was used for the data analysis. Subjects were classified according to their serum prolactin levels, antipsychotics in use, and sociodemographic variables. Doses of the antipsychotics used by the subjects were converted to their individual chlorpromazine equivalent doses. Tables were selected according to objectives, and Pearson's product-moment correlation was used for parametric variables, while the Chi-square test was used for nonparametric variables. In addition, logistic regression was used to determine the predictor for the prolactin level. All tests were two-tailed, with the level of significance at 0.05%.

3.7. Study Design

It was a descriptive cross-sectional study.

4. RESULTS

4.1. Sociodemographic Characteristics of Respondents

A total of 81 patients completed the study (Table 1).

4.2. Prevalence of Galactorrhea among Respondents

A total of 41 respondents had galactorrhea. The prevalence of respondents that were detected to have galactorrhea was 50.6%.

4.3. Correlation between Antipsychotic dosage and Galactorrhea

The mean antipsychotic dosage in chlorpromazine equivalent was 467 mg (205.55). A significant correlation was found between the presence of galactorrhea and antipsychotic dosage in CPZ equivalent ($r = 0.356$, $p = 0.001$).

4.4. Association between Class of Antipsychotic Medication and Galactorrhea

Most of the respondents (42 = 51.85%) received typical antipsychotic medications and 26(32.10%) of them had galactorrhea.

There was a significant difference between the presence of galactorrhea among those respondents on typical antipsychotic medications when compared with those on atypical antipsychotic medications ($\chi^2 = 4.521$, $df = 1$, $p = 0.033$)

4.5. Association between Duration of Antipsychotic Medication Use and Prolactin Level

The mean duration of antipsychotic use was 111 weeks. There was statistically significant association between duration of antipsychotic use and prolactin level ($\chi^2 = 999.098$, $df = 912$, $p = 0.035$).

Table 1: Sociodemographic characteristics of respondents.

Variables	Frequency (%) N = 81
Age (years)	
18-27	15(18.5)
28-37	28(34.6)
38-47	25(30.9)
48-57	12(14.8)
58-67	1(1.2)
Mean age	36.74(10.01)
Marital Status	
Single	22(27.2)
Married	48(59.2)
Separated	5(6.2)
Divorced	6(7.4)
Education	
None	8(9.9)
Primary	17(21.0)
Secondary	30(37.0)
Tertiary	26(32.1)
Employment	
Employed	23(28.4)
Unemployed	47(58.0)
Student	11(13.6)

Table 2: Prevalence of galactorrhea.

Galactorrhea	Frequency (%) N = 81
Present	41(50.6)
Absent	40(49.4)

Table 3: Class of antipsychotic and galactorrhea.

Variable (Antipsychotic)	Galactorrhea		χ^2	df	p-Value	
	Cases	Yes				No
Typical	42	26	16	4.521	1	0.033
Atypical	39	15	24			

Table 4: Predictors of galactorrhea.

Variables	B	SE	Wald	df	p-Value	Cox & Snell R^2	Nagelkerke R^2
						0.084	0.708
Age	0.010	0.037	0.066	1	0.798		
Duration of antipsychotic use	-0.036	0.008	20.436	1	0.000		
Dose of antipsychotics	0.017	0.012	1.996	1	0.158		
Class of antipsychotics	-1.505	0.794	3.593	1	0.058		

4.6. Predictors of Galactorrhea among the Respondents

Overall, the major predictor of galactorrhea is the duration of antipsychotic medication.

5. DISCUSSION

5.1. Prevalence of Galactorrhea among Respondents

In this study, the prevalence of galactorrhea is much higher than the prevalence of 32% reported in a 2012 study [1] on the evaluation and management of galactorrhea. The 50.6% prevalence in this study is not surprising in the light of the reported prevalence of a 1%-45% range among unmedicated normal women in a 2011 report. It is, therefore, not surprising that the prevalence of galactorrhea in this study is markedly higher than the reported prevalence among drug naïve respondents.

5.2. Correlation between Antipsychotic Dosage and Galactorrhea

A case report in India observed a dose-dependent relationship between antipsychotic use and the occurrence of galactorrhea in a female patient using Quetiapine [15]. This is similar to the finding of this study. A 2013 review article [16] on the effects of antipsychotics on women's menstruation also reported a dose-dependent relationship between antipsychotic medication usage and the occurrence of galactorrhea. A 1998 study [17], using 15 patients and their response of prolactin to haloperidol, showed a rapid increase during the first 6–9 days between the levels of 30 and 50 mg. Nevertheless, it goes on to report that the observed elevation was not influenced by dose and remained below 77 ng/ml during the study.

5.3. Association between Class of Antipsychotic Medication and Galactorrhea

A study [18], on hormonal side effects of antipsychotics reported that typical antipsychotics are significantly more likely to cause galactorrhea than atypical antipsychotics. This is in tandem with the findings reported by us.

5.4. Association between Duration of Antipsychotic Medication Use and Prolactin Level

This study showed that there was a significant association statistically between the duration of antipsychotic use and prolactin level. This finding is in agreement with a report in several other studies [16, 19–21] on the impact of antipsychotics on prolactin level all of which noted that there is a relationship between duration of antipsychotic use and prolactin level. Another study [22] had a contrary report, indicating that prolactin levels tend to marginally drop with increasing duration of use. The likely reason for this discrepant finding compared to the finding in our study is probably due to the fact that the respondents in the study with a contrary report used the medication for only 6 weeks at the time prolactin levels were retaken compared to a mean duration of 111 weeks in this study.

5.5. Predictors of Galactorrhea among the Respondents

In this study, among the various variables tested overall, the major predictor of the prolactin level is the duration of antipsychotic medication. This finding is similar to a report in a very recent retrospective study [23], which studied the etiological profile of galactorrhea among 40 women with galactorrhea referred to the department of endocrinology. Different from our study, some of the patients studied were taking other classes of drugs apart from antipsychotic medications.

6. ADDITIONAL POINTS

6.1. Strengths of This Study

(1) Exclusion of patients with medical conditions such as hypothyroidism, cirrhosis of the liver, chronic kidney failure, prolactinoma, and exclusion of patients taking medications such as verapamil, α -methyldopa, opioids, cimetidine, hormonal contraceptives, and selective serotonin reuptake inhibitors. This is because these conditions and medications have a propensity to cause hyperprolactinemia. This is to eliminate their effects as confounders. (2) It is a descriptive cross-sectional study. (3) The doctors attending to the respondents had the liberty to decide the type of antipsychotic and the dosages to be given to the respondents.

6.2. Limitations of This Study

(1) This is a cross-sectional study. (2) The respondents were hospital based; thus, findings from this study may not be generalizable to the larger population. In spite of these observations, the findings from this study can serve as a reference point for future studies and can add to the epidemiological database of galactorrhea in female mentally ill patients.

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Authors' Contributions

This work was conducted with the collaboration of all the authors. EOO, DCC, and COB designed the study, did the literature search and collected data, while EOO wrote the protocol for the study. Data analysis was done by EOO and COB. EOO wrote the initial draft of this publication, DCC prepared the tables, and all the authors made corrections for the final draft of this manuscript.

Conflict of Interest

The authors declare that there is no conflict of interest regarding this study and the publication of its findings.

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