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Original Research Article

Sexual function in patients with schizophrenia on anti-psychotics: a comparative study of hyperprolactinemia-inducing and hyperprolactinemia non-inducing antipsychotics

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ABSTRACT

Background: Sexual dysfunction is a common but often under-recognized adverse effect in patients with schizophrenia receiving antipsychotic therapy. Hyperprolactinemia induced by certain antipsychotics has been implicated as a major contributing factor. This study aimed to compare sexual function among patients receiving hyperprolactinemia-inducing and hyperprolactinemia non-inducing antipsychotics and to assess whether sexual dysfunction is related to antipsychotic-induced hyperprolactinemia or the underlying illness itself.

Methods: A prospective observational study was conducted in the Department of Psychiatry at Sri Ramachandra Hospital, Chennai, from March to July 2025. Sixty patients diagnosed with schizophrenia according to ICD-10 criteria and receiving antipsychotic therapy were enrolled. Patients were categorized into two groups: hyperprolactinemia-inducing antipsychotics (olanzapine, haloperidol, risperidone) and hyperprolactinemia non-inducing antipsychotics (aripiprazole, cariprazine, lurasidone). Sexual function was assessed using the Arizona Sexual Experience Scale (ASEX), and serum prolactin levels were measured. Statistical analyses included independent t-tests and one-way ANOVA, with $p<0.05$ considered significant.

Results: Of the 60 participants, 32 (53.3%) were males and 28 (46.7%) were females. Patients receiving hyperprolactinemia-inducing antipsychotics demonstrated significantly higher ASEX scores compared with those receiving hyperprolactinemia non-inducing agents (21.53±2.97 vs 15.70±2.93; $p=0.0005$). Serum prolactin levels were also significantly elevated in the hyperprolactinemia-inducing group (137.5±51.60 ng/mL vs 33.2±17.14 ng/mL; $p=0.0005$). Within-group analysis revealed that haloperidol was associated with the highest ASEX scores and prolactin levels among prolactin-raising agents, while aripiprazole exhibited the lowest values among prolactin-sparing drugs.

Conclusions: Sexual dysfunction was significantly more prevalent among patients receiving hyperprolactinemia-inducing antipsychotics and was strongly associated with elevated serum prolactin levels. However, the presence of sexual dysfunction in some patients receiving prolactin-sparing agents suggests that factors related to schizophrenia itself may also contribute. Careful selection of antipsychotic therapy and routine monitoring of sexual function and prolactin levels may improve treatment adherence and quality of life in patients with schizophrenia.

Keywords: Antipsychotics, Arizona sexual experience scale, Hyperprolactinemia, Schizophrenia, Sexual dysfunction

INTRODUCTION

Schizophrenia is a chronic and debilitating psychiatric disorder characterized by disturbances in perception, thought processes, emotions, and behavior. It affects approximately 24 million people worldwide and remains a major contributor to disability and reduced quality of life. Antipsychotic medications are the cornerstone of schizophrenia management and have significantly improved clinical outcomes by reducing psychotic symptoms and preventing relapse. However, long-term antipsychotic treatment is frequently associated with adverse effects that may compromise treatment adherence and overall patient well-being.[1]

Among these adverse effects, sexual dysfunction is one of the most common yet least discussed complications of antipsychotic therapy. Sexual dysfunction may manifest as reduced libido, impaired arousal, erectile dysfunction, menstrual irregularities, difficulty achieving orgasm, or reduced satisfaction with sexual activity.[2] These symptoms can negatively affect self-esteem, interpersonal relationships, and quality of life, often leading to poor adherence to treatment and increased risk of relapse.[3] Despite its clinical significance, sexual dysfunction remains under-recognized in routine psychiatric practice because patients are often reluctant to report such symptoms and clinicians may not routinely inquire about them.[4]

Hyperprolactinemia is considered one of the major mechanisms underlying antipsychotic-induced sexual dysfunction. Dopamine exerts an inhibitory effect on prolactin secretion through the tuberoinfundibular pathway. Antipsychotics that strongly block dopamine D_2 receptors, such as risperidone and haloperidol, frequently cause elevations in serum prolactin levels.[5] Elevated prolactin concentrations can suppress gonadal hormone secretion, leading to decreased libido, erectile dysfunction, menstrual disturbances, infertility, and other sexual adverse effects.[6] Studies have demonstrated a strong association between antipsychotic-induced hyperprolactinemia and sexual dysfunction, particularly among patients receiving prolactin-elevating agents.[7]

The propensity of antipsychotic medications to induce hyperprolactinemia varies considerably. Risperidone, paliperidone, and many first-generation antipsychotics are associated with significant prolactin elevation, whereas newer agents such as aripiprazole, cariprazine, and lurasidone are generally considered prolactin-sparing.[8,9] Aripiprazole, due to its partial dopamine agonist activity, has been shown not only to minimize prolactin elevation but also to reverse hyperprolactinemia induced by other antipsychotic medications.[10] Several studies have reported improved sexual function and normalization of prolactin levels following a switch from prolactin-raising antipsychotics to aripiprazole-based therapy.[11,12]

Although the relationship between hyperprolactinemia and sexual dysfunction has been widely studied, evidence suggests that sexual dysfunction in schizophrenia may not be solely attributable to elevated prolactin levels. Factors related to the illness itself, including negative symptoms, depressive symptoms, psychosocial impairment, and neurobiological alterations, may also contribute to sexual dysfunction.[13] Furthermore, comparative studies evaluating the impact of hyperprolactinemia-inducing and hyperprolactinemia non-inducing antipsychotics on sexual function remain limited, particularly in the Indian population.[14]

Therefore, the present study was undertaken to compare the effects of hyperprolactinemia-inducing and hyperprolactinemia non-inducing antipsychotics on sexual function in patients with schizophrenia and to assess whether sexual dysfunction is primarily related to antipsychotic-induced hyperprolactinemia or to the underlying disease process.

METHODS

Study design and setting

A prospective observational study was conducted in the Department of Psychiatry at Sri Ramachandra Hospital and Sri Ramachandra Medical Centre, Chennai, Tamil Nadu, India. The study was carried out over a period of five months from March 2025 to July 2025 after obtaining approval from the Institutional Ethics Committee (Ref. No. CSP/25/MAR/159/187).

Study population

Patients diagnosed with schizophrenia according to the International Classification of Diseases, 10th Revision (ICD-10) criteria and receiving antipsychotic therapy were screened for eligibility. A total of 60 patients were enrolled in the study after obtaining written informed consent.

Inclusion criteria

Patients of either sex aged 18-40 years; diagnosed with schizophrenia according to ICD-10 criteria; receiving either hyperprolactinemia-inducing or hyperprolactinemia non-inducing antipsychotic medications; and willing to participate in the study were included.

Exclusion criteria

Patients with significant endocrine, cardiovascular, neurological, or other psychiatric disorders; pregnant or lactating women; and patients receiving medications known to independently cause sexual dysfunction, such as selective serotonin reuptake inhibitors or beta-blockers, were excluded.

Sample size

The sample size was calculated using Epi Info software version 2.1.3 with a confidence interval of 95%. The estimated sample size was 60 participants. Considering a 10% attrition rate, the required sample size was calculated as 66. However, 60 eligible patients completed the study and were included in the final analysis.

Study procedure

Demographic and clinical details including age, gender, marital status, educational status, duration of illness, medical history, medication history, and current antipsychotic therapy were collected using a structured data collection form. Patients were categorized into two groups based on the type of antipsychotic prescribed: Group 1 (hyperprolactinemia-inducing antipsychotics): olanzapine, haloperidol, and risperidone and Group 2 (hyperprolactinemia non-inducing antipsychotics): aripiprazole, cariprazine, and lurasidone.

Sexual function was assessed using the Arizona Sexual Experience Scale (ASEX). Serum prolactin levels were obtained from laboratory records and analyzed for comparison between the two groups.

Assessment of sexual function

Sexual dysfunction was evaluated using the Arizona Sexual Experience Scale (ASEX), a validated five-item questionnaire that assesses sexual drive, arousal, penile erection/vaginal lubrication, ability to reach orgasm, and satisfaction from orgasm. Each item is scored on a six-point Likert scale ranging from 1 (normal function) to 6 (severe dysfunction). Total ASEX scores range from 5 to 30, with higher scores indicating greater sexual dysfunction. A total score of ≥19, a score of ≥5 on any individual item, or scores of ≥4 on any three items were considered indicative of clinically significant sexual dysfunction.

Outcome measures

The primary outcome measure was the difference in ASEX scores between patients receiving hyperprolactinemia-inducing and hyperprolactinemia non-inducing antipsychotics. Secondary outcomes included comparison of serum prolactin levels between the two groups and evaluation of differences among individual antipsychotic agents.

Statistical analysis

Data were entered and analyzed using Statistical Package for Social Sciences (SPSS) version 27.0. Descriptive statistics were expressed as mean±standard deviation (SD) for continuous variables and frequencies with percentages for categorical variables. Independent sample t-tests were used to compare age, duration of illness, ASEX scores, and serum prolactin levels between the two study groups. One-way analysis of variance (ANOVA) was performed to compare ASEX scores and prolactin levels among individual antipsychotic medications within each group. A p value of <0.05 was considered statistically significant.

RESULTS

A total of 60 patients diagnosed with schizophrenia receiving antipsychotic therapy were included in the study. The study population comprised 32 (53.33%) males and 28 (46.67%) females (Table 1). The majority of patients belonged to the age group of 37-40 years (31.67%), followed by 28-32 years (25.00%). The mean age of the study participants was 31.94±6.29 years.

Among the study participants, 38 (63.33%) were married and 22 (36.67%) were unmarried. Regarding educational status, 37 (61.67%) patients were illiterate and 23 (38.33%) were literate. Most patients belonged to the lower-middle socioeconomic class (30.00%), followed by the upper-middle class (25.00%)

Group- level comparison

The study participants were divided into two groups based on the type of antipsychotic medications. Group 1 patients received hyperprolactinemia inducing drugs like olanzapine, haloperidol, risperidone. Group 2 patients received hyperprolactinemia non inducing drugs like cariprazine, aripiprazole and lurasidone and the between group analysis was done as depicted in Table 1.

Table 1: Group level comparison.

Variables	Group 1 Mean±SD	Group 2 Mean±SD	P value
Age (years)	31.1±6.35	32.77±6.22	0.309
ASEX Score	21.53±2.97	15.7±2.93	0.0005
Prolactin (ng/ml)	137.5±51.60	33.2±17.14	0.0005
Duration of illness	5.21±4.83	4.98±4.45	0.843

The comparison of mean±standard deviation (SD) for age, ASEX score, prolactin levels, and duration of illness between Group 1 and Group 2. There was no statistically significant difference in age (31.1±6.35 vs. 32.77±6.22, p=0.309) and duration of illness (5.21±4.83vs. 4.98±4.45, p=0.843). However, Group 1 showed significantly higher ASEX scores (21.53±2.97 vs. 15.7 ± 2.93, p=0.0005) and prolactin levels (137.5±51.60 vs. 33.2±17.14, p=0.0005), indicating notable sexual dysfunction and hyperprolactinemia, as depicted in Table 1.

Within-group drug comparison

Within group analysis was performed to assess the effects of individual antipsychotics on sexual function and serum prolactin levels. In Group 1, each drug's effect was compared to identify the differences in the degree of hyperprolactinemia and sexual dysfunction. Similarly, in Group 2, individual agents were analyzed to evaluate variations in outcomes despite being prolactin sparing. Group 1 patients received hyperprolactinemia inducing drugs like olanzapine, haloperidol, risperidone. Group 2 patients received hyperprolactinemia non inducing drugs like cariprazine, aripiprazole and lurasidone.

Table 2: Comparison of age in Group 1.

Drug names	N	Mean±SD	P value
Olanzapine	10	30.0±5.37	0.243
Haloperidol	10	34.5±5.08	
Risperidone	10	28.8±7.43	

Table 2 depicts the age distribution in Group 1 across the 3 drugs (olanzapine:30.0±5.37 years; haloperidol: 34.5±5.08 years and risperidone: 28.8±7.43 years). No significant age difference was found within Group 1 (p=0.243). This shows age is not a confounding factor in sexual dysfunction difference between groups.

Table 3: Comparison of ASEX score in Group 1.

Drug names	N	Mean±SD	P value
Olanzapine	10	19.8±1.87	<0.001
Haloperidol	10	24.6±2.63	
Risperidone	10	20.2±1.54	

Table 3 depicts the ASEX score comparison in Group 1 across the 3 drugs. Haloperidol (24.6±2.63) shows the highest ASEX Scores in Group 1 compared to olanzapine (19.8±1.87) and risperidone (20.2±1.54). The p value was found to be <0.001.

Table 4: Comparison of prolactin levels in Group 1.

Drug names	N	Mean±SD	P value
Olanzapine	10	115.40±39.43	<0.001
Haloperidol	10	186.70±42.87	
Risperidone	10	110.60±33.90	

Table 5: Comparison of age in Group 2.

Drug names	N	Mean±SD	P value
Cariprazine	10	32.4±5.42	<0.001
Aripiprazole	10	31.5±7.57	
Lurasidone	10	34.4±5.75	

Table 4 depicts the prolactin levels comparison in Group 1 across the 3 drugs; haloperidol (186.70±42.87 ng/ml) shows the highest prolactin levels in Group 1 compared to olanzapine (115.49±39.43 ng/ml) and risperidone (110.60±33.90 ng/ml). The p value was found to be <0.001 shows a statistically significant difference between the drugs.

Table 5 depicts the age distribution in Group 2 across the 3 drugs (cariprazine 32.4±5.42 years; aripiprazole 31.5±7.57 years; lurasidone 34.4±5.75 years). No significant age difference was found within Group 2 (p=0.243). This shows age is not a confounding factor in sexual dysfunction difference between groups.

Table 6: Comparison of ASEX score in Group 2.

Drug names	N	Mean±SD	P value
Cariprazine	10	15.6±3.16	<0.001*
Aripiprazole	10	14.9±3.54	
Lurasidone	10	16.6±1.89	

*Statistically significant.

Table 6 depicts the ASEX score comparison in Group 1 across the 3 drugs. Lurasidone (16.6±1.89) shows the highest ASEX Scores in Group 2 compared to cariprazine (15.6±3.16) and aripiprazole (14.9±3.54). The p value was found to be <0.001, indicating a statistically significant difference within Group 2.

Table 7: Comparison of prolactin levels in Group 2.

Drug names	N	Mean±SD	P value
Cariprazine	10	33.00±18.68	<0.001*
Aripiprazole	10	31.20±12.51	
Lurasidone	10	35.40±20.78	

*Statistically significant.

Table 7 depicts the prolactin levels comparison in Group 2 across the 3 drugs; lurasidone (35.22±20.84 ng/ml shows the highest prolactin levels in Group 2 compared to cariprazine (32.89±18.82 ng/mL) and aripiprazole (31.12±12.37 ng/ml). The p value was found to be <0.001 shows a statistically significant difference between the drugs within Group 2.

DISCUSSION

The present study compared sexual dysfunction and serum prolactin levels among patients with schizophrenia receiving hyperprolactinemia-inducing and hyperprolactinemia non-inducing antipsychotics. The findings demonstrated significantly higher ASEX scores and serum prolactin levels among patients receiving prolactin-raising antipsychotics compared to those receiving prolactin-sparing agents. These results suggest a strong association between antipsychotic-induced hyperprolactinemia and sexual dysfunction.

Sexual dysfunction is a common but frequently under-recognized adverse effect of antipsychotic therapy. In the present study, patients receiving hyperprolactinemia-inducing antipsychotics exhibited significantly greater

sexual dysfunction than those receiving prolactin-sparing agents. Similar findings were reported by Montejo et al, who observed a high prevalence of sexual dysfunction among patients receiving antipsychotic medications and highlighted its detrimental effects on treatment adherence and quality of life.[4] Serretti and Chiesa also reported that sexual dysfunction is one of the most frequent adverse effects associated with antipsychotic treatment and is often underreported in clinical practice.[5]

The significantly elevated prolactin levels observed in the hyperprolactinemia-inducing group support the established role of dopamine D_2 receptor blockade in the pathogenesis of antipsychotic-induced hyperprolactinemia. Peuskens et al demonstrated that antipsychotics with a greater propensity to elevate prolactin levels are associated with increased risks of sexual and endocrine adverse effects.[8] Similarly, Holt and Peveler reported that hyperprolactinemia contributes substantially to sexual dysfunction, infertility, menstrual disturbances, and reduced quality of life among patients receiving long-term antipsychotic therapy.[15]

Among the prolactin-raising antipsychotics evaluated in the present study, haloperidol was associated with the highest prolactin levels and ASEX scores. This finding may be attributed to its potent dopamine D_2 receptor antagonistic activity. Previous studies have similarly demonstrated that first-generation antipsychotics are associated with greater prolactin elevation than many second-generation agents.[8] The marked elevation of prolactin observed with haloperidol in the present study further supports its well-established endocrine adverse-effect profile.

Patients receiving aripiprazole exhibited the lowest prolactin levels and the least degree of sexual dysfunction among the prolactin-sparing antipsychotics. This finding is consistent with previous studies demonstrating the prolactin-sparing properties of aripiprazole. Kirino et al reported significantly lower prolactin levels and fewer prolactin-related adverse effects among patients treated with aripiprazole compared with other antipsychotics.[10] The unique mechanism of aripiprazole as a partial dopamine D_2 receptor agonist allows maintenance of dopaminergic inhibition of prolactin secretion while preserving antipsychotic efficacy. Furthermore, Kelly et al reported improvement in prolactin-related adverse effects and sexual functioning following a switch from prolactin-elevating antipsychotics to aripiprazole.[16]

An interesting observation of the present study was the mild elevation in prolactin levels among patients receiving lurasidone. Although lurasidone is generally considered a prolactin-sparing antipsychotic, previous studies have reported occasional increases in prolactin levels depending on dosage, treatment duration, and patient characteristics.[8] Nevertheless, the degree of sexual dysfunction observed in patients receiving lurasidone remained substantially lower than that observed with prolactin-elevating antipsychotics.

The present study also identified sexual dysfunction among a small proportion of patients receiving prolactin-sparing antipsychotics despite normal prolactin levels. This finding suggests that hyperprolactinemia may not be the sole mechanism underlying sexual dysfunction in schizophrenia. Yoshida and Takeuchi reported that disease-related factors such as negative symptoms, depressive symptoms, psychosocial impairment, and neurobiological alterations may independently contribute to sexual dysfunction.[13] Similarly, Besnard et al suggested that serotonin receptor activity, individual susceptibility, and genetic polymorphisms may influence sexual function independently of prolactin levels.[17] These observations support the multifactorial nature of sexual dysfunction in schizophrenia.

The demographic and clinical characteristics of the study groups were comparable with respect to age and duration of illness, reducing the likelihood of confounding effects. Therefore, the observed differences in prolactin levels and sexual dysfunction are more likely attributable to differences in the pharmacological profiles of the antipsychotic medications. Routine assessment of sexual function and monitoring of serum prolactin levels may facilitate early identification of treatment-related adverse effects and improve medication adherence.

The present study has certain limitations. The sample size was relatively small and the study was conducted at a single tertiary care center, limiting the generalizability of the findings. Additionally, the observational design precludes the establishment of a causal relationship between antipsychotic exposure and sexual dysfunction. Future multicentric studies with larger sample sizes and longer follow-up periods are required to further elucidate the relationship between antipsychotic-induced hyperprolactinemia and sexual dysfunction.

Overall, the findings of the present study support existing evidence that hyperprolactinemia-inducing antipsychotics are associated with significantly greater sexual dysfunction and higher serum prolactin levels than prolactin-sparing agents. Consideration of these adverse effects during antipsychotic selection may improve treatment adherence, quality of life, and long-term clinical outcomes in patients with schizophrenia.

This study has few limitations. Limited sample size was used due to the short duration. This study is done in a tertiary care hospital and not done in a community setting hence the result cannot be generalized.

CONCLUSION

The findings of the present study indicated that sexual dysfunction was more prominent in patients receiving Hyperprolactinemia inducing antipsychotics compared to those on Hyperprolactinemia non inducing antipsychotics. The study revealed that the ASEX scores were significantly greater in the Hyperprolactinemia inducing

group, along with a marked elevation in serum prolactin levels, suggesting a strong link between hyperprolactinemia and sexual dysfunction during antipsychotic treatment. However, a few patients in the prolactin-sparing group also experienced sexual dysfunction, even though their prolactin levels remained within normal range. This finding suggests that sexual dysfunction may also be partially illness-related, and not solely a result of antipsychotic-induced hyperprolactinemia. These results indicate that while elevated prolactin contributes significantly, the pathophysiology of schizophrenia itself may play an additional role in sexual dysfunction among affected individuals.

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