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Factors associated with sexual side effects of antipsychotics in patients with psychotic disorders

Md. Mamun Al Mujahid, Ahsan Aziz Sarkar, Md. Sultan-E-Monzur, Md. Anowar Hossain, Md. Shohedul Alam, A. D. M. Rifat Chowdhury, Md. Abdullah Al Mamun, Mohammad Hasibur Rahman

Abstract

Background: Various studies have revealed that sexual side effects are frequent in psychotic patients treated with antipsychotics. Although sexual side effects have a negative impact on adherence to treatment, information on factors associated with antipsychotic related sexual side effects are limited.

Objectives: To evaluate the factors associated with sexual side effects of antipsychotics in psychotic patients.

Methods: We employed a single center, cross-sectional, naturalistic study design to collect data from 146 patients with DSM-5 diagnosis of different psychotic disorders. In addition to assessing sexual functioning by Psychotropic-Related Sexual Dysfunction Questionnaire (PRSexDQ-SalSex), we recorded demographic data, medication history and relevant clinical information.

Results: Among the patients, 52.1% exhibited sexual dysfunction according to the assessment with PRSexDQ. Sexual dysfunction (SD) was common in both sexes with males exhibiting higher prevalence of SD (58.5%) than females (43.8%). Incidence of SD increased in male patients ($\chi2=3.14$, $p=.050$), when risperidone and typical antipsychotics were used ($\chi2=10.5$, $p=.030$), with higher doses ($t=15.1$, $p=.001$), with longer duration of treatment ($t=8.2$, $p=.001$) and period of illness ($t=14.7$, $p=.001$), with increased age of the patients ($t=39.5$, $p=.001$) and when the diagnoses were schizophrenia ($\chi2=50.8$, $p=.000$). Patients' route of taking medication ($\chi2=0.535$, $p=.380$) and poly pharmacy of antipsychotics ($\chi2=0.955$, $p=.220$) appeared to have no significant effect.

Conclusions: Sexual side effects were common in patients taking antipsychotics and antipsychotics should be carefully chosen to ensure compliance.

Declaration of interest: None

Keywords: Sexual side effects; sexual dysfunction; antipsychotics

Introduction

Proper sexual functioning is one of the most important components of the quality of life and of maintaining a satisfying intimate relationship. Sexual dysfunction (SD) however is increasingly becoming a medical phenomenon of concern, in particular among patients taking antipsychotic medication.[1] Antipsychotic drugs, by modulating neurotransmitters and hormones, lead to erectile dysfunction and abnormal ejaculation[2,3] as well as impair desire and arousal.[4] Sexual dysfunction has been considered by many patients as a more troublesome side effect compared to others.[5] It is essential to sustain compliance on patients taking antipsychotics as they may discontinue taking a prescribed medication if they discover that they are unable to have a natural sexual life because of it. Identifying the factors associated with SD in patients receiving antipsychotics can provide important clues for safe prescription and thus, ensure compliance.

Studies using structured interviews or self-report questionnaires tend to report a prevalence of 30-60% for sexual side effects related to treatment with antipsychotics.[6] Both typical and atypical antipsychotics are associated with a substantial impairment of sexual functioning and a review comparing different antipsychotics with regard to sexual dysfunction concluded that risperidone induces sexual dysfunction most frequently, followed by typical antipsychotics (e.g. haloperidol), olanzapine and quetiapine.[5] The majority of the studies focused on the impact of different dosages on SD rates, found significant dose-dependent SD rates at least for risperidone.[7,8] Only a few

patients spontaneously complain about the sexual problem when they mention side effects of antipsychotic drugs. Doctors are also reluctant to discuss it when not complained and patients suffer in silence and ultimately discontinue the drug. This study tried to estimate the magnitude of the problem of sexual dysfunction among patients taking antipsychotic medication which, if known, would become easier to recommend and justify appropriate measures to be taken to minimize the problem. Study findings may also help to guide prescription of antipsychotic medication in the at-risk population and improve treatment adherence.

Methods

This cross-sectional study was carried out in the Inpatient and Outpatient Departments of National Institute of Mental Health (NIMH), Dhaka in between January 2019 to September 2019. A total of 146 sexually active patients in the age range of 21 years and above, with a DSM-5 diagnosis of either schizophrenia, schizophreniform disorder, schizoaffective disorder, mood disorder with psychotic features or other psychotic disorders were conveniently recruited for the study. Patients receiving antidepressants, mood stabilizers, drugs that might interfere with sexual functioning like alpha blockers, beta blockers or who had medical conditions like hypertension, diabetes, etc. that might affect sexual performance were excluded from the study. Data were collected by face-to-face conversation using paper and pencil instrument and from those forms were entered into SPSS software.

A semi-structured questionnaire was used to collect sociodemographic data like age, sex, marital status, etc. and relevant clinical information like diagnosis, duration of treatment, name of the prescribed antipsychotic(s), route of drug administration, dose of the drug, etc. Bangla adapted version of Pyschotropic-Related Sexual Dysfunction Questionnaire (PRSexDQ) was used to evaluate sexual dysfunction. The PRSexDQ consists of seven items evaluating the occurrence of sexual dysfunction along with subjective report on decrease of libido, delay of orgasm or ejaculation, lack of orgasm or ejaculation, erectile dysfunction or decrease in vaginal lubrication and the level of patient's tolerance to dysfunction. Sexual dysfunction was defined as having a score equal to or greater than 1 in any of the five items of the PRSexDQ that evaluated the various dimensions of sexual function. Ethical approval was provided by the Institutional Review Board of NIMH. Following data collection, data analyses were completed on the full sample using SPSS 24.0.

Results

The characteristics of the participants are shown in Table 1. Mean age±SD of the patients was 32.6±9.9 years. They were receiving eight different types of antipsychotics and of the 146 patients, 116 (79.5%) were taking a single antipsychotic and 30 (20.5%) were taking two antipsychotics at the same time.

Table 1: Characteristics of the patients who were enrolled in the study (N=146)

Characteristic	Frequency (n)	Percentage (%)
Age group (year)		
21-28	66	45.2
29-39	44	30.1
40-50	28	19.2
≥51	08	5.5
Gender		
Male	82	56.2
Female	64	43.8
DSM-5 diagnosis		
Schizophrenia	96	65.8
Schizophreniform	30	20.5
Schizoaffective	2	1.4
Mood disorder with psychotic features	16	11
Other psychotic disorders*	2	1.4

* Other psychotic disorders included brief psychotic disorder and delusional disorder

Among the patients, 52.1% exhibited SD when measured by PRSexDQ, among who males reported a higher proportion of SD (58.5%) than females (43.8%). Among the patients with SD, 63.2% had shown problems in all three domains of sexual performance, 23.7% in desire and arousal, 5.3% in desire and orgasm, 5.3% in arousal and orgasm and 2.6% solely in desire domain. Desire was universally affected and only 5.3% had sole disturbance in arousal and orgasm without affecting the desire. Among patients taking different antipsychotics, it was observed that 60.7% patients receiving risperidone complained of sexual dysfunction followed by 55.1% patients receiving haloperidol and 47% receiving trifluoperazine. Atypical antipsychotic olanzapine appeared relatively safer with dysfunction as 32.2% of the patients receiving olanzapine complained of sexual dyfunction. Use of risperidone, haloperidol and trifluoperazine significantly increased the probability of SD ($\chi2=10.5$, p=.030) whereas olanzapine had significantly lower probability of causing SD as found in chi-square tests. Schizophrenia patients had increased probability of SD ($\chi2=50.8$, p=.000) compared to schizophreniform, mood disorder with psychotic features or other psychotic patients. Male patients showed a higher probability ($\chi2=3.14$, p=.050) of having SD. Probability of causing SD did not differ by the route of drug administration ($\chi2=0.535$, p=.380) and on mono or polytherapy ($\chi2=0.955$, p=.220). Results of chi-square tests are summarized in Table 2.

Table 2: Sexual dysfunction by DSM-5 diagnosis, type of antipsychotic, drug combination, route of administration and gender (N=146)

DSM-5 diagnosis	Sexual Dysfunction		Chi-squared	P
	Present (n/%)	Absent (n/%)		
Diagnosis				
Schizophrenia	70 (92.1)	26 (37.1)	50.8	.000
Schizophreniform	6 (7.9)	24 (34.2)		
Schizoaffective	-	2 (2.8)		

DSM-5 diagnosis	Sexual Dysfunction		Chi-squared	P
	Present (n/%)	Absent (n/%)		
Mood disorder with psychotic features	-	16 (22.8)		
Other psychotic disorders	-	2 (2.8)		
Name of the drug				
Haloperidol	16 (21)	13 (18.6)	10.5	.030
Trifluoperazine	8 (10.5)	9 (12.8)		
Risperidone	34 (44.7)	22 (31.4)		
Olanzapine	10 (13.1)	21 (30)		
Quetiapine	1 (1.3)	1 (1.4)		
Clozapine	1 (1.3)	1 (1.4)		
Fluphenazine	4 (5.2)	2 (2.8)		
Chlorpromazine	2 (2.6)	1 (1.4)		
Therapy				
Monotherapy	58 (76.3)	58 (82.9)	.955	.220
Polytherapy	18 (23.7)	12 (17.1)		
Route				
Oral	72 (94.7)	68 (97.1)	.535	.380
Parenteral	4 (5.3)	2 (2.9)		
Gender				
Male	48 (63.2)	34 (48.6)	3.14	.050
Female	28 (36.8)	36 (51.4)		

Haloperidol equivalent doses of different antipsychotic drugs[9,10] were calculated and independent sample t-test were performed between patients with SD and without SD groups. T-test results showed that dose of the antipsychotic, duration of illness, duration of current treatment and age of the patient differ across both groups and increase in dose, duration of psychotic illness, duration of current treatment and age of the patient significantly increased the risk of having SD (Table 3). Patients with SD, were receiving a haloperidol equivalent mean±SD dose of 9.7±7.7mg.

Table 3: Independent sample t-test for dose of drug, duration of illness, duration of current treatment, age between SD and non-SD groups (N=146)

	t	df	P
Haloperidol Equivalent dose (mg)	15.152	145	.001
Duration of illness (year)	14.706	145	.001
Duration of current treatment (year)	8.212	145	.001
Age of the patient (year)	39.54	145	.001

Discussion

Nazareth reported that prevalence of SD in the general population is 31%.[8] In comparison to the general population, this study found patients on antipsychotic medications had a higher prevalence of SD (52.1% vs. 31%). Male patients complaining about SD had higher prevalence than females. Apart from higher prevalence in males, previous studies also found equal or lower prevalence in males.[11,12] The reason behind comparatively low female SD could be cultural values like conservative attitude, lack of sex education and reluctance to divulge to male researchers.

Among the patients, 94.7% reported that the desire part of their sexual performance was affected after antipsychotic therapy. This finding suggests the role of dopamine blockade in motivational function along with other neurohormonal mechanisms that precipitate dysfunction of desire, arousal and orgasm in patients. Pertaining to phase-specific SD, decreased libido has often been associated with the inhibition of motivation and reward and hyperprolactinemia, both of which could be linked to the dopamine receptor antagonism.[3] Impaired arousal and orgasm have been linked to hyperprolactinemia, sedation and reduced peripheral vasodilatation, which in turn, seem to be associated with dopamine D2 receptor antagonism, histamine receptor antagonism, cholinergic and alpha-adrenergic antagonism.[13]

Overall study finding suggests risperidone, followed by first-generation antipsychotics and finally other second-generation antipsychotics was the lineup for increased to decreased tendency of causing SD. Bearing this in mind, it is not surprising that SD rates are usually higher in patients treated with drugs associated with a strong D2 receptor antagonism and with a higher likelihood of inducing hyperprolactinemia such as in haloperidol, trifluoperazine and risperidone compared with other drugs such as olanzapine, aripiprazole, quetiapine and ziprasidone. In addition, the notion that drugs such as ziprasidone, olanzapine and quetiapine, which act as antagonists of the 5HT2c receptors, are less likely to induce SD.[14]

Frequency of SD increased as the dose of the antipsychotic drugs, duration of illness, duration of current treatment and age of the patients increased. Bobes et al. reported that the adverse effects of antipsychotics mainly occur in the long-term treatment and suggested that if the symptoms are not fully controlled in short time, the psychotic disease itself could cause sexual dysfunction, particularly decreased libido.[15] Mosaku et al. explained in his study that the duration of medication use is also significantly associated with orgasmic functions, sexual desires and overall sexual satisfaction.[16] Bitter et al. found that the rate of sexual dysfunction is highest between 3 to 6 months of treatment duration with antipsychotic medication and demonstrated that haloperidol is attributed to higher rates of sexual dysfunction in patients in acute phases and for long term treatment, a high rate of sexual dysfunction is detected in those patients taking risperidone.[17]

When considering effect of mono and dual therapy of antipsychotics in causing SD, it was found that use of multiple antipsychotic drugs did not significantly increase the risk of SD. This finding was contrary to the common sense assumption that multiple drugs would further increase SD. The reason behind this finding could be that using two drugs at lower doses decreased drug specific side effects, thus also SD. Another explanation could be that commonly a first and a second-generation combination were in use; adding a second-generation antipsychotic decreased risk of SD. Gallego found that switching to or adding a second generation antipsychotic to other

antipsychotics were associated with a marked improvement in overall sexual functioning, a decrease in erectile and ejaculatory difficulties in men and a reduction in menstrual dysfunction in women.[18] It was found that long-acting depot preparations had similar sexual side effect profile as oral antipsychotics. However, number of patients receiving long-acting injections were small, so this finding needs further evaluation.

Conclusions

The cross-sectional design of the study limits the strength of the causal relationship. Also, the long treatment duration with the antipsychotics might be associated with a survival bias, i.e. patients who exhibited more severe forms of sexual dysfunction were more prone to discontinue their treatment and therefore were not captured in the study. Despite these limitations, this study helped to conclude that sexual side effects were common in patients taking antipsychotics, especially first generation antipsychotics. So antipsychotics should be carefully chosen to ensure compliance. Larger studies are required for in-depth analysis of the sexual side effects of antipsychotic medication.

Md. Mamun Al Mujahid, Assistant Professor, Psychiatry, TMSS Medical College, Bogura, Bangladesh; **Ahsan Aziz Sarkar,** Assistant Registrar, Psychiatry, NIMH, Dhaka, Bangladesh; **Md. Sultan-E-Monzur,** Former Assistant Professor, Psychiatry, North Bengal Medical College, Sirajganj, Bangladesh; **Md. Anowar Hossain,** MD Psychiatry Resident, NIMH, Dhaka, Bangladesh; **Md. Shohedul Alam,** Consultant Psychiatrist, Islami Bank Medical College Hospital, Rajshahi, Bangladesh; **A. D. M. Rifat Chowdhury,** HMO, NIMH, Dhaka, Bangladesh; **Md. Abdullah Al Mamun,** Registrar, Psychiatry, NIMH, Dhaka, Bangladesh; **Mohammad Hasibur Rahman,** MD Resident, Psychiatry, NIMH, Dhaka, Bangladesh.

Correspondence: Ahsan Aziz Sarkar, Assistant Registrar, Department of Psychiatry, National Institute of Mental Health, Sher-E-Bangla Nagar, Dhaka, Bangladesh-1207.
Email: ahsan.psychiatry@gmail.com

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