Sexual Dysfunction in Male Schizophrenia Remitted Patients Treated with Risperidone and Olanzapine - A Comparative Study in a Tertiary Care Hospital in Northern Kerala

Ben Thekkekutte Varghese[1], Yesudas Kalathara Francis[2], Deepak Koyilerian Prabhakaran[3]

[1, 2, 3] Department of Psychiatry, Government Medical College, Kannur, Kerala, India.

ABSTRACT

BACKGROUND

Patients on antipsychotics frequently report sexual dysfunction as a side effect. Antipsychotics from the second generation are favoured since they are less likely to induce negative effects, second-generation antipsychotics such as risperidone and olanzapine, on the other hand, have a sexual side effect that affects treatment compliance and leads to marked distress and interpersonal problems. A pleasurable sexual encounter is an essential component of all human life. A normal sexual function provides a sense of psychological, bodily, and social well-being. The sexual difficulty has an impact on one's mood, self-esteem, interpersonal functioning, treatment adherence, and quality of life. The purpose of this study was to see if the second-generation antipsychotics risperidone and olanzapine were linked to sexual dysfunction.

METHODS

This was a hospital-based cross-sectional study of 70 male schizophrenia remitted patients treated with risperidone or olanzapine who met the inclusion and exclusion criteria and were seen in the outpatient department. The patients were assessed with socio-demographic proforma, brief psychiatric rating scale was used to assess clinical stability, clinical information sheet and ICD- 10 DCR were used to make a diagnosis of schizophrenia, Arizona Sexual Experiences Scale was used to assess the sexual dysfunction. The statistical analysis was carried out with the help of the Statistical Package for Social Sciences (SPSS). Frequency (%) and mean + / - SD were used to express categorical and quantitative values, respectively. The chi-square test was employed to determine whether categorical variables were related.

RESULTS

Among the 70 male patients, 35 were on treatment with risperidone and 35 were on treatment with olanzapine. 71.4 % of risperidone treated patients and 45.7 % of olanzapine treated patients' experienced sexual dysfunction.

CONCLUSIONS

This study concluded that sexual dysfunction is common in male schizophrenia remitted patients treated with risperidone and olanzapine and it is highest with risperidone (71.4 %), while in olanzapine (45.7 %) had dysfunction. Clinicians should ask and systematically evaluate the sexual side effect associated with these antipsychotics and address it or else it may lead to noncompliance with treatment.

KEY WORDS

Sexual Dysfunction in Atypical Antipsychotics, Risperidone, Olanzapine, ASEX.

Corresponding Author:
Dr. Deepak Koyilerian Prabhakaran,
Swetha, Kunhipally, Kottaly P.O.,
Kannur-670005, Kerala, India.
E-mail: dkpswetha@gmail.com

DOI: 10.14260/jemds/2022/94

How to Cite This Article:
Varghese BT, Francis YK, Prabhakaran DK. Sexual dysfunction in male schizophrenia remitted patients treated with risperidone and olanzapine - a comparative study in a tertiary care hospital in Northern Kerala. J Evolution Med Dent Sci 2022;11(04):470-474, DOI: 10.14260/jemds/2022/94

Submission 25-01-2022,
Peer Review 30-01-2022,
Acceptance 25-02-2022,
Published 11-03-2022.

BACKGROUND

"Sexual dysfunction (SD) is defined as a disorder of sexual behaviour and sexual sensation that appears as an abnormality or absence of sexual psychology and physiological reaction."[1] Sexual dysfunction (SD) is one of the commonest and bothersome side effects in patients taking antipsychotic drugs and it affects treatment compliance. Sexual dysfunction occurs due to a multitude of reasons. The causes of sexual dysfunction can be organic to psychogenic. Organic causes include chronic disease, drugs, medical and surgical causes. Psychogenic causes include individual factors like depression, anxiety, relationship issues, psychosexual factors like negative learning and attitudes, performance anxiety.[2] Among the drugs, antihypertensives, antihistamines, diuretics, anti-depressants, benzodiazepines and antipsychotics are the common causes of sexual impairment.[3]

The human sexual response study of Masters and Johnson (1966) shed light on the male and female sexual responses.[4] The various phases in the sexual response cycle are the Excitement phase, Plateau Phase, Orgasmic phase and Resolution phase.

Depending upon the various areas of sexual functions affected, the spectrum of sexual dysfunction includes:

1. Decreased sexual desire
2. Difficulty in erection
3. Sexual aversion disorders
4. Premature ejaculation
5. Difficulty in achieving orgasm.

The common sexual dysfunctions experienced in patients on atypical antipsychotics include impairment of libido, orgasmic function, erectile and ejaculatory function.[5]

The mechanisms of sexual dysfunction are mainly because of problems in one or more of three areas of the sexual response cycle: sexual interest (libido), arousal (vaginal lubrication in females and erection in males) and orgasm. The degree of affection depends on the pharmacological profile of the drug.[6]

Antipsychotics Induced Sexual Dysfunction Occurs by the Following Mechanisms

1. Histamine receptor antagonism.
2. Dopamine receptor antagonism especially dopamine 2 receptor antagonism.
3. Cholinergic receptor antagonism.
4. Alpha-adrenergic alpha receptor antagonism.[7]

A study done by G Sullivan et al. regarding the sexual side effects of antipsychotic medication found that it occurred in 30 to 60 percent of persons taking antipsychotics and it included mainly difficulties in erection and ejaculation, changes in sexual desire in men while in women it included decreased sexual desire, orgasmic dysfunction and menstrual irregularities.[8] Studies have shown that second-generation antipsychotics have an advantage with regard to sexual function compared with first-generation antipsychotics.[9]

Risperidone and olanzapine are atypical antipsychotics approved for the treatment of schizophrenia and bipolar disorder. Anil Kumar et al. conducted comparative research of risperidone, quetiapine, and olanzapine in an Indian population with sexual dysfunction. It involved a total of 102 subjects in which 25 patients were on quetiapine, 25 were on risperidone, 22 were on olanzapine and 30 were healthy subjects. They were evaluated for sexual functioning using SFQ (Sexual functioning questionnaire). The following results were obtained from the study, 23 % of healthy subjects had some impairment, 96 % of patients on risperidone had sexual dysfunction, 88 % of patients on quetiapine and 90 % of the patients on olanzapine had sexual dysfunction.[5]

A large international population study in schizophrenic outpatients over one-year comparing sexual function in patients treated with atypical and typical antipsychotics was done. The entered patients were on monotherapy (olanzapine 2638, risperidone 860, quetiapine 142 or haloperidol 188). The results were that sexual dysfunction rates were lower for a patient treated with olanzapine and quetiapine, compared to patients who received risperidone or haloperidol.[10]

These studies show that sexual dysfunction is common in patients getting treatment with atypical antipsychotics like risperidone and olanzapine. Patients rarely report the sexual side effects associated with these drugs due to fear of shame. Male being the active partner in sexual intercourse, the sexual dysfunction can have a significant effect on his mood, interpersonal functioning, self-esteem and life satisfaction. This aspect if not addressed can lead to poor drug compliance. So the treating psychiatrist must actively enquire about these side effects.

There are several international studies related to sexual dysfunction due to antipsychotics and the treatment for the same, but there are only limited studies done in this regard in the Indian population and there is only poor attention for these side effects in patients suffering from schizophrenia. So there is a need to examine the prevalence of sexual dysfunctions of these antipsychotics in the Indian and Kerala population and how it affects treatment compliance.

Objectives

Primary objective

To determine the prevalence and compare the effects of risperidone and olanzapine on sexual function in male schizophrenia remitted patients.

Secondary Objective

- To compare the types of sexual dysfunction related to risperidone and olanzapine in male schizophrenia patients who have had their schizophrenia remitted.
- To determine the length of drug use and its impact on sexual function.

METHODS

This is a cross-sectional study conducted in a hospital. Male schizophrenia remitted patients on risperidone or olanzapine who attended the outpatient branch of the Department of Psychiatry, Government Medical College, Kannur were included in the study after receiving ethics committee approval. The research was conducted over one year, from February 1, 2020, to February 29, 2021.

The minimum sample size calculated was 27 subjects in each group (sample size was calculated using formula $n = (Z_{1-\alpha/2} + Z_{1-\beta})^2 (p_1 (1- p_1)+ p_2 (1- p_2))/(p_1- p_2)^2$ with an assumed prevalence of sexual dysfunction, 86 % in risperidone and 48.3 % in olanzapine with 5 % level of significance and 90 % power).[11] However, a convenient sample of 35 subjects in each group was taken. Patients who met the inclusion and exclusion criteria were enrolled for the study.

Inclusion Criteria

1. Patients attending psychiatry OPD in GMC, Kannur who consented to the study.
2. Sexually active married male subjects between age 21 and 50 yrs.
3. Those patients satisfying ICD 10 criteria for schizophrenia from history, who were maintaining remission either on risperidone or olanzapine determined by the score of BPRS < 4.

Exclusion Criteria

1. Patients having comorbid medical illnesses like diabetes, hypertension, and peripheral vascular disease.
2. Patients with primary sexual dysfunction.
3. Schizophrenia patients who were mentally retarded.
4. Those on multiple antipsychotic medications or being treated with other drugs that impact sexual function, such as antidepressants, benzodiazepines, or antihypertensives.

Alcohol or Tobacco Use

The sociodemographic data, clinical information sheet, brief psychiatric rating scale, and Arizona sexual experiences scale were used to assess the samples.

Sociodemographic Data Sheet

The investigator created this datasheet to gather and record information on the patient's name, age, educational status, occupation, monthly income, history, contact address, and family type.

Clinical Information Sheet

It is used to get treatment records, the history of the patient and the diagnosis made by the doctor and the current treatment and dosing of the drug on which the patient is maintaining clinical stability.

Brief Psychiatric Rating Scale (BPRS)[12]

It is a commonly used scale to evaluate the positive, negative and affective symptoms in psychotic disorders like schizophrenia. It is divided into 18 categories, each of which is evaluated from 1 (not present) to 7 (present) (extremely severe). Remission of clinical stability is when scoring is less than 4 in all items. It is useful in documenting the efficacy of treatment.

Arizona Sexual Experiences Scale (ASEX)

A simple rating scale that measures sex drive, arousal, vaginal lubrication / penile erection, orgasm ability, and orgasm satisfaction. The score ranges from 5 to 30. Sexual dysfunction is defined as a total score ≥ 19, or a score of ≥ 5 on any item, or ≥ 4 on three items.[13]

Statistical Analysis

Frequency (%) and mean SD were used to express categorical and quantitative values, respectively. The chi-square test was employed to determine whether categorical variables were related. The statistical significance threshold for all statistical interpretations was set at $P < 0.05$. Statistical analyses were carried out using SPSS 20.0, a statistical software package.

RESULTS

Among the 70 male patients, 35 were on treatment with risperidone and 35 were on treatment with olanzapine. The majority of the patients were between the ages of 41 and 50. (47.1%). The majority of the patients (54.3 %) came from a rural background, had a nuclear family (54.3 %), had an annual income of more than 10,000 (40 %) and were unskilled employees (42.9 percent). 51.4 % of patients belonged to the Hindu religion. In both risperidone and olanzapine treated patients, paranoid schizophrenia patients were the majority (42.9 % and 54.3 % respectively) and the majority of patients were maintaining clinical stability for 8 months to < 1 year (34.3 %) in both the groups. 71.4 % of risperidone treated patients and 45.7 % of olanzapine treated patients experienced sexual dysfunction. In risperidone treated patients, most common sexual dysfunction was difficulty in getting and keeping an erection (45.7 %) while in olanzapine there was dysfunction with sexual drive (25.7 %). We could not get an association between the duration of treatment and sexual dysfunction.

		Risperidone		Olanzapine		χ^2	p
		Count	Percent	Count	Percent		
Sexual dysfunction	Present	25	71.4	16	45.7	4.77*	0.029
	Absent	10	28.6	19	54.3		
ASEX Sexual dysfunction	> = 19	15	42.9	9	25.7	2.28	0.131
	< 19	20	57.1	26	74.3		
ASEX Sexual drive	> = 5	15	42.9	9	25.7	2.28	0.131
	< 5	20	57.1	26	74.3		
ASEX Sexual arousal	> = 5	13	37.1	7	20.0	2.52	0.112
	< 5	22	62.9	28	80.0		
ASEX Getting and keeping an erection	> = 5	16	45.7	7	20.0	5.25*	0.022
	< 5	19	54.3	28	80.0		
ASEX Reaching orgasm	> = 5	13	37.1	7	20.0	2.52	0.112
	< 5	22	62.9	28	80.0		
ASEX Satisfaction orgasm	> = 5	15	42.9	7	20.0	4.24*	0.039
	< 5	20	57.1	28	80.0		

DISCUSSION

Our research was carried out in a tertiary care facility in Kerala's northern district. As a result, the sample was reflective of the vast majority of patients in Kerala receiving therapy. The inclusion of only male subjects with remitted schizophrenia excluding the female population was necessitated due to the difficulty of administering ASEX

scoring in female subjects. Earlier landmark studies were done by kotin and co-workers also had male subjects only.[14] Because of hormonal changes, sexual functionality varies with age, and most previous research had included the age criterion of the sample as 50 and even 60 in some studies. In our study, 47.1 percent of the patients (N = 33) were between the ages of 41 and 50. The majority of our study population had completed high school (58.6 %), had a monthly salary of more than 10,000 rupees (40 %) and came from a rural background (54.28 %). Unskilled workers were the most common occupation (42.85 percent). Hinduism was practised by 51.4 percent of the participants. All the subjects were married and reported a monogamous relationship with their wives.

When we go to previous studies, a study done by knegtering et al.[15] had 49 subjects and a study done by melkersson et al.[16] had 75 subjects with a diagnosis of schizophrenia

In our research, we discovered that risperidone was linked to a higher rate of overall sexual impairment (71.4 %) than olanzapine (45.7 percent). This is similar to a study conducted by Sathish Kumar et al. at the Central Institute of Psychiatry to examine sexual dysfunction and serum prolactin levels in schizophrenia remitted patients treated with olanzapine, risperidone, and clozapine. The Udvalg för Kliniske Undersogelser (UKU) Side Effect Rating Scale and Sexual Functioning Questionnaire were used to evaluate 31 patients on olanzapine, 23 on risperidone, 19 on clozapine, and 30 healthy controls. It showed that 86 % on risperidone, 48.3 % on olanzapine and 31 % on clozapine showed one or the other form of sexual dysfunction[11]

A cross-sectional study conducted by Bobes et al. to assess the sexual side effects of schizophrenia patients treated with risperidone, olanzapine, quetiapine, or haloperidol found that risperidone had higher sexual adverse effects. A total of 636 patients were evaluated using the UKU scale, which showed that risperidone showed 43.2 % sexual dysfunction while olanzapine showed 35.3 % dysfunction.[17]

In our study, it was found that erectile dysfunction was the most prevalent problem in the risperidone group (45.7 %), followed by difficulty in sexual drive and satisfaction with orgasm (42.9 %), followed by difficulty in sexual arousal and reaching orgasm (37.1 %) While in the olanzapine group, sexual drive dysfunction was the most common (25.7 %), all other dysfunctions were equal (20 %)

A study was done by Sathish Kumar et al. also showed that risperidone showed more erectile difficulty in 83 % while 48 % in olanzapine treated patients[11] In a randomised open-label comparison trial of olanzapine versus risperidone on sexual functioning, Knegtering H et al. found that olanzapine had fewer side effects and a significant difference in erectile dysfunction. Risperidone showed 31.6 % while olanzapine showed 0 % erectile dysfunction.[18]

A study done by Anilkumar et al., showed that impaired sexual drive occurred in 80 % of risperidone treated and 72 % of olanzapine treated patients.[5] In our study, difficulties with sexual drive occurred in 42.9 percent of risperidone-treated patients and 25.7 percent of olanzapine-treated patients, with problems with the sexual drive being the most frequent sexual dysfunction in olanzapine-treated patients.

Similar to our study, when compared to erection and arousal problems produced by antipsychotics, the majority of research showed that orgasmic side effects were less typically observed. Ejaculatory issues are frequently linked to erection issues. This is because, even if a person's orgasmic potential is intact, he won't be able to ejaculate. After all, he won't be able to get a complete erection.

In a study done by Anil Kumar et al., ejaculation impairment was reported in 32 % of risperidone treated patients and 27 % of olanzapine treated patients,[5] in our study risperidone showed 37.1 % ejaculation impairment while only 20 % in the olanzapine group.

On exploring the association between sociodemographic variables and sexual dysfunction like age, education, occupation, monthly income, background, religion, the family type we could not find any relation.

About 34.3 percent of both the risperidone and olanzapine groups maintained clinical stability for 8 months to 1 year, and about 20 % in the risperidone group and 25.7 percent in the olanzapine group maintained clinical stability for > = 1 year, but we couldn't find any statistically significant value between the effect of treatment duration and sexual dysfunction in the two medication groups.

CONCLUSIONS

Sexual dysfunction is a serious clinical problem that, regrettably, isn't often treated in the clinic. The goal of this study was to look at sexual dysfunction in people who were taking risperidone or olanzapine. The study concluded that male schizophrenia remitted patients on treatment with risperidone or olanzapine had sexual dysfunction as a side effect and it was maximum in risperidone treated patients compared with olanzapine. Hence there's a requirement that clinicians should ask and systematically evaluate for the sexual side effect associated with these antipsychotics and address it. Conveying this issue may increase the adherence to treatment and increase the quality of life, or else it may lead to noncompliance with treatment.

Strengths of the Study

Sexual dysfunction in patients treated with risperidone and olanzapine was the focus of this study, which is a significant area of need that is largely unmet. Given that it was conducted in an outpatient setting of a tertiary care hospital, the study population was representative of those receiving treatment in the country. We used standardised instruments that have been widely used in similar groups.

Limitations of the Study

There was no control group; therefore a comparison with age or sex-matched normal people was impossible. Only male schizophrenia treated patients were included in the study, inclusion of female subjects is also needed for better generalization of the result. Because patients' accounts are less credible during the symptomatic phase, only clinically stable patients were included with rigorous BPRS assessment. In schizophrenia, however, complete remission is uncommon, especially in terms of negative and cognitive

symptoms. If the problem of causation is to be addressed, there is a critical need for a long-term prospective study.

REFERENCES

[1] Chen L, Shi GR, Huang DD, et al. Male sexual dysfunction: a review of literature on its pathological mechanisms, potential risk factors, and herbal drug intervention. Biomed Pharmacother 2019;112:108585.

[2] Halvorsen JG, Metz ME. Sexual dysfunction, Part I: classification, etiology, and pathogenesis. J Am Board Fam Pract 1992;5(1):51-61.

[3] Nagaraj AKM, Nizamie HS, Akhtar S, et al. A comparative study of sexual dysfunction due to typical and atypical antipsychotics in remitted bipolar-I disorder. Indian J Psychiatry 2004;46(3):261-6.

[4] Masters W, Johnson VE. Human sexual response boston. Little Brown 1966.

[5] Nagaraj AKM, Pai NB, Rao S. A comparative study of sexual dysfunction involving risperidone, quetiapine, and olanzapine. Indian J Psychiatry 2009;51(4):265-71.

[6] Bella AJ, Shamloul R. Psychotropics and sexual dysfunction. Cent European J Urol 2013;66(4):466-71.

[7] Park YW, Kim Y, Lee JH. Antipsychotic-induced sexual dysfunction and its management. World J Mens Health 2012;30(3):153-9.

[8] Sullivan G, Lukoff D. Sexual side effects of antipsychotic medication: evaluation and interventions. Hosp Community Psychiatry 1990;41(11):1238-41.

[9] Cutler AJ. Sexual dysfunction and antipsychotic treatment. Psychoneuroendocrinology 2003;28 Suppl 1:69-82.

[10] Dossenbach M, Dyachkova Y, Pirildar S, et al. Effects of atypical and typical antipsychotic treatments on sexual function in patients with schizophrenia: 12-month results from the Intercontinental Schizophrenia Outpatient Health Outcomes (IC-SOHO) study. Eur Psychiatry 2006;21(4):251–8.

[11] Sathish Kumar SV, Sinha VK. Comparative study of sexual dysfunction and serum prolactin level associated with olanzapine, risperidone, and clozapine in patients with remitted schizophrenia. Indian J Psychiatry 2015;57(4):386-91.

[12] Zanello A, Berthoud L, Ventura J, et al. The Brief Psychiatric Rating Scale (version 4.0) factorial structure and its sensitivity in the treatment of outpatients with unipolar depression. Psychiatry Res 2013;210(2):626-33.

[13] McGahuey A, Gelenberg AJ, Laukes CA, et al. The Arizona sexual experience scale (ASEX): reliability and validity. J Sex Marital Ther 2000;26(1):25-40.

[14] Kotin J, Wilbert DE, Verburg D, et al. Thioridazine and sexual dysfunction. Am J Psychiatry 1976;133(1):82-5.

[15] Knegtering R, Castelein S, Bous H, et al. A randomized open-label study of the impact of quetiapine versus risperidone on sexual functioning. J Clin Psychopharmacol 2004;24(1):56-61.

[16] Melkersson K. Differences in prolactin elevation and related symptoms of atypical antipsychotics in schizophrenic patients. J Clin Psychiatry 2005;66(6):761-7.

[17] Bobes J, Garc A-Portilla MP, Rejas J, et al. Frequency of sexual dysfunction and other reproductive side-effects in patients with schizophrenia treated with risperidone, olanzapine, quetiapine, or haloperidol: the results of the EIRE study. J Sex Marital Ther 2003;29(2):125-47.

[18] Knegtering H, Boks M, Blijd C, et al. A randomized open-label comparison of the impact of olanzapine versus risperidone on sexual functioning. J Sex Marital Ther 2006;32(4):315-26.