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A Comparative Study on Evaluation of Sexual Dysfunction in Patients Treated With Atypical Antipsychotics Involving Risperidone, Olanzapine and Quetiapine

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Abstract
Background and aims*: Sexual impairment is commonly seen with antipsychotics but most patients do not report it. The aim of the study was to determine and compare frequency of sexual dysfunction associated with atypical antipsychotics Risperidone, Olanzapine and Quetiapine, in clinically stable schizophrenics.*
Materials and methods*: Prospective cross-sectional study in sexually active patients with Schizophrenia, in the age group 18-40 years. Purposive sampling technique was employed. Sample was divided into four groups, healthy volunteers, olanzapine group, quetiapine group and risperidone group. Brief psychiatric rating scale (BPRS) and changes in sexual functioning questionnaire (CSFQ) were used to assess sexual domains. Kruskal Wallis test and Chi-square tests were used to test significance of difference.*
Results*: 100 subjects were included (25 in each group). Mean age was 33.2 ± 5.4 years and 61% were from nuclear family. 60% of patients were males, 54.66% were from rural background, 52% were employed, all were married, 28% had a family member with psychiatric illness and paranoid schizophrenia was seen in 46.67%. Loss of desire was seen in 53% followed by loss of arousal in 47%. There was no difference between sexes. Most developed dysfunction when drugs were continued more than a year.*
Conclusion*: Compared to Risperidone and Olanzapine, Quetiapine showed lower sexual side effects. Impairment in sexual desire/libido was the commonest side effect observed. Sexual dysfunction escalates with extended duration of treatment.*

Keywords: *Loss of desire, Quetiapine, Risperidone, schizophrenia, sexual dysfunction.*

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I. Introduction

Sexual dysfunction can occur even in normal persons occasionally and shows variability in frequency of sexual desire and activity, between person to person, time to time. It can be caused by physical conditions like ageing process and thriving condition and pathological conditions like medical illness, psychiatric diseases and drugs. Sexual dysfunction is commonly seen in mood disorders, schizophrenia and other psychotic disorders. The reported prevalence is 40-80% in women and 45-85% in men.[1,2,3]

Antipsychotics are one of the common drugs causing sexual impairment but rarely reported by patients suffering from psychiatric diseases on treatment. Studies have revealed significant sexual impairment with both typical and atypical antipsychotics, which affects subject's self esteem, causes problem for their sexual partners, compromises treatment compliance and interferes with quality of life.[4]

Atypical antipsychotics, compared to typical antipsychotics, produce less extra pyramidal symptoms like tremors, rigidity, tardive dyskinesia, dystonia and least sexual dysfunction.As the prevalence of sexual dysfunction in Schizophrenics on antipsychotics ranges from 25% to 60%, knowing the sexual side effects, of individual atypical antipsychotics, help in safe and effective administration of medication to the patients.[5,6]

Researches in these aspects have limitations, as patients tend not to talk with their clinician about their sexual life. Fewer studies have compared the sexual dysfunction caused by atypical antipsychotics in Schizophrenic patients, especially in Indian population.It has been shown in studies that while Risperidone

elevates serum Prolactin in a dose dependent manner with reduced sexual desire and impaired arousal, Olanzapine elevates prolactin level only temporarily and Quetiapine does not increase prolactin levels.[7,8]

The aim of the study was to determine and compare the frequency of sexual dysfunction associated with antipsychotics risperidone, olanzapine and quetiapine, in clinically stable schizophrenics.

II. Materials And Methods

This was a prospective cross sectional study conducted at the outpatient department of the Institute of Mental Health, Chennai, Tamilnadu, India between January 2015 and June 2015. Patients with Schizophrenia fulfilling ICD 10 criteria who were clinically stable with treatment, belonging to age group 18-40 were recruited. Sexually active patients of both sexes were included in the study by employing purposive sampling technique. Patients with co-morbid medical illness or psychiatric illness, those with primary sexual dysfunction and those taking other drugs which affect sexual function (more than one antipsychotic, antidepressants or antihypertensives) were excluded from the study. Institutional ethics committee approval was obtained prior to the study and protocols were followed throughout the study. Both patients and informants were explained about the study in detail and informed consent was obtained prior to enrolment in study. The sample was divided into four groups viz., group 1 – 25 healthy volunteers, group 2 – 25 patients already on drug Olanzapine, group 3 – 25 patients already on drug Quetiapine and group 4 – patients already on drug Risperidone. None of the drugs were administered for the purpose of the study. Socio demographic data and clinical information were entered in preformed proforma sheet, Brief psychiatric rating scale (BPRS)[1] was used to assess symptoms of schizophrenia and also to document efficacy of treatment and Changes in sexual functioning questionnaire (CSFQ) with specific versions for males and females was used to assess sexual functioning in all domains. Data entry and statistical analysis was performed with SPSS version 22.0 (IBM, New York, USA). Descriptive data was given in summary statistics, KruskalWallis test was used to test significance of difference between quantitative variables and Chi-square test was used for qualitative variables. $p< 0.05$ was considered significant.

III. Results

A total of 100 subjects (75 patients with schizophrenia and 25 healthy controls) were included in the study of whom 58 were males (58%) (n= 58/100) and 42 were females (42%) (n = 42/100).43% of the subjects were in the age group 36 – 40 years. The mean age of the group (n = 100) was 33.2 ± 5.4 years. 61% of the subjects (n = 61/100) were from a nuclear family.

60% of the patients (n = 45/75) were males.34.67% of the patients (n = 26/75) had completed only high school education while 28% of them had either completed higher secondary education or had completed bachelor's degree (n = 21/75 each). 54.66% of the patients (n = 41/75) were from a rural residence.58.67% were from a nuclear family (n = 44/75). All the study participants were married at the time of study. 52% of the patients (n = 39/75) were currently employed at the time of study. 60% of the patients (n = 45/75) were receiving a monthly income of Rs. 5000-10000 while 30.66% (n = 23/75) were receiving a monthly income of less than Rs. 5000 at the time of present study. 28% of the patients (n = 21/75) had a family member with psychiatric illness.Paranoid schizophrenia was the most common type seen in the present population (46.67%) (n = 35/75).

The mean daily dose of the three drugs compared was 12.8 ± 4.8 mg for Olanzapine (Chlorpromazine equivalent dose of 256 mg), 112 ± 43.4 mg for Quetiapine (Chlorpromazine equivalent dose of 149.3 mg) and 5.6 ± 2.0 mg for Risperidone (Chlorpromazine equivalent dose of 280 mg). The comparison data of sexual dysfunction in various domains in the three different groups are given in Table 1.

Table 1. Comparison of sexual dysfunction in domains across study groups

Sexual dysfunction in domains across study groups (n = 100)							
Sl. No.	**Domains**	**Control group (n = 25)**	**Olanzapine group (n = 25)**	**Quetiapine group (n = 25)**	**Risperidone group (n = 25)**	**Pearson χ^2value**	**p value**
1.	Loss of Desire/ Libido	7/25 (28.0%)	16/25 (64.0%)	12/25 (48.0%)	18/25 (72.0%)	11.361	0.010
2.	Loss of arousal/ Erectile dysfunction	6/25 (24.0%)	14/25 (56.0%)	11/25 (44.0%)	16/25 (64.0%)	10.856	0.012
3.	Impairment in ejaculation/ Orgasm	5/25 (20.0%)	11/25 (44.0%)	8/25 (32.0%)	11/25 (44.0%)	4.352	0.226
4.	Impairment in sexual pleasure	6/25 (24.0%)	14/25 (56.0%)	14/25 (56.0%)	17/25 (68.0%)	10.684	0.014
5.	Overall sexual impairment	5/25 (20.0%)	13/25 (52.0%)	12/25 (48.0%)	15/25 (60.0%)	9.172	0.027

The differences observed with different treatment groups of schizophrenic patients were not seen gender wise. The difference in overall sexual impairment between both sexes had a p value of 0.226 and was not statistically significant (Table 2).

Table 2. Comparison of domains of sexual dysfunction across both sexes

Domains of sexual dysfunction	Impairment in Desire/ Libido		Impairment in Erection/ Arousal		Impairment in Ejaculation/ Orgasm	
Treatment groups	Male (Desire)	Female (Libido)	Male (Erection)	Female (Arousal)	Male (Ejaculation)	Female (Orgasm)
Control group (25/100)	3/13 (23.07%)	4/12 (33.33%)	3/13 (23.07%)	3/12 (25.00%)	2/13 (15.38%)	3/12 (25.00%)
Olanzapine group (25/100)	11/14 (71.00%)	5/11 (45.45%)	8/14 (57.14%)	6/11 (54.54%)	6/14 (42.85%)	5/11 (45.45%)
Quetiapine group (25/100)	8/16 (50.00%)	4/9 (44.44%)	7/16 (43.75%)	4/9 (44.44%)	5/16 (31.25%)	3/9 (33.33%)
Risperidone group (25/100)	12/15 (80.00%)	6/10 (60.00%)	10/15 (66.66%)	6/10 (60.00%)	7/15 (46.66%)	5/10 (50.00%)
χ^2	1.609		0.351		0.688	
p - value	0.657		0.950		0.875	

The comparison of effects of duration of drug treatment on sexual dysfunction is given in Table 3. Even though patients on longer duration of drug treatment showed significant sexual impairment, the differences between individual drugs was not statistically significant (Pearson Chi square value = 3.6216, p value = 0.459).

Table 3. Effects of duration of treatment on sexual dysfunction

Duration of drug treatment and prevalence of sexual dysfunction (n = 75)							
Sl. No.	Duration of treatment	Olanzapine group (n = 25)		Quetiapine group (n = 25)		Risperidone group (n = 25)	
		No. of Subjects	With sexual dysfunction	No. of Subjects	With sexual dysfunction	No. of Subjects	With sexual dysfunction
1.	0 – 6 months	7/25 (28%)	1/7 (14.3%)	9/25 (36%)	3/9 (33.3%)	9/25 (36%)	4/9 (44.4%)
2.	6 – 12 months	12/25 (48%)	6/12 (50%)	13/25 (52%)	7/13 (53.8%)	10/25 (40%)	6/10 (60%)
3.	> 12 months	6/25 (24%)	6/6 (100%)	3/25 (12%)	2/3 (66%)	6/25 (24%)	5/6 (83.3%)

IV. Discussion

Sexual functioning wanes with age and this can hinder results of studies on sexual dysfunction. The present study had set the age criteria only up to the age of 40 years which rules out sexual dysfunction due to hormonal changes of ageing. Most of the studies on sexual dysfunction did not include females, but the present study includes females along with an appropriate sex specific scale for assessment. The Changes in sexual functioning questionnaire (CSFQ - F), with scores for individual domains of pleasure, desire, arousal and orgasm with cut off values, was collected by female health personnel. Clayton et al. had also found that CSFQ was an appropriate scale with good internal consistency and good reliability even in treatment resistant patients.[9]Overall sexual impairment was diagnosed when individuals had a score of 47 or less for males and 41 or less for females.

In the present study, 20% of the healthy volunteers of the control group (n = 5/25) also had overall sexual impairment. This was comparable to the study by Hallward and Ellison who reported that 10-15% of normal population in the west suffered from sexual dysfunction while Nagaraj et al. found the prevalence to be 23% in healthy volunteers.[10,11]Byerlyet al. had also compared the sexual side effects between risperidone, quetiapine and olanzapine in 238 patients of Schizophrenia.[12]

In the present study, it was found that Risperidone was frequently associated with overall sexual impairment (60%) compared to Olanzapine (52%) and Quetiapine (48%). This was similar to the results obtained in the studies by Knegtering et al. and Bobes et al.[13,14] In the present study, both sexes have been included and restricted age group upto 40 years only to avoid bias. Effect of duration of drug intake was also studied.

Impairment in libido/ desire was one of the commonest reported sexual dysfunction among all medication groups in the present study and it was statistically significant. This was similar to the results in the study by Atmaca at al. who reported impaired libido with Risperidone.[15] but drugs alone are not responsible for impaired sexual desire as the illness per se can play a larger role along with elevated prolactin by antipsychotics.

Erectile/ arousal dysfunction was the second most common sexual adverse effect in the present population. Risperidone was the commonly associated drug (64%) seen in both the sexes. It is easier for patients

to appreciate and complain erectile/arousal difficulties and still easier to measure by nocturnal tumescence and penile plethysmography. Nagaraj et al. had not found statistically significant difference between the drugs but Gharidian et al. reported more patients with erectile dysfunction.[10,16]

When compared to dysfunctions in libido and erection, impairment in ejaculation/ orgasm was less prevalent in the present study. There was no significant difference between the three groups. Nagaraj et al. had reported a reduced incidence of ejaculatory impairment for all three drugs in their study while Sathishkumar et al. had reported increased incidence with Risperidone.[10,17]Almost each sexual stage depends upon other stages of sexual excitation. Most dysfunctions in ejaculation were also associated with erection difficulties and hence difficult to assess alone. Even though the person's orgasmic capacity was intact, he may not ejaculate and experience orgasmic joy as he cannot achieve complete erection. This could not be explained and hence a limitation in the present study.

68% of study subjects on Risperidone had reported reduction in sexual pleasure after drug initiation while 56% of study subjects on Olanzapine and Quetiapine had reported inability to achieve sexual pleasure. Duration of drug treatment for Schizophrenia had a significant effect on sexual dysfunction. While only 14% of subjects on Olanzapine for less than 6 months showed sexual dysfunction, all the subjects (100%) on Olanzapine for more than a year showed sexual impairment. But there was no statistically significant difference between the individual drugs.

In conclusion, compared to Risperidone and Olanzapine, Quetiapine showed significant lower sexual side effects in the present study. Even though it is difficult to pinpoint drug effect at a single sexual domain, impairment in sexual desire was the commonest side effect observed in the present study with atypical antipsychotics. Sexual dysfunction escalates with extended duration of treatment.

PS conceptualized, designed and compiled the study. ST analyzed data and appraised results.

DECLARATIONS

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Conflict of interest: None declared
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