ORIGINAL ARTICLE

ANTI-PSYCHOTICS INDUCED SEXUAL DYSFUNCTION

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Background: Sexual dysfunction associated with the use of antipsychotic drugs is quite prevalent affecting the patients' quality of life and one of the reasons for non-compliance. This important aspect is underestimated and overlooked by the treating professionals, partly because patients rarely talk about their dysfunction. Due to the scarcity of local data on the subject the objective of the present study was to explore and compare the prevalence of sexual dysfunction associated with antipsychotic drugs. **Methods:** This was a hospital-based cross-sectional study comprising of comparative assessment among five antipsychotics being consumed by 91 male patients under this study. **Results:** Risperidone, haloperidol and olanzapine collectively as a group were associated with increased incidence of sexual dysfunction (42.43%) compared to quetiapine and aripiprazole group (16%) which was statistically significant. Individually risperidone (48%) and haloperidol (45.81%) were associated with highest incidence of sexual dysfunction followed by olanzapine (29.41%). Quetiapine (16.67%) and aripiprazole (15.38%) were associated with the lowest incidence of sexual dysfunction. **Conclusion:** Risperidone and haloperidol are associated with a higher rate of sexual dysfunction compared to olanzapine. Quetiapine and aripiprazole have a significantly lower profile of adverse effects on sexual function.

Keywords: Sexual dysfunction, Antipsychotics, Erectile dysfunction, Ejaculatory dysfunction, Orgasmic dysfunction, Libido

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INTRODUCTION

Sexual dysfunction is associated with use of antipsychotic drugs due to their mode of action, greatly affecting patient's quality of life and drug compliance.[1] The prevalence ranges from 40–71% for all drug groups.[2] This important aspect is underestimated by the treating professionals, and also patients rarely talk about their dysfunction.[3]

The problem is encountered frequently with first-generation or typical antipsychotics. Whereas second-generation or atypical antipsychotics like risperidone are not even free of sexual dysfunction.[4] Studies reveal that risperidone and other typical antipsychotics are associated with a higher rate of sexual dysfunction as compared to olanzapine, clozapine, quetiapine, and aripiprazole.[5,6] This is mainly due to dopamine blockade, autonomic side-effects and hyperprolactinemia caused by these drugs.[2] However olanzapine, clozapine, quetiapine and aripiprazole are somewhat prolactin-sparing having lesser degree of sexual side-effects.[5,7]

Decrease in libido, erectile dysfunction, abnormal ejaculations, problems in orgasm and overall sexual contentment are the main dysfunctions reported by the patients taking antipsychotic drugs.[2,8–10]

Keeping in view the scarcity of research data regarding the subject at country level, the objective of the present study is to explore and compare the prevalence of sexual dysfunction associated with various antipsychotics including haloperidol, risperidone, olanzapine, quetiapine and aripiprazole, used by patients presenting to the psychiatry department Ayub Teaching Hospital, Abbottabad.

MATERIAL AND METHODS

This was a hospital-based cross-sectional study recruiting the patients by purposive sampling. It comprised of comparative assessment of different types of sexual dysfunction caused by various antipsychotics consumed by the patients under study.

Ninety-one consecutive and married male patients attending the psychiatry outpatients' department in Ayub Teaching Hospital, Abbottabad, receiving monotherapy either with haloperidol, risperidone, olanzapine, quetiapine, or aripiprazole for more than twelve weeks for various psychiatric indications were included who were in a remission phase at the time of interview. Patients with any chronic medical illness including diabetes mellitus, hypertension, cardiovascular disease, gonadal injury, endocrinal problems, substance misuse, in ability to reply to our questions and sexual dysfunction before starting antipsychotic medications were not included. Those patients were also excluded who were on antidepressants, anticonvulsants, lithium and beta-blockers.

Informed consent was taken in prior and their identity was kept confidential. Patients were divided in to two groups. Group one comprised of patients taking risperidone, haloperidol and olanzapine whereas Group two comprised of patients taking quetiapine and

aripiprazole. However sexual side-effects were also studied individually for each drug.

For assessment of the patients' sexual function, 'Arizona Sexual Experience Scale' (ASEX) developed by McGahuey, *et al*[11] was administered. Patients were interviewed by a trained interviewer who decoded and explained the questions to the patients in local language. Data was collected which included record of patients' demographic data, psychiatric diagnosis, medication history and questions about sexual function including libido, sexual arousal, penile erection, ejaculation, orgasm and overall sexual satisfaction.

Patients were recorded to have sexual dysfunction as measured by a total score of 18 or higher on ASEX or any individual item score greater than 5 or any 3 individual item scores equal to 4.

Statistical analysis was carried out using SPSS-16. Means and standard deviations for age and ASEX scores of patients with sexual dysfunction for each drug were calculated. Chi-square test was used to identify and compare the frequency of various types of sexual dysfunction between the two drug groups.

RESULTS

Overall 91 outdoor male patients presenting to the psychiatry outdoor unit were interviewed having a mean age of 34.09±9.44 years (Table-1).

Majority of the patients 69 (75.82%) had chronic schizophrenia. Whereas 22 (24.18%) were suffering from bipolar affective disorder. Sexual dysfunction was present in 35.17% of patients overall. Highest incidence of sexual dysfunction was observed with risperidone 48% and haloperidol 45.84%. (Table-2).

Erectile and ejaculatory dysfunctions were the two main problems observed especially with risperidone (48% and 44%) and haloperidol (45.83% and 41.67%) (Table-3).

Table-1: Mean age and number of patients taking various antipsychotics (n=91)

Drug in use	Number of patients	Age (Year) (Mean±SD)	Dose range
Risperidone	25	34.24±9.59	2–8 mg
Haloperidol	24	33.26±7.98	2–15 mg
Olanzapine	17	34.18±11.55	2.5–20 mg
Quetiapine	12	35.16±8.19	25–600 mg
Aripiprazole	13	34.31±9.53	10–30 mg
Total	91	34.09±9.44	

Table-2: Comparative assessment of sexual dysfunction induced by the antipsychotics (n=91)

Drugs in use by the patients	Sexual dysfunction (%)	
Risperidone (n=25)	48	
Haloperidol (n=24)	45.84	
Olanzapine (n=17)	29.41	
Quetiapine (n=12)	16.67	
Aripiprazole (n=13)	15.38	
Risperidone, Haloperidol and Olanzapine collectively (Group-1) (n=66)	42.43	$p<0.05$*
Quetiapine and Aripiprazole collectively (Group-2) (n=25)	16	
Sexual dysfunction (Overall) (n=91)	35.17	

*Significant

Table-3: Sexual dysfunction induced by the antipsychotics (%)

Anti-psychotic drug in use	Reduced Libido	Erectile Dysfunction	Ejaculatory Dysfunction	Orgasmic Dysfunction
Risperidone (n=25)	36	48	44	32
Haloperidol (n=24)	33.34	45.83	41.67	33.33
Olanzapine (n=17)	23.53	29.41	23.55	17.66
Quetiapine (n=12)	16.66	16.67	16.67	8.34
Aripiprazole (n=13)	7.69	15.38	15.38	7.69
Risperidone, Haloperidol and Olanzapine collectively (Group 1) (n=66)	31.82	42.42	37.88	28.79
Quetiapine and Aripiprazole collectively (Group 2) (n=25)	12	16	16	8
***p*-values comparing Group 1 and 2**	p=0.055	p=0.018*	p=0.04*	p=0.03*

*Significant

DISCUSSION

Sexual dysfunction has been a side-effect of various antipsychotic medications in majority of patients and is one of the causes of poor quality of life.[1,12]

Majority of the patients (n=69) during the present study were suffering from Chronic schizophrenia (75.82%) whereas 22 patients had underlying Bipolar affective disorder (24.18%). These figures are almost in semblance with the figures of 74% and 26% reported by Khawaja[10] and slightly higher than the figures (71%) reported by Montejo *et al*.[13]

Overall the prevalence of impairment in one or more domains of sexual functioning was 35.17% in the present study which is exactly in line with the figures (35.5%) reported by Park *et al*[14] and slightly lower than the range of 40–71% reported in literature[2], whereas the percentage of sexual dysfunction associated with risperidone, haloperidol and olanzapine collectively (Group-1) was 42.43% which is in close proximity with figures of 40.40%, 40–60% and 45% reported by Oyekanmi *et al*[15], Serretti *et al*[16] and Smith *et al*[17] respectively. However sexual dysfunction associated with quetiapine and aripiprazole (Group-2) was comparatively lower (16%) which falls within the range of 16–27% as reported by Serretti *et al*.[16] These results reflect that patients on risperidone, haloperidol or olanzapine are more prone to have sexual dysfunction as

compared to the patients taking quetiapine or aripiprazole.

Frequently reported sexual problems by the patients consuming risperidone, haloperidol and olanzapine are declines in libido or arousal, erectile dysfunction, abnormal ejaculations and problems in achieving or maintaining orgasm.[8,9] Erectile and ejaculatory dysfunction were the main problems encountered by our patients. Patients (42.42%) taking monotherapy with risperidone, haloperidol and olanzapine group of drugs suffered from erectile dysfunction falling exactly in line with the figures (42%) reported by Nagaraj, *et al*[18] and in proximity with the figures (48%) reported by Khawaja.[10] However our figure is higher than figures of 34.5% and 32% reported by Oyekanmi *et al*[15] and Knegtering *et al*[19] respectively.

In our study 37.88% of patients on risperidone, haloperidol and olanzapine group had ejaculatory dysfunction, a figure falling in between the figures of 46% and 32% as reported by Khawaja[10] and Knegtering *et al*[19] respectively. However 31.82% and 28.79% of our patients had reduced libido and impaired orgasm respectively which is clearly higher than the figures of 17.1% and 18.5% as reported by Oyekanmi *et al*[15] and 8% and 14% as reported by Khawaja[10] respectively.

Risperidone was overall the most notorious drug (48%) to be associated with sexual dysfunction in our patients which is in agreement with the facts reported globally.[5–7] However our percentage is lower as compared to the figures of 55% and 86% reported by Shah[4] and Sathish Kumar *et al*[12] respectively.

Diminished libido as a result to risperidone intake was reported by 36% of patients which is almost in semblance with the figures (37.8% and 35.5%) reported by Bobesk *et al*[20] and Bitter *et al*[21] respectively and clearly lower than the percentage reported (64%) by Wirshing *et al*.[22]

Erectile dysfunction was the most prominent problem reported by 48% of our patients consuming risperidone which is higher than the figures of 32.1%, 31.6% and 40% recorded by Bobes *et al*[20], Knegtering *et al*[23] and Wirshing *et al*[22] respectively.

Ejaculatory dysfunction was reported by 44% of our patients on risperidone which is in between the figures of 32.6% and 86% reported by Bobes *et al*[20] and Wirshing *et al*[22] respectively.

Orgasmic dysfunction was present in 32% of patients taking risperidone which is exactly similar to the figures (32%) reported by Nagaraj *et al*[24]. However our percentage is clearly lower than the percentage reported (86%) by Wirshing *et al*[22].

Haloperidol was the next frequent drug after risperidone leading to sexual dysfunction in our patients as 45.84% of those on haloperidol had sexual impairment, a fact which is in agreement with the worldwide literature.[5,6,15]

Haloperidol caused decreased libido in 33.34% of our patients which is almost corresponding to 30.8% as reported by Bobes *et al*[20] and lower than the figures (38.7%) reported by Bitter *et al*[21]. Erectile dysfunction was present in 45.83% of our patients which is in-between the figures of 30.8% and 50% reported by Bobes *et al*[20], and Bitter *et al*[21] respectively. However ejaculatory dysfunction was reported in 33.33% of our patients, which is slightly higher than the figure of 27.7% recorded by Bobes *et al*[20] and lower than the figure of 50% recorded by Wirshing *et al*[22].

Olanzapine was next to follow as 29.41% of patients consuming it had sexual dysfunction which is lesser in comparison to risperidone and haloperidol a fact in line with the findings recorded during global research.[5,6,9] However our figures are lower in comparison to the figures (48.3%) reported by Sathish Kumar *et al*[12] and (40–60%) reported by Serretti *et al*[16]. Schmidt *et al*[8] found that switching to olanzapine may rather improve sexual functioning in affected patients.

In our study 23.3% of patients taking olanzapine suffered from diminished libido which is higher than the percentages of 17.8% and 0% reported by Bitter *et al*[21] and Knegtering *et al*[23] respectively.

Ejaculatory dysfunction was reported by 23.55% of patients which is in proximity with results (27%) reported by Nagaraj *et al*[24]. However, orgasmic dysfunction recorded in our study was 17.66% which is lower than that reported by Nagaraj *et al*[24]. Therefore olanzapine looks safer contrary to risperidone and haloperidol with comparatively lesser incidence of sexual side-effects.

Our patients using quetiapine had a remarkably lower percentage (16.67%) of sexual adverse effects as compared to risperidone, haloperidol, and olanzapine. These findings are almost analogous to the findings (16–27%) recorded by Serretti *et al*[16] and Nakonezny *et al*[25], whereas in close proximity with 18.2% as reported by Bobes *et al*[20]. Byerly *et al*[26] found that quetiapine was rather associated with clinically and statistically significant improvement in ASEX total scores after patients were shifted to quetiapine from risperidone and haloperidol. Quetiapine was associated with comparatively lesser degree of diminished libido (16.66%) contrary to risperidone, haloperidol, and olanzapine which is lower in comparison to the figures reported (31.8%) by Atmaca *et al*[27].

A considerably lower percentage (8.34%) revealed orgasmic impairment which reflects that patients on quetiapine have better orgasmic function in comparison to risperidone, haloperidol, and olanzapine which is in agreement with the findings of Kelly *et al*[28].

Considerably lower percentage (15.38%) of our patients using aripiprazole suffered from sexual

dysfunction almost corresponding to the results (14.3%) reported by Shah[7] and others[9,10,13]. Jeong *et al*[29] found that sexual dysfunction in schizophrenia patients rather improved after switching to aripiprazole from other atypical antipsychotics.

The findings of our study are mostly in agreement with the previous work. However, disparity at a few points in the present study could be attributed to the differences in factors such as dose and duration of treatment, differing psychosocial backgrounds, genetic variation among races, and probable patient-related errors in answering the questionnaire.

CONCLUSIONS

Risperidone and haloperidol are associated with a higher rate of sexual dysfunction as compared to olanzapine whereas the newer generation drugs including quetiapine and aripiprazole have a significantly lower profile of adverse effects.

LIMITATIONS

Following were the limitations of the present study:

1. The reliability and authenticity of the information gathered by questionnaires might be jeopardized by reporting errors, incomplete reminiscence, misapprehension of the relevant questions, feeling of embarrassment, selective involvement by the patients and interviewer's prejudice.
2. Any difference in sexual dysfunction due to higher and lower doses of each drug has not been compared here. However, such a comparison may yield useful inferences.
3. Sample size was comparatively smaller in our study. Larger sample could produce more accurate conclusion.

RECOMMENDATIONS

Further studies are needed, investigating the effects of dosage reduction, drug-free days, symptomatic therapy, risk factor alteration, shifting the antipsychotic medications and addition of other agents, thus leading us towards more effective and safe solutions.

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