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Original Research Article

A Comparative Study of Sexual Dysfunction Associated With Typical and Atypical Anti-Psychotics in Outdoor Patients

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ABSTRACT

Background: Antipsychotics are a class of drugs used to treat a variety of mental health problems, including schizophrenia, bipolar disorder and severe depression. The advent of the newer 'atypical' antipsychotic medications has revolutionized the pharmacological treatment of these disorders. Antipsychotic can cause various side effects and one of the distressing side effect people may experience with antipsychotics is a problem of sexual dysfunction. Sexual dysfunction which can result from the use of antipsychotics over prolonged time causes a decline in their quality of life and medication acceptance. Dopamine antagonism, increased serum prolactin, serotonergic, adrenergic and cholinergic mechanism are all proposed to be the mechanisms of sexual dysfunction.

Materials and Methods: The total sample size was 120 patients divided into 6 groups of 20 patients each on Olanzapine, Risperidone, Trifluperazine, Haloperidol, Quetiapine and Pimozide over three months. Sexual dysfunction was assessed in outpatients on antipsychotics using Arizona Sexual Experience Scale (ASEX) and using prolactin as a biochemical marker. To analyse the sexual dysfunction, the mean scores on all the domains of sexual functional questionnaire (SFQ) were compared across the study groups by using chi-square test for proportion. Relation between ASEX score and prolactin were assessed by Spearman's rank order partial correlation and prolactin levels before and after drug intake by students t-test.

Results: Among drugs, correlation between ASEX score and prolactin was highest for trifluperazine group (0.726) and lowest for quetiapine group (0.123) while risperidone caused highest change changes in prolactin levels ($p = 0.000$) and quetiapine caused least ($p = 0.020$). Among domains desire and erection were most commonly impaired. Desire was most impaired in risperidone group (60%) while erectile dysfunction in olanzapine group (75%). However statistically, the parameter most effected was erectile domain ($p = 0.005$).

Conclusion: Trifluperazine, Haloperidol showed a higher risk of sexual dysfunction than risperidone. Quetiapine showed a lowest risk of sexual dysfunction during treatment period.

Key Words: Schizophrenia, sexual dysfunction, antipsychotics, ASEX, erectile dysfunction.

INTRODUCTION

Psychosis is a symptom of mental illness characterized by a distorted or non-existent sense of reality with major disturbances in reasoning often with delusions and hallucination. [1] The antipsychotic drugs or major tranquilizers are chemically diverse but posses the common property of alleviating the symptoms of both functional and organic psychosis. [2] They are effective not only in the acute phase of psychotic disorders but also as a maintenance therapy, to reduce the risk of relapse and interact with multiple neurotransmitter systems. Whereas the therapeutic effects of these drugs are believed to result from competitive blockage of dopamine receptors and serotonin (5HT) receptors, the adverse effects are attributed to blockage of variety of receptors like blockage of alpha1adrenergic receptors, dopamine D_2 receptors, dopamine D_4 receptors, histamine H_1 receptors, muscarinic receptors and serotonin $5HT_2$ receptors. Typical antipsychotic drugs have an equal or greater affinity for D_2 receptors than for $5HT_2$ receptors. [3]

Adverse effects often are extensions of many pharmacological actions of these drugs. The most important are those on the cardiovascular, central and autonomic nervous and endocrine systems. [1, 4] Endocrine changes occur because of effects of antipsychotic drugs on the hypothalamus or pituitary, including their antidopaminergic action. [5] The hyperprolactinemic activity is presumed to be responsible for breast engorgement and galactorrhea that occasionally are associated with their use, sometimes even in male patients given high dose of neuroleptics. Perhaps due to effects of hyperprolactinemia, some antipsychotic drugs reduce the secretion of gonadotropins and sex steroids, which can cause amenorrhea in women and sexual dysfunction or infertility in man. [6] Patients often refuse to take their medication on a regular basis because of unacceptable sexual effects and sexual function is often sacrificed "for the sake of sanity" in psychotic disorders. [7]

Objectives

1. To compare and evaluate the frequency of sexual dysfunction associated with typical and atypical antipsychotics in outdoor patients.
2. To assess the frequency of sexual dysfunction in a sample of out patients with schizophrenia and schizo-affective disorders under antipsychotic therapy.
3. An attempt to identify the least sexually adverse antipsychotic drug among the groups.

METHODS

After approval from board of studies and institutional ethics committee, the study was conducted in the Department of Pharmacology in association with Department of Psychiatry, Govt. Medical College, Srinagar with average monthly attendance of about 3000 patients from April 2011 to October 2011.

Patient Selection

Patients receiving antipsychotics and diagnosed with Schizophrenia and other psychiatric ailments according to diagnostic and statistical manual of mental disorders (DSM-IV, American Psychiatric Association, 1994) criteria were included. [8]

It was a prospective, comparative study on 120 patients comprising 20 patients in each group. Six classes of antipsychotics (three typical and three atypical) were included in the study. An informed consent was taken from the patients found fit for the study. At present there are three scale available to assess sexual dysfunction in patients under antipsychotic treatment and among them ASEX is preferred. [9] The

ASEX was developed for Mc Gahuey et al. in the University of Arizona in response to the need for evaluating psychotropic drug induced sexual dysfunction. The ASEX can be completed in approximately 5 minutes.[10] And it was designed to be self or clinician administrated. In addition, ASEX questionnaire can be used for heterosexual and homosexual population as well for those without sexual partners.

ARIZONA SEXUAL EXPERIENCE SCALE (ASEX)
Ref. McGahuey et al. J Sex Marital Ther 2000; 26: 25-40

Sexual drive, arousal, penile erection /vaginal lubrication, ability to reach orgasm and satisfaction with orgasm over the past week. Items are rated on a 6 point scale ranging from 1 (hyperfunction) through to 6 (hypofunction), providing a total score range between 5 to 30. A total score > 18 or a score of ≥5 (very difficult) on any single item or any three items with individual scores ≥ 4 is indicative of clinically significant sexual dysfunction

1 How strong is your sex drive?
(a) Extremely strong; (b) Very Strong; (c) Somewhat strong;
(d) Somewhat weak; (e) Very weak; (f) Absent

2. How easily are you sexually aroused?
(a) Extremely easily; (b) Very easily; (c) Somewhat easily
(d) Somewhat difficult; (e) Very difficult; (f) Never

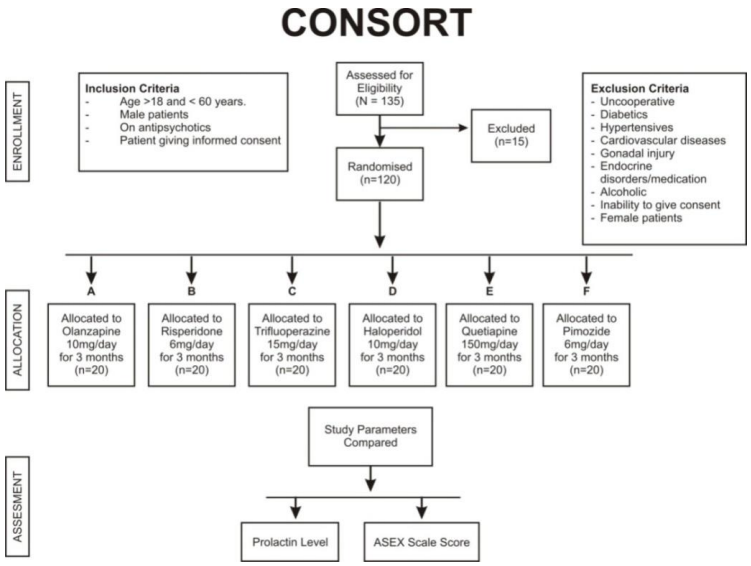
3a. Can you easily get and keep an erection?
(a) Extremely easily; (b) Very easily; (c) Somewhat easily
(d) Somewhat difficult; (e) Very difficult; (f) Never

3b. How easily does your vagina become moist?
(a) Extremely easily; (b) Very easily; (c) Somewhat easily
(d) Somewhat difficult; (e) Very difficult; (e) Never

4. How easily can you reach orgasme?
(a) Extremely easily; (b) Very easily; (c) Somewhat easily
(d) Somewhat difficult; (e) Very difficult; (f) Never

5. Are your orgasms satisfying
(a) Extremely satisfying; (b) Very satisfying; (c) Somewhat satisfying
(d) Somewhat unsatisfying;(e) Extremely unsatisfying;(f)Never achieve orgasme

Scoring for sexual dysfunction was done by ASEX after 3 months of treatment. The biochemical marker used for assessing sexual dysfunction was serum prolactin estimated before and after completion of 3 months using ELISA.



Statistical Methods

Data was expressed as mean ± standard deviation and percentage. The intergroup comparison of the parametric data was done by Student's 't' test and Analysis of Variance (ANOVA). P value < 0.05 was considered significant. The software used was Statistical Package for Social Sciences (SPSS) and Microsoft Excel. Change in prolactin levels before and after completing three months of antipsychotic therapy was done by Students 't' test. Correlation between final prolactin levels and ASEX score was done by using Spearman's correlation coefficient with r = 0.8 and above indicating high correlation coefficient, r = 0.5 (around) → moderate correlation, r = 0.3 → low correlation coefficient and r = 0.0 → absolutely no correlation while as statistical analysis of ASEX score of treatment groups was done by ANOVA.

RESULTS

Total number of sexual dysfunction patients as per scoring using ASEX scale were 41 in all (Table 1).

Table – 1: Distribution of Effected Parameters (Dsyfunction = 41)

Parameter	O	R	T	H	Q	P
Sexual desire dysfunction	3	5	5	4	1	2
Arousal dysfunction	0	0	0	0	0	0
Erectile dysfunction	4	2	2	2	1	1
Orgasmic dysfunction	0	0	0	0	0	0
Overall satisfaction dysfunction	0	2	2	2	1	2
Total	7	9	9	8	3	5

O = Olanzapine; R = Risperidone; T = Trifluperazine; H = Haloperidol;
Q = Quetiapine; P = Pimozide

Highest number of cases of dysfunction patients were 11 (32.35%) each in the age group of 31-40 and 51-60 years. 10 (29.4%) patients were in the age group of 41-50 years while as only 9 (31.0%) patients were in the age group of 20-30 years. Highest number of effected patients were in trifluoperazine group [(9)] followed by haloperidol [(8)] in typical. Among atypical highest number was in risperidone group [(9)] followed by olanzapine. [(7)] While as least patients [(3)] of dysfunction patients were in quetiapine group. Overall parameter most effected was desire (equal in trifluoperazine and risperidone) while as erectile dysfunction was highest in olanzapine group (Table 2).

Table – 2. Statistical Analysis of the ASEX Score of Treatment Groups

Study Group	Mean±SD	P-Value
Olanzapine	11.75±4.29	0.006 (Significant)
Risperidone	13.00±5.36	
Trifluoperazine	15.3±3.81	
Haloperidol	16.3±4.45	
Quetiapine	15.1±2.5	
Pimozide	14.5±2.82	

Among atypical antipsychotics highest changes in prolactin levels were seen in risperidone group (p = 0.001) while as quetiapine caused least changes in the prolactin levels (p = 0.06). While as in typical antipsychotic group highest changes in prolactin levels were seen in trifluoperazine (p = 0.005) while as the least changes were seen in the pimozide (p = 0.015). Correlation coefficient between ASEX score of group I and final prolactin levels was 0.496 in case of olanzapine, 0.549 in risperidone, 0.727 in trifluoperazine, 0.679 in haloperidol, 0.502 in pimozine and 0.339 in quetiapine (Table 3).

Table – 3. Change in Prolactin Levels Before and After Treatment in Six Groups

Variable	N	Mean±SD	P-Value
OLANZAPINE			
I-PL1	20.000	10.760±3.35	0.024 (Significant)
F-PL1	20.000	16.670±12.46	
RISPERIDONE			
I-PL2	20.000	11.71±2.96	0.001 (Significant)
F-PL2	20.000	19.87±8.14	
TRIFLUOPERAZINE			
I-PL3	20.000	13.54±3.38	0.005 (Significant)
F-PL3	20.000	21.88±11.02	
HALOPERIDOL			
I-PL4	20.000	11.62±2.68	0.006 (Significant)
F-PL4	20.000	25.33±20.95	
QUETIAPINE			
I-PL5	20.000	12.16±3.13	0.06 (Non-Significant)
F-PL5	20.000	14.07±4.22	
PIMOZIDE			
I-PL6	20.000	12.09±3.04	0.015 (Significant)
F-PL6	20.000	16.61±7.94	

DISCUSSION

Sexual and reproductive function side effects of antipsychotics are frequent, often under-estimated and badly tolerated. It effects self-esteem, causes trouble for their sexual partners, interferes with their quality of life and compromises treatment compliance. [11-15] Patients themselves report that the sexual side effects of medication are distressing. [16] Men may perceive sexual dysfunction as more distressing than women [17] and can be a significant reason for non-adherence to prescribed antipsychotic treatment. [18-21]

The objectives of our study were to assess the frequency of sexual dysfunction and to identify the least sexually adverse antipsychotic drug. In the present comparative study 135 male patients were enrolled. A majority of patients had received the diagnosis of schizophrenia 80 (66.66%), followed by bipolar disorders 20 (16.67%), depression with psychotic features 14 (11.67%) and miscellaneous (psychosis, anxiety neurosis) constituted only 6 (5%). All patients had at least two weeks drug-free period before the drug study was started. The total number of patients was 120 divided into six groups of 20 each by using simple random sampling. The mean age of patients was 35.8±9.62 in olanzapine group, 40.7±7.7 in risperidone group, 39.7±9.92 in trifluoperazine, 39.45±10.52 in haloperidol, 44.2±8.90 in quetiapine group and

40.4±10.19 in pimozide group with p value of 0.166 which is statistically insignificant.

The highest percentage (28.3%) of study population was in the age group of 41-50 years, and (28.3%) were in the age group of 31-40 years. 28.33 of patients were non-smokers, 14.7% were ex-smokers 19.17% were smokers. Literates constituted 63.34% with majority of them educated upto secondary school (85%), illiterates constituted 36.66%. Most of the people were from rural areas constituting 69.16% and 30.84% were from urban areas. Most of the study subjects were unemployee (33.34%), skilled workers (25.00%), shopkeepers (19.16%), farmers (16.66%) and government employee constituted the rest (5.84%). Muslims constituted 91.67% of patients, others being Hindus (4.16%), Sikhs (2.5%) and Buddhist (1.67%). A majority of them had received the diagnosis of schizophrenia (mostly paranoid), other having diagnosis of bipolar disorders (16.67%), depression with psychotic features (11.67%) and miscellaneous (psychosis and anxiety neurosis) constituted 5.0%

There are various aspects that make assessment of sexual dysfunction related to psychotropic drugs difficult. These include the potential biases associated with

a. Patient selection (the study may include a greater number of patients who pay more attention to sexual matter and who are more willing to report on such matter)
b. The assessment procedure used (self report, questionnaire or direct questioning)
c. The type of measurement used (objective versus subjective) measurements.
d. The gender differences in the assessment.
e. The lack of baseline assessment. [(22)]

An added difficulty is the differentiation between the effects of psychopathology and its course and the effect of psychotropic medication. [(23)] The best way of finding whether antipsychotic medication has a negative effect on sexual function is to compare subjects before and after they start medication. However, drug free patients are too unwell to answer intimate questions about sexual functioning. In this study ASEX is in English, questions had to be translated and explained to the responders in local language. The advantage of this approach is that responders were able to understand any points they do not within the questionnaires. However the disadvantage of this method is responders don't have privacy, which they would have in questionnaire. This leads to embarrassment during interview, some interviewer's bias and responders may be less honest in answering such questions. However in the current circumstances this was the best possible option.

CONCLUSION

- Atypical antipsycotics are not as a group much better than typical antipsychotics and among them, risperidone seems to induce more and quetiapine less sexual dysfunction.
- Quetiapine does appear to significantly improve this profile in short term treatment, however, long term and larger sample studies are required to systematically evaluate this profile and confirm our results.
- An attempt should also be made to compare individual drugs at higher versus lower

doses. Also higher the sample size, better the inference. Procedures like nocturnal penile tumescence or penile plethysmography should be used which can rule out any organic sexual disorder.

- Elevated prolactin levels along with low estrogen levels have been associated with increase in blood pressure and cardiovascular diseases and associated with osteoporosis, cancers of breast and endometrium.

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