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Sexual Dysfunction with Risperidone in Male and Female Patients of Schizophrenia

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Abstract

Background: *Sexual side-effects due to use of Antipsychotic drugs have become one of the most important determinants of treatment compliance. Studies regarding sexual side-effects associated with antipsychotics comprise only a handful in the Indian population, especially so in this north-eastern part of the country.*

Aims and Objectives

1. *To assess the sexual dysfunction associated with Risperidone in male and female patients of Schizophrenia.*
2. *To compare the sexual dysfunction associated with Risperidone between male and female patients of Schizophrenia.*

Materials and Methods: *This was a hospital based comparative study conducted on 50 clinically stable male and female patients of Schizophrenia on **Risperidone** only. A Sexual Functioning Questionnaire (SFQ) was administered after assessing the clinical stabilities with the Brief Psychiatric Rating Scale (BPRS). Sexual dysfunction was assessed by calculating the mean scores on all the domains of sexual functioning in SFQ which were then compared across the study groups using the Chi square test . The results were analysed using SPSS Version 16.0 setting the significance threshold at **p <0.05**.*

Results: *From this study, we inferred that with **Risperidone**, impairment is seen in desire disorders **(12%),** arousal disorders **(14%)**, orgasmic difficulties **(26%)** and overall sexual dysfunction **(20%)** although not statistically significant. It was also found that in females, Risperidone caused more desire disorders, more arousal disorders and a more overall sexual dysfunction; whereas in case of males, Risperidone caused more arousal disorders, more orgasmic difficulties, more sex related pain problems and a more overall sexual dysfunction;*

Conclusion: *Sexual dysfunction is an important side-effect of Antipsychotic drugs. So clinicians should try to address these side-effects to help patients' attain a better compliance.*

Introduction

Sexual function is an important determinant of one's quality of life. WHO defines *sexual health* as "integration of physical, emotional, intellectual & social aspects of sexual being in ways that are positively enriching & that enhance personality, communication & love. Every person has a right to receive sexual information & to consider sexual relationship for pleasure as well as for procreation."(WHO Technical Report, Series 572).[1] According to Aizenberg et al 1995,Marques et al 2012, Fujii et al 2010, Malik et al 2011, sexual dysfunction in patients with schizophrenia may be actually due to the disease process itself (example negative symptoms), physical health or use of psychotropic medications.[2,3,4],

According to ICD 10, the schizophrenic disorders are characterized in general by fundamental and characteristic distortions of thinking and perception, and by inappropriate or blunted affect. Clear consciousness and intellectual capacity are usually maintained, although certain cognitive deficits may evolve in the course of time. The normal requirement for a diagnosis of schizophrenia is a minimum of one very clear symptom (and usually two or more if less clear-cut) belonging to any one of the groups listed as (a) to (d) below, or symptoms from at least two of the groups referred to as (e) to (h), should have been clearly present for most of the time during a period of 1 month or more. [5]

a) Thought echo, thought insertion or withdrawal, and thought broadcasting;
b) Delusions of control, influence, or passivity, clearly referred to body or limb movements or specific thoughts, actions, or sensations;delusional perception;
c) Hallucinatory voices giving a running commentary on the patient's behaviour, or discussing the patient among themselves, or other types of hallucinatory voices coming from some part of the body;
d) Persistent delusions of other kinds that are culturally inappropriate and completely impossible, such as religious or political identity, or superhuman powers and abilities (e.g. being able to control the weather, or being in communication with aliens from another world);
e) Persistent hallucinations in any modality, when accompanied either by fleeting or half-formed delusions without clear affective content, or by persistent over-valued ideas, or when occurring every day for weeks or months on end;
f) Breaks or interpolations in the train of thought, resulting in incoherence or irrelevant speech, or neologisms;
g) Catatonic behaviour, such as excitement, posturing, or waxy flexibility, negativism, mutism, and stupor;
h) "Negative" symptoms such as marked apathy, paucity of speech, and blunting or incongruity of emotional responses, usually resulting in social withdrawal and lowering of social performance; it must be clear that these are not due to depression or to neuroleptic medication;
i) A significant and consistent change in the overall quality of some aspects of personal behaviour, manifest as loss of interest, aimlessness, idleness, a self-absorbed attitude, and social withdrawal.

Baggaley et al in 2008 found that risperidone induces sexual dysfunction most frequently followed by haloperidol, olanzapine, quetiapine & least by aripiprazole.[6] Knegtering et al 2003, 2004, 2006, 2008 & Boer et al 2011 also found a comparable order, in the following ascending array- risperidone, haloperidol, olanzapine, quetiapine & aripiprazole.[7,8,9,10,11]

Risperidone is a benzisoxale with a half life of 20 hours. Risperidone is an antagonist at serotonin 5HT 2a, dopamine D2, alpha-1 and alpha-2 adrenergic and histamine H_1 receptors[12]

Around half of all patients treated with

antipsychotics experience sexual dysfunction; the associated distress and frustration may have a profound effect on the quality of life of the patient as well as making personal relationships more difficult, and sexual dysfunction may lead to non-compliance with the antipsychotic treatment regimen.[13]. Finn et al (1990) showed that patients are more concerned with the sexual side-effects of their medications than any other side-effect.[14] Structured interviews reveal 30 to 60% of sexual side effects associated with antipsychotic treatment (Knegtering 2008 & 2003).[8,9,]

According to the current classification established by the American Psychiatric Association, disorders of sexual function are divided into 4 categories:

1) Disorders of sexual desire,
2) Disorders of arousal,
3) Disorders of orgasm,
4) Sexual pain disorders (American Psychiatric Association 1994).

Serrati & Chiesa 2011 reported 12 to 38% decrease in desire with antipsychotics. Knegtering et al 2008, Boer et al 2011 found 6 to 50% reduction in sexual desire with the use of antipsychotic medications. Aizenberg et al 1995 reported a diminution in sexual desire in patients using antipsychotics that in those not using antipsychotics.[2,8,16] Patients being treated with antipsychotics often report being less easily sexually aroused (Aizenberg et al 1995).[2]

The meta-analysis of Serrati & Chiesa 2011 shows that 7 to 46% of patients using antipsychotics experience dysfunction of arousal like erection & lubrication and 4 to 49% of patients experience orgasmic dysfunction. Knegtering et al 2008, Boer et al 2011 reported 0 to 39% for the same. [8,11,16] Knegtering et al 2008, Serrati & Chiesa 2011 reported a decrease in vaginal lubrication with the use of antipsychotic drugs.[8,16]Another study done by Knegtering et al 2008, Boer et al 2011 revealed 3 to 46% (46% for risperidone) of orgasmic disturbances with antipsychotic use. Ghadirian et al in 1982 also reported a disturbance in quality of orgasm with use of antipsychotic medications.[17] Pain during orgasm with the use of antipsychotic drugs was reported by Ghadirian et al 1982 whereas Berger et al in 1979 and Donnellan et al in 2001 reported painful ejaculation in patients using antipsychotics.[17,18,29]

Rated on a sexual functioning questionnaire developed by Burke et al.(1994), the majority of risperidone (71%) and haloperidol / fluphenazine (61%) treated subjects but less of clozapine (40%) treated subjects reported overall worsening of sexual functioning including desire, erection and orgasm.[23]

Bobes and colleagues cross-sectionally studied sexual dysfunction with risperidone, olanzapine, quetiapine and haloperidol among 636 patients of schizophrenia. Frequency of sexual dysfunction was 38% with haloperidol, 35.3% with olanzapine, 43.2% with risperidone and 18.2% with quetiapine.[24]. Knegtering and associates studied 49 patients of schizophrenia and other psychotic disorders for sexual dysfunction due to quetiapine (200-1200 mg/day) (n=25) and risperidone (1-6 mg/day) (n=24) in a randomized open label study. 16% of those on quetiapine reported sexual dysfunction as compared to 50% on risperidone thus concluding that sexual dysfunction is significantly less common in quetiapine than risperidone.[9,10]

Most antipsychotics are potent dopamine blockers leading to sustained elevation of prolactin (Knegtering et al 2008,Ghadirian et al 1982)[8,17] and this increase in prolactin inhibits tuberoinfundibular dopaminergic neurons leading to sexual disturbances (Fitzgerald and Dinan 2008).[19]

Studies have also revealed significant contribution of dopaminergic, adrenergic, serotonergic and cholinergic actions of antipsychotics for sexual dysfunction. [20] In fact a recent study has reported that the mostly responsible mechanism of sexual dysfunction is the direct consequence of dopamine antagonism.[21]

Risperidone causes greater degree of prolactin

elevation, olanzapine has only marginal effect and quetiapine has no effect on prolactin elevation.[30] A number of studies on antipsychotic induced sexual dysfunction have incorporated the procedure of measurement of prolactin level. Almost all of them have found a positive correlation between hyperprolactinemia and sexual dysfunction. [21,30,31] . Risperidone seems to be the antipsychotic associated with a greater risk of sexual dysfunction. Reduced libido, erectile dysfunction, ejaculatory difficulties, impaired orgasm were noted in men whereas amenorrhoea, decreased libido, impaired orgasm, decreased vaginal lubrication were noted in women. Antipsychotics with strong α1- and α2-antagonistic properties seem to induce priapism most frequently. Risperidone has a high affinity, followed by clozapine and quetiapine[21,30,31].

In a study done by Nagaraj and his associates it was reported that desire was most commonly impaired in the risperidone group (80%) as compared to 72% in the quetiapine group and 78% in the olanzapine group. Erectile dysfunction was most common in the olanzapine group (50%). It was 40% in the risperidone group and 36% in the quetiapine group. However, it was not statistically significant. Orgasmic dysfunction was equally common to both the risperidone and quetiapine (32%) groups and 27% in the olanzapine group. [26]

Aims and Objectives

1. To assess the sexual dysfunction associated with Risperidone in male and female patients of Schizophrenia.
2. To compare the sexual dysfunction associated with Risperidone between male and female patients of Schizophrenia.

Methods and Materials

This was a hospital based comparative study carried out in a tertiary medical institution located in the upper part of Assam, India. The study duration was one year (August 2016-July 2017). The study received the ethical approval from the institutional review board. An informed written consent was obtained from every participant and they were free to withdraw their consent at any point of time. The total sample size was 50 (30 males and 20 females). The cases were selected from patients, attending the outpatient department or admitted in the institution between August 2016 and July 2017, who were diagnosed as **Schizophrenia (as per ICD 10)** and were on **Risperidone** tablets only, who fulfilled the inclusion and exclusion criteria and gave an informed written consent for participating in the study. The diagnosis was confirmed by Consultant Psychiatrists of the same institution.

Inclusion Criteria

- Patients of age group between 18 to 56 years.
- Patients of both the genders.
- Patients who give consent for the study.

Exclusion Criteria

- Patients with other comorbid medical illnesses like diabetes mellitus, hypertension, cardiovascular diseases, endocrine disorders.
- Patients with other comorbid psychiatric illness.
- Patients using alcohol or any other substances.
- Post-menopausal females
- Patients on more than one antipsychotic drug or other drugs that affect sexual functioning like antidepressants are not included. (But Trihexiphenidyl was allowed in the patients).

Assessment Tools –

- Informed consent form
- The ICD-10 classification of Mental and Behavioural disorders
- Kuppuswamy's Socio-economic Status Scale (Modified version 2014)
- Semi-Structured Proforma
- Brief Psychiatric Rating Scale (BPRS)
- Sexual Functioning Questionnaire (SFQ)

- Statistical Program for Social Sciences (SPSS) windows version 16.0

Procedure

All patients in the age group of 18 -56 years who attended the outpatient department or who were admitted in the Department of Psychiatry, AMCH within the time period of August 2016 to July 2017, and diagnosed as Schizophrenia as per ICD-10, confirmed by the Consultant Psychiatrists of the Department, maintaining well on tablets **Risperidone only,** for at least 6 weeks were taken. Every consecutive case who attended or who was admitted in the study period was selected till the total sample size was reached. A written informed consent was taken from each participant. They were free to withdraw their consent at any given point of time. A socio-demographic data of each patient was tabulated in the demographic sheet by interview method. After this, clinical stabilities of the patients were assessed with the Brief Psychiatric Rating Scale (BPRS) following which a Sexual Functioning Questionnaire (SFQ) was provided to every patient. Analysis of the observed data was done using tests like **Chi square test and unpaired t-test** in SPSS windows version 16.0. The significance threshold for the tests were set at **p<0.05**.

Results and Observations

Table 1: Distribution of Cases on Risperidone on the basis of age

AGE IN YEARS	CASES ON RISPERIDONE	
	N	%
18-30	26	52
31-43	15	30
44-56	9	18

It is seen from the above table that cases were mainly in the age group of 18 to 30 years.

Table.2: Mean age distribution of cases on Risperidone

	CASES ON RISPERIDONE	
	MEAN±SD	RANGE
AGE IN YEARS	32.04±10.776	18-56

Table.3: Distribution of cases on Risperidone according to sex

SEX	CASES ON RISPERIDONE	
	N	%
MALE	30	60
FEMALE	20	40

Table 4: Comparison of sexual desire in cases on Risperidone between males and females

SFQ SCORE FOR DESIRE DISORDERS		NORMAL(N)(%)	ELEVATED(N)(%)	p-value
RISPERIDONE	Male	28 (93%)	2 (7%)	0.202
	Female	16 (80%)	4 (20%)	

*SFQ- Sexual functioning questionnaire *p-value significant at <0.05

It was seen that with Risperidone, 4 out of 20 females and 2 out of 30 males are affected. On applying chi-square test the p value is found to be 0.202 which denotes that there is no significant statistical difference in sexual desire among males and females.

Table 5: Comparison of sexual arousal in cases on Risperidone between males and females

SFQ SCORE FOR AROUSAL DISORDERS		NORMAL(N)(%)	ELEVATED(N)(%)	p-value
RISPERIDONE	Male	25 (83%)	5 (17%)	0.687
	Female	18 (90%)	2 (20%)	

*SFQ- Sexual functioning questionnaire *p-value significant at <0.05

From the above table it is seen that with Risperidone, 2 out of 20 females and 5 out of 30 males are affected. On applying chi-square test the p value is found to be 0.687 which denotes that there is no significant statistical difference in sexual arousal among males and females.

Table 6: Comparison of orgasmic difficulties in cases on Risperidone between males and females

SFQ SCORE FOR ORGASMIC DISORDERS		NORMAL(N)(%)	ELEVATED(N)(%)	p-value
RISPERIDONE	Male	19 (63%)	11 (37%)	0.050
	Female	18 (90%)	2 (10%)	

*SFQ- Sexual functioning questionnaire *p-value significant at <0.05

We can see that 2 out of 20 females and 11 out of 30 males are affected. On applying chi-square test the p value is found to be 0.050 for Risperidone which denotes that there is no significant statistical difference in orgasmic difficulties among males and females.

Table 7: Comparison of sex related pain disorders in cases on Risperidone between males and females

SFQ SCORE FOR PAIN DISORDERS		NORMAL(N)(%)	ELEVATED(N)(%)	p-value
RISPERIDONE	Male	29 (97%)	1 (3%)	0.556
	Female	18 (90%)	2 (10%)	

*SFQ- Sexual functioning questionnaire *p-value significant at <0.05

We can see that 2 out of 20 females and 1 out of 30 males are affected. On applying chi-square test the p value is found to be 0.556 which denotes that there is a significant statistical difference in sex related pain disorders among males and females.

Table 8: Comparison of overall sexual dysfunction in cases on Risperidone between males and females

SFQ SCORE FOR OVERALL SEXUAL DYSFUNCTION		NORMAL(N)(%)	ELEVATED(N)(%)	p-value
RISPERIDONE	Male	22 (73%)	8 (27%)	0.279
	Female	18 (90%)	2 (10%)	

*SFQ- Sexual functioning questionnaire *p-value significant at <0.05

We can see that 2 out of 20 females and 8 out of 30 males are affected. On applying chi-square test the p value is found to be 0.279 which denotes that there is no significant statistical difference in overall sexual disorders among males and females between the groups.

Discussion

Most of the subjects in the group belonged to the age group 18-30 years. The mean age was **32.04±10.776** years. There was no significant difference between the mean ages. Majority of subjects were males (**60%**). There was no significant difference when it comes to distribution of subjects in both the groups on the basis of gender.

Our results corroborate with the study by Hummer and his colleagues [22] who compared sexual dysfunction among patients of schizophrenia on atypical antipsychotics with those on typical antipsychotics and found atypical group to have 21% orgasmic difficulties. Also the meta-analysis of Serretti and Chiesa[16] which showed that 4%–49% of patients using atypical antipsychotics experience orgasmic dysfunction. Out of 50 patients on Risperidone, only **3** had sex related pain disorders, that is, 94% had no pain and only **6%** had sex related pain disorders .Similar studies which elicited pain during orgasm with the use of antipsychotic drugs was reported by Ghadirian et al 1982, whereas Berger et al in 1979 and Donnellan et al in 2001 reported painful ejaculation in patients using antipsychotics.[17,18,29] However which group of antipsychotics were used was not mentioned.

When the overall sexual dysfunction was calculated it was found that out of 50 patients on Risperidone, **10** of them had sexual dysfunction. The rest 40 were normal, that is **20%** had sexual dysfunction. This is supported by the study of Nagaraj et al who found that 16% to 60% of the patients using atypical antipsychotics experience sexual dysfunctions. [26] Also supported by the study of Bains et al who concluded that Risperidone seems to be the antipsychotic more associated with sexual dysfunction [27]. Serrati and Chiesa too stated that with Risperidone, 19-82% have sexual dysfunction,8-82% desire problems,16-93% arousal problems,13-86% orgasmic problems[16] These findings also strongly corroborate with the findings of Kotin and co-workers [25] who studied sexual dysfunction among 87 patients of schizophrenia and found 25% of those on typical antipsychotics to have reported sexual dysfunction.

Conclusion

From the present study we can conclude that with **Risperidone**, impairment is seen in desire disorders **(12%),** arousal disorders **(14%),** orgasmic difficulties (**26%)** and overall sexual dysfunction **(20%)**; although none of these findings were statistically significant.

Across **females**, Risperidone was found to cause more desire disorders, more arousal disorders and a more overall sexual dysfunction; whereas in case of **males,** Risperidone was found to cause more arousal disorders, more orgasmic difficulties, more sex related pain problems and a more overall sexual dysfunction.

Limitations in this study include that here an initial assessment of the participants' sexual dysfunction before treatment was not assessed. Thus, it is difficult to distinguish psychotropic-induced sexual dysfunction if they were already having any sexual problems pre-morbidly. Also self-reporting scales were employed in the study and although scales were reported to be well correlated with observer's ratings, there is a possibility of discrepancies between self-reports and actual problems. Besides self-reports have been subjected to biases.

The fact that sexual side effects of antipsychotics may not subside over time emphasizes the importance of effective treatment strategies for these side effects (Boer et al) [11] ; and this should therefore be a focus of future research. This should include psychosocial interventions for patients and partners, as well as pharmacological treatment strategies.

Also more research is needed on the possible interaction between sexual side effects and the symptoms of schizophrenia, eg negative symptoms, lack of motivation and initiative. There may be an overlap in underlying neurobiological mechanisms. Fortier et al highlighted that current scientific knowledge regarding sexuality cannot fully explain the neuro- physiology, neuro-endocrinology and psychological mechanism induced by drugs. In most cases, side-effects that impact on sexual functions are idiosyncratic and unpredictable with no apparent relationship between the type of drug used, dose and the incidence of a specific sexual dysfunction. [28]

Finally the variation in outcome between different studies could be the result of the study design and the instruments used. Taking into account the cognitive symptoms that many patients with a psychotic disorder experience, these questionnaires should be relatively short and simply formulated.

Conclusively, when clinicians are better informed about sexual functioning in patients with severe mental illness, they will be probably more willing to discuss this topic with the patient.

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