

A Cross-sectional Study of Antipsychotic Drugs Induced Sexual Dysfunction among Married Males with Remitted Schizophrenia Attending Tertiary Health Care Centre from Central India

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ABSTRACT

Introduction: Schizophrenia is a chronic debilitating disease having a major impact on the sufferers' lives. Antipsychotic drugs are the mainstay of the treatment of schizophrenia. But, antipsychotics can lead to a variety of sexual dysfunctions among the males with schizophrenia, which may affect their treatment compliance.

Aim: To assess the prevalence and the types of sexual dysfunctions among married males with remitted schizophrenia who were on a single oral antipsychotic drug from either class (i.e., typical or atypical type).

Materials and Methods: The present cross-sectional study was conducted in a tertiary health-care centre from Central India, with a sample size of 100 married males with schizophrenia who were in the remission phase on a single oral antipsychotic drug. Data were collected by using a convenient sampling method. Socio-demographic profile and clinical variables were recorded in a specific case report form

prepared for the study using the Arizona Sexual Experiences (ASEX) scale and the Udvalg for Kliniske Undersogelser (UKU) side-effect rating scale to assess the prevalence and the types of oral antipsychotic drugs induced sexual dysfunctions among study participants.

Results: The prevalence of antipsychotic drug induced sexual dysfunction was 54%. The most common type of sexual side-effect of oral antipsychotic treatment was Decreased Sexual Desire/Drive (DSD) as assessed by both ASEX (94.4%) and UKU (63.0%) scales. Sexual dysfunctions like DSD and Ejaculatory Dysfunction (EJD) were associated with the treatment of schizophrenia with typical antipsychotic drugs.

Conclusion: The present study shows that the treatment with typical antipsychotics was significantly associated with sexual side-effects. So, routine inquiry during the follow-ups should be done regarding the evaluation of sexual side-effects of antipsychotic agents in order to improve treatment compliance and disease prognosis.

Keywords: Ejaculatory dysfunction, Sexuality, Sexual desire, Treatment compliance, Treatment emergent sexual dysfunctions

INTRODUCTION

Human sexuality has always been one of the most important subjects in medical science. Sexuality has an important role in human behaviour [1]. Sexual dysfunctions are manifested as disruption in sexual desire and psychophysiological changes associated with the sexual response cycle in both genders [2]. The prevalence of sexual dysfunctions among the general population is high. About 10-52% of the men and 25-63% of the women have sexual dysfunctions [3-5].

According to Diagnostic and Statistical Manual of Mental Disorders 5th Edition (DSM-5) [2], schizophrenia is a psychiatric disorder characterised by disturbance in the relation between thoughts, emotions and behaviours. Schizophrenia leads to functional impairment through loss of acquired capability to earn a livelihood and through the psychosocial impairment [6]. Peak age of onset of schizophrenia is during the reproductive period, so impaired sexual functioning among the persons who have schizophrenia can affect their ability to have their own family, and thus to fulfil traditional social expectations [7].

Antipsychotics are the mainstay drugs in the treatment for schizophrenia. Role of antipsychotic drugs in sexual dysfunction in persons with schizophrenia has become a recent topic of interest for researchers as antipsychotic drugs induced sexual dysfunction is one of the important side-effects leading to poor treatment compliance, particularly among the males than the females as males tend to be more concerned about sexual dysfunctions than females [8-13].

Old or previous antipsychotics are known as typical or First Generation Antipsychotics (FGAs) or Dopamine Receptor Antagonists (DRAs). Newer antipsychotics are known as atypical or Second-Generation Antipsychotics (SGAs) or Serotonin Dopamine Antagonists (SDAs). To improve the treatment adherence and compliance of persons with schizophrenia, it is a need in current period to consider antipsychotic drugs induced sexual dysfunctions, particularly among the persons with schizophrenia taking SGAs. SGAs can improve the symptoms of schizophrenia, but they can also impair ejaculation and orgasm [13-19]. Sexual dysfunction has also been reported amongst the persons with schizophrenia receiving FGA like Haloperidol [20].

A study from central India had observed that among the psychotropic medicines like antipsychotics and antidepressants, sexual dysfunction was highest among the antipsychotic group. This study had divided sexual dysfunction into levels of severity like mild, moderate and severe but did not assessed the various types of sexual dysfunctions due to psychotropic medicines and their respective prevalences [21].

After reviewing the literature, data on this topic from central India was found to be sparse; hence there was a need for a comprehensive study on assessing the prevalence and the types of sexual dysfunction in the persons diagnosed with schizophrenia receiving oral antipsychotic treatment. Moreover, an international study from 27 countries had observed that the prevalence of sexual dysfunction among the persons with schizophrenia varied significantly across the regions as perceived by the psychiatrists. The same study concluded that the psychiatrists underestimated the presence of impotence and loss of libido significantly compared to the reports from the patients [22]. Such geographical variation was evident in both the perceptions of psychiatrists and the reports of sexual dysfunction by the patients [22].

Therefore, this study aimed to find the prevalence and the types of sexual dysfunction among a clinical sample of males suffering from schizophrenia who were on a single oral antipsychotic treatment from a tertiary health care centre from central India.

MATERIALS AND METHODS

This cross-sectional study was conducted in an Out-Patient Department of Psychiatry of Dr Panjabrao Alias Bhausaheb Deshmukh Memorial Medical College, Amravati, Maharashtra, India; from September 2016 to November 2017. Prior to the commencement, the study was approved by the Institutional Ethics Committee with a reference letter number:-{PDMMC/SS/ Ethical 6036/ 2016}. Informed written consent was taken from all the study participants after explaining them the nature and the purpose of the study.

All participants were subjected to detailed clinical and mental state examinations to rule out any major co-morbid medical, surgical, and psychiatric illnesses other than schizophrenia.

Sample size calculation: Based on the fact that the prevalence of sexual dysfunction among males with a diagnosis of schizophrenia is as high as 50% [22], and applying the formula of sample size determination for cross-sectional study design $(n=4pq/L^2)$ [23]. In the formula mentioned, 'p' is the prevalence of sexual dysfunction in persons with schizophrenia, q=100-p, and L is an allowable error and it is 20% of the 'p'. So, at p=50% [22], 95% confidence interval and 20% allowable error of margin, the required sample size was 100.

Inclusion criteria: Married males in the age group of 21 to 40 years, those who fulfilled DSM-5 diagnostic criteria for schizophrenia [2], those who were on a single antipsychotic drug of one class (i.e., either typical or atypical antipsychotic drug) within effective therapeutic dose range [24,25] for atleast six months, those who were well maintained/ in remission phase for at least six months [26] (i.e., without any active psychotic symptoms), and those who were willing to give the consent. Remission in schizophrenia as the relative absence of core positive and negative symptoms of schizophrenia such as hallucination, delusions, and disorganised speech as well as behaviour for at least six months [27].

In the present study, the participants who were on a single antipsychotic agent from the respective classes were chosen, as the previous study had observed that person with schizophrenia who were in combination therapy on both of typical and atypical antipsychotics had more sexual dysfunction than any one class [28]. Among the typical antipsychotic class, males who were receiving Haloperidol (dose range 10 to 20 mg/day) were included while among the atypical antipsychotic class, males who were receiving Olanzapine (does range 10 to 20 mg/day) were included [24,25]. Among the persons with schizphrenia who were receiving Haloperidol, Trihexiphenidyl was given concurrently in a dose range of 2 to 8 mg/day in order to prevent an occurrence of Haloperidol induced Extrapyramidal disorders/Parkinsonism [29].

Exclusion criteria: Males who did not gave the consent, unmarried males, widower males, who did not fulfilled the DSM-5 diagnostic criteria for schizophrenia [3], those who were not in remission phase, those who were on treatment with more than one

antipsychotic drug of same or different classes, those who had a history suggestive of primary sexual dysfunction (i.e., history of sexual dysfunction prior to initiation of antipsychotic medications), those who were suffering from major psychiatric disorders other than Schizophrenia like mood disorders, other psychotic disorders, neurotic disorders and substance dependence except for nicotine [30,31], those who had local injuries to genitalia or had any genital anomalies, those who had major medical and surgical disorders, and those who were on the medications like antihypertensive, antidepressant etc., known to interfere with sexual functioning.

Data were collected by a convenient sampling method after fulfilling inclusion criteria by using a pre-designed, semi-structured questionnaire. It was used to record the socio-demographic data, general examination, systemic examination, and mental status examination of the study participants.

Arizona Sexual Experience Scale (ASEX): It is a clinician administered questionnaire. It is an user friendly 5 item rating scale based on a 6 point Likert scale. It particularly determines modifications and alterations of sexual functions in relation to the intake of medicines or psychotropic substances. Each item explores a particular domain of sexuality, such as "sexual drive, sexual arousal, penile erection, ability to reach orgasm and satisfaction from orgasm". Possible total scores range from 5 to 30, with higher scores indicating more sexual dysfunction. Using the ASEX scale, subjects with a total ASEX score of \geq 19, any one item with a score of \geq 5, or any three items with a score of \geq 4 would have sexual dysfunction. These criteria were used in subsequent analyses to define whether subjects met ASEX criteria for sexual dysfunction [32].

Udvalg for Kliniske Undersogelser (UKU) side-effect rating scale: UKU scale helps in assessing the treatment emergent sexual side-effects of the drugs. Side-effect assessment part is rated on a four-point scale. UKU mainly measures the five components - Increased Sexual Desire (ISD), DSD, ED, EJD, and Orgasmic Dysfunction (OD). For statistical analysis, persons with a score of one or higher on any of the relevant items of the UKU side-effect rating scale were considered [33].

STATISTICAL ANALYSIS

Data from both the ASEX and the UKU clinician rated scales were entered with Microsoft Excel version 2007. Final data were analysed with Statistical Package for the Social Sciences (SPSS) statistical software version 22 (IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp.). Continuous data were presented as mean and Standard Deviation (SD); categorical data were presented as frequency and percentage. Chi-square and Fisher-exact tests were used to determine the level of significance. Central tendencies and dispersion of variables were studied using the descriptive statistical methods such as mean and SD. Study groups with sexual dysfunction and without sexual dysfunction were matched according to the socio-demographic profiles to identify confounding variables. Matching was performed according to the type of variable using the Chi-square test and the Student's t-test. The level of significance was set at 0.05.

RESULTS

Socio-demographic variables and schizophrenia related variables among the study participants:

[Table/Fig-1] shows that an equal number of participants (50%) were present in age groups 21 to 30 years and 31 to 40 years. The majority of participants were literate (90%), unemployed (74%), from an urban area (79%), and belonged to the Hindu religion (78%).

Among schizophrenia related variables, the majority of participants had 6 to 10 years of illness duration (34%), were on atypical antipsychotic drug (67%), had a duration of antipsychotic exposure for up to 12 months (61%), and had a negative family history of Schizophrenia (51%). The mean dose of typical antipsychotic (Haloperidol) was 17.27±3.14 mg/day. The mean dose of atypical antipsychotic (Olanzapine) was 15.11±3.67 mg/day.

Socio-demographic variables and Schizophrenia related variables	n
Age group (years)	Mean age±SD 31.32±6.05 Range=21-40 years
21-30	50
31-40	50
Education	
Literate	90
Illiterate	10
Employment	
Employed	26
Unemployed	74
Residence	
Urban	79
Rural	21
Religion	
Hindu	78
Muslim	13
Others	9
Duration of Schizophrenia illness (years)	Mean±SD=8.51±5.49
Up to 5	33
6 to 10	34
11 to 15	22
16 and above	11
Antipsychotic medication type	
Typical (Haloperidol)	33
Atypical (Olanzapine)	67
Duration of antipsychotic treatment (months)	Mean±SD=23.39±19.93
Up to 12	61
13 to 36	15
37 and above	24
Doses of antipsychotics (mg/day) Typical	Mean±SD=17.27±3.14
10 to 15	14
16 to 20	19
Atypical	Mean dose±SD=15.11±3.67
10 to 15	43
16 to 20	24
Family history of Schizophrenia	
Present	49
Absent	51
[Table/Fig-1]: Socio-demographic variables and among the males with schizophrenia (n=100).	schizophrenia related variables

Distribution of cut-off scores of ASEX and prevalence of Alterations of Sexual Functions in Males with Schizophrenia:

[Table/Fig-2] shows that out of 100 males with schizophrenia, 54 had antipsychotic induced alterations of sexual functions.

Profile of Distribution of Types of Alterations of Sexual Functions in Males with Schizophrenia according to ASEX Scale Scores:

[Table/Fig-3] shows that out of 54 males with antipsychotic induced alterations of sexual functions, based on the ASEX scale scores, the

ASEX cut-off scores	Persons with Schizophrenia on antipsychotic treatment having sexual dysfunction according to ASEX cut-off scores n, (%)
ASEX total score of ≥19	11 (20.4%)
ASEX scores of 4 in three domains but a total score of <19	33 (61.1%)
ASEX score of 5 in 1 domain but total score of <19	10 (18.5%)
[Table/Fig 2], Distribution of out of	off approach ACEV in maloo with application

[1able/Fig-2]: Distribution of cut off scores of ASEX in males with schizophrenia (n=54). ASEX: Arizona sexual experience scale

Types of alterations of sexual functions according to ASEX scale	n (%)
Low sexual drive/desire	51 (94.4)
Difficulty in sexual arousal	46 (85.2)
Erectile Dysfunction (ED)	36 (66.7)
Difficulty in reaching orgasm	30 (55.6)
Dysfunction of orgasmic satisfaction	24 (44.4)
[Table/Fig-3]: Distribution of types of alterations of sexual functions ac to ASEX scores in males with schizophrenia receiving oral antipsychotic (n=54). ASEX Arizona sexual experience scale	

most common alteration of the sexual function was low sexual drive which was present in 51 (94.4%).

Profile of distribution of types of sexual dysfunction according to UKU scale scores in males with Schizophrenia receiving antipsychotic treatment:

[Table/Fig-4] shows that based on UKU scale scores, 63 had DSD, 43 had ED, 44 had EJD, and 42 had OD.

Types of sexual dysfunction according to UKU scale	n						
Diminished Sexual Desire (DSD)							
Present	63						
Absent	37						
Erectile Dysfunction (ED)	<u>`</u>						
Present	43						
Absent	57						
Ejaculatory Dysfunction (EJD)							
Present	44						
Absent	56						
Orgasmic Dysfunction (OD)							
Present	42						
Absent	58						
[Table/Fig-4]: Distribution profile of types of sexual dysfur scores in males with schizophrenia (n=100). UKU: Udvalg for KliniskeUndersogelser side-effect rating scale	nction according to UKU						

Relationship between Socio-demographic Variables as well as Schizophrenia-related Variables and Types of Alterations of Sexual Functions According to ASEX Scale Scores:

[Table/Fig-5] shows that, among the socio-demographic variables, study participants in age group of 31 to 40 years had significant penile ED and those belonged to urban area of residence had impaired sexual drive/desire. Among the schizophrenia related variables, presence of family history of schizophrenia was associated with impaired sexual drive/desire, impaired sexual arousal, ED and absence of orgasmic satisfaction.

Relationship between Socio-demographic Variables as well as Schizophrenia Related Variables and Types of Sexual Dysfunction According to UKU Scale Scores:

[Table/Fig-6] shows that the antipsychotic induced sexual dysfunctions like DSD, EJD and OD in males with schizophrenia were associated with illiteracy. Rest of the socio-demographic variables were not associated with any type of sexual dysfunction.

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				A	Iterations	of sexua	I function	s accord	ing to AS	EX scale	scores				
Socio-demographic		drive/ desire 1=100)			arousal 100)			erection 100)			to reach n (n=100)		Orgasmic satis- faction (n=100)		
variables and schizophrenia related variables	- (n1 =51)	+ (n2 =49)	р	- (n1 =46)	+ (n2 =54)	р	- (n1 =36)	+ (n2 =64)	р	- (n1 =30)	+ (n2 =70)	р	- (n1 =24)	+ (n2 =76)	р
Age group (years)															
21 to 30	26	24	0.04	23	27	0.00	14	36	0.04*	18	32	0.00	13	37	0.00
31 to 40	25	25	0.84	23	27	0.99	22	28	0.04*	12	38	0.09	11	39	0.63
Education															
Literate	46	44		40	50	0.07	32	58	0.77	27	63		23	67	
Illiterate	5	5	0.94	6	4	0.37	4	6	0.77	3	7	0.97	1	9	0.3
Occupation															
Employed	14	12	0.70	11	15		12	14		8	18		5	21	
Unemployed	37	37	0.73	35	39	0.66	24	50	0.21	22	52	0.92	19	55	0.5
Residence															
Urban	44	35		39	40		29	50		22	57	0.36	19	60	0.98
Rural	7	14	0.03*	7	14	0.09	7	14	0.38	8	13		5	16	
Religion													,		
Hindu	44	34		36	42		29	49		24	54		22	56	0.17
Muslim	5	8	0.09 6	6	7	0.99	4	9	0.89	4	9	0.86	1	12	
Other	2	7	1	4	5		3	6		2	7		1	8	
Duration of Schizop	hrenia (ye	ars)													
Up to 5	17	16		12	21		6	27		10	23		9	24	0.76
6 to 10	19	15	1	18	16		16	18		14	20	-	6	28	
11 to 15	10	12	0.86	10	12	0.52	10	12	0.06	5	17	0.18	6	16	
16 and above	5	6	1	6	5		4	7		1	10		3	8	
Duration of antipsyc	hotic trea	tment (month	is)												
Up to 12	32	29		25	36		19	42		21	40		16	45	0.22
13 to 36	8	7	0.84	9	6	0.37	9	6	0.10	5	10	0.26	1	14	
37 and above	11	13	1	12	12		8	16		4	20		7	17	
Doses of antipsycho	tics (mg/	day)													
10 to 15	26	29	0.10	28	27	0.07	18	37	0.15	19	36	0.07	11	44	
16 to 20	25	20	0.40	18 27	27	0.27	18	27	0.45	11	34	0.27	13		0.3
Family history of Scl	nizophren	ia													
Present	34	15	0.0005	34	15		29	20		18	31	0.07	17	32	
Absent	17	34	0.0003*	12	39	0.01*	7	44	0.01*	12	39	0.07	7	44	0.01*

Among the schizophrenia related variables, none were associated with the sexual dysfunction assessed by UKU scale scores.

Relationship between Types of Antipsychotic Drugs and Types of Alterations of Sexual Functions Assessed by ASEX Scale:

[Table/Fig-7] shows that none of the types of alterations of sexual functions according to ASEX scale scores were associated with any particular type of antipsychotic drugs.

Relationship between Types of Antipsychotic Drugs and Types of Sexual Dysfunction Assessed by the UKU Scale:

[Table/Fig-8] shows that sexual dysfunctions like DSD (p=0.02) and EJD (p=0.02) in males with schizophrenia were associated with the treatment with typical antipsychotic drugs.

DISCUSSION

Socio-demographic profile of the study participants: In the present study, there were 100 males with schizophrenia in the age range of 21 to 40, with mean age of 31.32 ± 6.05 years [Table/Fig-1]. Minimum age of the study participants was kept at 21 years because the legal age of marriage for Indian males is 21 years. The maximum age of the study participants was kept at 40 years because 40% of the males are affected by sexual dysfunction, mainly by the Erectile

Dysfunction (ED) at this age [27]. In the present study, majority of study participants (79%) were from the urban area [Table/Fig-1]. Present study finding reflects that access to experts like sexologists, urologists and andrologists is available primarily to men living in urban areas, where there is a higher concentration of tertiary health care hospitals and specialists [34]. A study from rural Northern India had concluded that, there is a shortage of trained psychiatrists in rural areas. Therefore, it is a need of the hour to train primary care physicians in identifying and treating less severe or referring complicated cases of sexual health disorders to specialists [35].

Sexual dysfunction profile among the study participants: In the present study, according to ASEX scale score, prevalence of sexual dysfunction in clinical population of schizophrenia receiving antipsychotic drugs was 54% [Table/Fig-2]. This finding was similar to previous study finding where the prevalence of sexual dysfunction among persons with Schizophrenia was 50% [22]. In contrast to present study, Aggarwal S et al., observed a low prevalence of sexual dysfunction among persons with schizophrenia and it was relatively 40.8% [36]. The low prevalence in their study might be due to the fact that they had not assessed impact of antipsychotics in causation of sexual dysfunction in persons with schizophrenia [36].

							ion accordin	<u> </u>			(100)	1
Socio-demographic		n=100)	-		=100)	-		n=100)	-		i=100)	-
Variables and schizophrenia related variables	+ (n1=63)	- (n2 =37)	р	+ (n1=43)	- (n2 =57)	р	+ (n1=44)	- (n2 =56)	р	+ (n1=42)	- (n2 =58)	р
Age group (years)												
21 to 30	34	16	0.00	23	27	0.54	25	25	0.00	25	25	0.1
31 to 40	29	21	0.30	20	30	0.54	19	31	0.22	17	33	0.1
Education												
Literate	54	36	0.00*	37	53	0.00	36	54	0.00*	35	55	
Illiterate	9	1	0.03*	6	4	0.20	8	2	0.03*	7	3	0.0
Occupation												
Employed	18	8	0.44	12	14	0.70	14	12	0.24	14	12	
Unemployed	45	29	0.44	31	43	0.70	30	44	0.24	28	46	0.15
Residence												
Urban	47	32	0.15	31	48	0.14	32	47	0.17	30	49	0.1
Rural	16	5	0.15	12	9	0.14	12	9	0.17	12	9	0.11
Religion												
Hindu	50	28	0.75	34	44		36	42		33	45	0.12
Muslim	7	6		5	8	0.93	3	10	0.22	3	10	
Other	6	3		4	5		5	4		6	3	
Duration of Schizophrenia (ye	ars)											
Up to 5	25	8		18	15		17	16		19	14	
6 to 10	21	13	0.00	11	23		15	19	0.55	14	20	
11 to 15	11	11	0.23	9	13	0.32	0.32 7	15	0.55	6	16	- 0.10
16 and above	6	5		5	6		5	6	1	3	8	
Duration of antipsychotic trea	tment (mont	hs)										
Up to 12	43	18		28	33		30	31		28	33	
13 to 36	9	6	0.10	7	8	0.54	8	7	0.09	8	7	0.1
37 and above	11	13		8	16		6	18		6	18	
Doses of antipsychotics (mg/d	day)											
10 to 15	32	23		21	34		21	34		23	32	
16 to 20	31	14	0.27	22	23	0.28	23	22	0.19	19	26	- 0.9
Family history of Schizophren	ia											
Present	31	18		23	26		23	26	0	20	29	_
Absent	32	19	0.95	20	31	0.43	21	30	0.56	22	29	0.8

Types of alterations of	Types of Antipsychotic drugs						
sexual functions as- sessed by ASEX scale	Typical (Haloperidol) n1=33 (%)	Atypical (Olanzapine) n2=67 (%)	p- value				
Sexual drive/desire							
Absent	14 (42.4)	37 (55.2)	0.00				
Present	19 (57.6)	30 (44.8)	0.22				
Sexual arousal							
Absent	14 (42.4)	32 (47.8)	0.61				
Present	19 (57.6)	35 (52.2)	0.61				
Penile erection							
Absent	10 (30.3)	26 (38.8)	0.40				
Present	23 (69.7)	41 (61.2)	0.40				
Ability to reach orgasm							
Absent	9 (27.3)	21 (31.3)	0.07				
Present	24 (72.7)	46 (68.7)	0.67				
Orgasmic satisfaction							
Absent	5 (15.2)	19 (28.4)	0.14				
Present	28 (84.8)	48 (71.6)	0.14				

"-": absent; Chi-square and Fis

They had assessed the relationship between the schizophrenia and sexual dysfunction without an attempt to study the association of sexual dysfunction with any specific antipsychotic drugs [36].

There is ample evidence that antipsychotics lead to high rate of sexual dysfunction ranging from 30-80% [37], which was similar to present study finding. A study has found that 38.1% persons with schizophrenia had sexual dysfunction while on treatment with haloperidol [20]. Same study had also found that 35.3% of the persons with schizophrenia with sexual dysfunction were on olanzapine, 18.2% were on Quetiapine, and 43.2% were on Risperidone [20]. Prevalence of sexual dysfunction in persons with schizophrenia was investigated as a part of a large (n=7655), prospective, international (27 countries) study. Based on the patient reports, sexual dysfunction affected approximately 50% of the persons, and the prevalence of complaints varied significantly between the regions (p<0.0001) [22].

In the present study, out of those 54 persons who had sexual dysfunction according to ASEX scale scores, majority (94.4%) had low sexual drive [Table/Fig-3]. Findings similar to present study was observed by Aggarwal S et al., where in majority of the study participants (44.7%) had low sexual drive according to ASEX scale score [36]. In the present study, according to UKU scale scores, majority (63%) had DSD, which also matches with finding on ASEX

Types of sexual	Types of Antip							
dysfunction assessed by UKU scale	Typical (Haloperidol) n1=33 (%)	Atypical (Olanzapine) n2=67 (%)	p- value					
Decreased Sexual Desire (DSD)								
Present	26 (78.8)	37 (55.2)	0.00*					
Absent	7 (21.2)	30 (44.8)	0.02*					
Erectile Dysfunction (E	D)							
Present	16 (48.5)	27 (40.3)	0.40					
Absent	17 (51.5)	40 (59.7)	0.43					
Ejaculatory Dysfunction (EJD)								
Present	19 (57.6)	25 (37.3)	0.00*					
Absent	14 (42.4)	42 (62.7)	0.02*					
Orgasmic Dysfunction	(OD)							
Present	15 (45.5)	27 (40.3)	0.00					
Absent	18 (54.5)	40 (59.7)	0.62					
sexual dysfunction accor	ding to UKU scale scores Udvalg for kliniske undersog	ipsychotic drugs and type s. elser side-effect rating scale; (

scale where low sexual drive/desire was the most common sexual dysfunction based on ASEX scale scores (94.4%) [Table/Fig-3,4]. Nagaraj AK et al., found that according to UKU scale score, majority of their study participants (41.7%) had ED, which is in contrast to present study finding [38]. Such a difference in profile might be secondary to differences in inclusion criteria adopted for studies.

Nagaraj AK et al., had included study participants of ages between 18 to 50 years which was broader than present study age range [38]. In their study, ED was most common sexual dysfunction which might be due to fact that about 40% of men above age 40 years suffer from ED [27]. A study had observed that among men, less desirability for sex, less achievable, and maintainable penile erection, premature ejaculation, and reduced orgasmic satisfaction were noted [22].

Relationship between Socio-demographic Characteristics, Schizophrenia Related Variables and Various Types of Sexual Dysfunctions in Study Participants

In the present study, among the socio-demographic characteristics of study participants, age group of 31 to 40 years was associated with ED and those belonged to urban area of residence had impaired sexual drive/desire based on ASEX scale scores [Table/ Fig-5]. Based on UKU scale scores, among the socio-demographic characteristics, only educational status (mainly illiteracy) was associated with presence of various types of sexual dysfunctions mainly decrease sexual desire, EJD and OD [Table/Fig-6]. In contrast to present study finding, Nagaraj AK et al., found that none of the socio-demographic variables had association with sexual dysfunction [38]. Prabhakaran DK et al., concluded that people with higher education level tend to had awareness and less stigmatising attitude towards reporting sexual dysfunction which is in contrast to present study finding [39].

In the present study, among schizophrenia related variables, presence of family history of schizophrenia was associated with impaired sexual drive/desire, impaired sexual arousal, ED and absence of orgasmic satisfaction according to scores on ASEX scale [Table/Fig-5]. In the present study, among schizophrenia related variables, none of variable was associated with sexual dysfunctions assessed by UKU scale scores [Table/Fig-6]. Such a difference in findings using two different scales (i.e., ASEX and UKU) may be due to different types of sexual dysfunctions assessed by these two scales apart from their different structural styles of items/ questions included.

Relationship between Doses of Antipsychotics, Duration of Antipsychotic Treatment, Types of Antipsychotic Drugs and Various Types of Sexual Dysfunctions in Study Participants In the present study, doses of antipsychotics in therapeutic dose range were not associated with any type of sexual dysfunctions based on both ASEX and UKU scale scores [Table/Fig-5,6]. A study observed that typical antipsychotic drug like Haloperidol raises serum prolactin level in therapeutic dose range which leads to sexual dysfunction [15]. Same study concluded that lowering the dosage of offending drug like Haloperidol or switching to a prolactin-sparing antipsychotic like olanzapine often reduces sexual side-effects [15]. In present study, duration of antipsychotic treatment was not associated with occurrence of any type of sexual dysfunction based on both ASEX and UKU scale scores [Table/Fig-5,6]. It was a novel finding in the present study as a systematic review conducted by Costa AM et al., found that none of the studies had assessed the effect of duration of antipsychotic treatment on antipsychotic induced sexual dysfunctions among the persons with schizophrenia [40].

In the present study, none of the types of sexual dysfunctions assessed by ASEX scale scores were associated with any particular type of antipsychotic drugs [Table/Fig-7]. Sexual dysfunctions assessed according to UKU scale scores, like DSD and EJD in persons with schizophrenia were associated with treatment with typical antipsychotic like haloperidol [Table/Fig-8]. Nagaraj AK et al., also observed a similar finding that, sexual dysfunction was significantly higher with typical than atypical antipsychotics [38]. In their study, ED was the most common sexual dysfunction [38]. In the present study, none of the types of sexual dysfunction was associated with treatment with atypical antipsychotic agents [Table/ Fig-7,8]. Mahmoud A et al., had observed a similar finding [41]. They concluded that atypical antipsychotics could improve sexual dysfunction in persons with schizophrenia [41]. Bobes J et al., had observed a similar finding that majority of persons with schizophrenia had sexual dysfunction while on treatment with typical antipsychotic like haloperidol [20]. In their study, majority (38.1%) had haloperidol induced sexual dysfunction, while lesser i.e., 35.3% had sexual dysfunction while on olanzapine [20].

Limitation(s)

First, due to the cross-sectional study design, temporal assessment was not done. Secondly, the other fairly key drawbacks were recall bias and social desirability bias. As participants were questioned about details of their sexual functioning, they might have answered in such a way as to portray themselves in a good light. Hence, social desirability bias could be present. Thirdly, future studies should assess the relation between the couples' satisfaction between the males with schizophrenia on treatment with antipsychotics and their wives.

CONCLUSION(S)

In conclusion, persons with schizophrenia receiving antipsychotic treatment frequently experience sexual side-effects. Treatment with typical than atypical antipsychotics was significantly associated with sexual side-effects. So, routine inquiry during follow-ups should be made regarding the evaluation of the sexual side-effects of antipsychotic agents in order to improve treatment compliance and disease prognosis.

REFERENCES

- Sadock VA. Normal Human Sexuality and Sexual Dysfunctions. In: Sadock BJ, Sadock VA, Ruiz P. Kaplan and Sadock's Synopsis of Psychiatry, 11th ed. Philadelphia: Wolters Kluwer; 2015; 4993.
- [2] American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition. Arlington, VA, American Psychiatric Association, 2013.
- [3] Frank E, Anderson C, Rubinstein D. Frequency of sexual dysfunction in normal couples. N Engl J Med. 1978;299:111-15.
- [4] Rosen RC, Taylor JF, Leiblum SR, Bachmann GA. Prevalence of sexual dysfunction in women: Results of a survey study of 329 women in an outpatient gynecological clinic. J Sex Marital Ther. 1993;19:171-88.
- [5] Spector IP, Carey MP. Incidence and prevalence of the sexual dysfunctions: A critical review of the empirical literature. Arch Sex Behav. 1990;19:389-408.

- [6] Tamminga CA. Schizophrenia and other Psychotic disorders: Introduction and Overview. In: Sadock BJ, Sadock VA, Ruiz P. Kaplan and Sadock's Synopsis of Psychiatry, 11th ed. Philadelphia: Wolters Kluwer; 2015; 3613.
- [7] Hafner H, Riecher-Rossler A, Der Heiden WA, Maurer K, Fatkenheuer B, Loffler W. Generating and testing a causal explanation of the gender difference in age at first onset of schizophrenia. Psychol Med. 1993;23:925-40.
- [8] Lambert M, Conus P, Eide P, Mass R, Karow A, Moritz S, et al. Impact of present and past antipsychotic side-effects on attitude toward typical antipsychotic treatment and adherence. Eur Psychiat. 2004;19:415-22.
- [9] Seeman MV. Loss of libido in a woman with schizophrenia. Am J Psychiatry. 2013;170:471-75.
- [10] Mahmoud A, Drake RJ, Lewis SW, Hayhurst KP, Barnes TR. The ANNSERS (antipsychotic non-neurological side-effects rating scale): Validation of sexual side-effect measurement. Ther Adv Psychopharm. 2011;1:97-100.
- [11] Inder WJ, Castle D. Antipsychotic-induced hyperprolactinaemia. Aust NZ J Psychiat. 2011;45:830-37.
- [12] Dossenbach M, Dyachkova Y, Pirildar S, Anders M, Khalil A, Araszkiewicz A, et al. Effects of atypical and typical antipsychotic treatments on sexual function in persons with schizophrenia: 12-month results from the Intercontinental Schizophrenia Outpatient Health Outcomes (IC-SOHO) study. Eur Psychiat. 2006;21:251-58.
- [13] Haddad PM, Sharma SG. Adverse effects of atypical antipsychotics. CNS Drugs. 2007;21:911-36.
- [14] Byerly MJ, Nakonezny PA, Fisher R, Magouirk B, Rush AJ. An empirical evaluation of the Arizona sexual experience scale and a simple one-item screening test for assessing antipsychotic-related sexual dysfunction in outpersons with schizophrenia and schizoaffective disorder. Schizophr Res. 2006;81:311-16.
- [15] Knegtering H, van der Moolen AE, Castelein S, Kluiter H, van den Bosch RJ. What are the effects of antipsychotics on sexual dysfunctions and endocrine functioning? Psychoneuroendocrinology. 2003;28:109-23.
- [16] Atmaca M, Kuloglu M, Tezcan E. A new atypical antipsychotic: Quetiapineinduced sexual dysfunctions. Int J Impot. 2005;17:201-03.
- [17] Wesby R, Bullmore E, Earle J, Heavey A. A survey of psychosexual arousability in male persons on depot neuroleptic medication. Eur Psychiat. 1996;11:81-86.
- [18] Cohen S, Kühn KU, Sträter B, Scherbaum N, Weig W. Adverse side-effect on sexual function caused by psychotropic drugs and psychotropic substances. Der Nervenarzt. 2010;81:1129-37.
- [19] Smith S, O'Keane VE, Murray R. Sexual dysfunction in persons taking conventional antipsychotic medication. Brit J Psychiat. 2002;181:49-55.
- [20] Bobes J, Garc A-Portilla MP, Rejas J, Hern Ndez G, Garcia-Garcia M, Rico-Villademoros F, et al. Frequency of sexual dysfunction and other reproductive side-effects in persons with schizophrenia treated with risperidone, olanzapine, quetiapine, or haloperidol: The results of the EIRE study. J Sex Marital Ther. 2003;29:125-47.
- [21] Atram U, Pradeep B, Desai S, Maidapwad S. Prevalence of sexual dysfunction in patients receiving psychotropic medications. Indian J Neurosci. 2019;5:145-49.
- [22] Dossenbach M, Hodge A, Anders M, Molnár B, Peciukaitiene D, Krupka-Matuszczyk I, et al. Prevalence of sexual dysfunction in persons with schizophrenia: International variation and underestimation. Int J Neuropsychopharmacol. 2005;8:195-201.
- [23] Ghogare AS, Patil PS. A cross-sectional study of comorbid generalized anxiety disorder and major depressive disorder in persons with tension-type headache attending tertiary health care centre in central rural India. Niger Postgrad Med J. 2020;27:224-29.

- [24] Stahl SM. Haloperidol. In: Stahl SM, Grandy MM, Muntner N, editor. Stahl's Essential Psychopharmacology Prescriber's Guide, 5th edn. New York: Cambridge University Press; 2014; 293.
- [25] Stahl SM. Olanzapine. In: Stahl SM, Grandy MM, Muntner N, editor. Stahl's Essential Psychopharmacology Prescriber's Guide, 5th edn. New York: Cambridge University Press; 2014; 487.
- [26] Andreasen NC, Carpenter Jr WT, Kane JM, Lasser RA, Marder SR, Weinberger DR, et al. Remission in schizophrenia: Proposed criteria and rationale for consensus. Am J Psychiatry. 2005;162:441-49.
- [27] Feldman HA, Goldstein I, Hatzichristou DG, Krane RJ, McKinlay JB. Impotence and its medical and psychosocial correlates: Results of the Massachusetts Male Aging Study. J Urol. 1994;151:54-61.
- [28] Stahl SM. Trihexiphenidyl. In: Stahl SM, Grandy MM, Muntner N, editor. Stahl's Essential Psychopharmacology Prescriber's Guide, 5th edn. New York: Cambridge University Press; 2014; 697.
- [29] Ucok A, Incesu C, Aker T, Erkoc S. Sexual dysfunction in patients with schizophrenia on antipsychotic medication. Eur Psychiatry. 2007;22:328-61.
- [30] Kelkar PN, Vankar GK, Mishra KK, John S, Ghogare AS. Prevalence of substance abuse in patients with schizophrenia. J Clin Diagn Res. 2020;14:VC01-VC05.
- [31] Ghogare AS, Saboo AV. A cross-sectional study of cognitive impairment in patients of alcohol use disorder attending a tertiary health care center in Central India. Ann Indian Psychiatry. 2019;3:155-60.
- [32] McGahuey CA, Gelenberg AJ, Laukes CA, Moreno FA, Delgado PL, McKnight KM, et al. The Arizona Sexual Experience Scale (ASEX): Reliability and validity. J Sex Marital Ther. 2000;26:25-40.
- [33] Lingjaerde O, Ahlfors UG, Bech P, Dencker SJ, Elgen K. The UKU side-effect rating scale. A new comprehensive rating scale for psychotropic drugs and a cross-sectional study of side-effects in neuroleptic-treated patients. Acta Psychiatr Scand Suppl. 1987;334:1-100.
- [34] Deo MG. Doctor population ratio for India- The reality. Indian J Med Res. 2013;137:632-35.
- [35] Singh AK, Kant S, Abdulkader RS, Lohiya A, Silan V, Nongkynrih B, et al. Prevalence and correlates of sexual health disorders among adult men in a rural area of North India: An observational study. J Family Med Prim Care. 2018;7:515-21.
- [36] Aggarwal S, Grover S, Chakrabarti S. A comparative study evaluating the marital and sexual functioning in persons with schizophrenia and depressive disorders. Asian J Psychiatr. 2019;39:128-34.
- [37] Haddad PM, Wieck A. Antipsychotic-induced hyperprolactinemia: Mechanism, clinical features and management. Drugs. 2004;64:2291-314.
- [38] Nagaraj AK, Nizamie HS, Akhtar S, Sinha BN, Goyal N. A comparative study of sexual dysfunction due to typical and atypical antipsychotics in remitted bipolar-I disorder. Indian J Psychiatry. 2004;46:261-66.
- [39] Prabhakaran DK, Nisha A, Varghese PJ. Prevalence and correlates of sexual dysfunction in male personswith alcohol dependence syndrome: A crosssectional study. Indian J Psychiatry. 2018;60:71-77.
- [40] Costa AM, Lima MS, Mari J. A systematic review on clinical management of antipsychotic-induced sexual dysfunction in schizophrenia. Sao Paulo Med J. 2006;124:291-97.
- [41] Mahmoud A, Hayhurst KP, Drake RJ, Lewis SW. Second generation antipsychotics improve sexual dysfunction in schizophrenia: A randomised controlled trial. Schizophr Res Treatment. 2011;2011:596898.

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