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Sexual functioning in females with depression in remission receiving escitalopram

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***Background & objectives*: Sexual functioning is a strong determinant of quality of life. Sexual dysfunction has been widely reported due to depressive disorder as well as selective serotonin reuptake inhibitors. Thus, treatment with antidepressants can culminate in a double-edged sword, leading to drug discontinuation and symptom relapse. The objective of this study was to assess the sexual functioning of sexually active females with depression, currently in remission, receiving escitalopram and to compare with healthy controls.**

***Methods*: Fifty female patients with depression, currently in remission, with self-reported normal pre-morbid sexual function and receiving escitalopram for at least three months, were assessed on female sexual function index (FSFI) questionnaire and compared with healthy controls.**

***Results*: Half of the patients (n=25, 50%) in group A were found to have sexual dysfunction (FSFI score <26.55), while, 90 per cent (n=45) had decreased desire, 86 per cent (n=43) had decreased arousal, 54 per cent (n=27) had decreased lubrication, 68 per cent (n=34) had decreased orgasm, 62 per cent (n=31) had decreased satisfaction and 32 per cent (n=16) had pain during sexual activity. Patients receiving escitalopram had significantly higher sexual dysfunction as compared to healthy controls in mean total FSFI score (*P*<0.001) and all mean domain scores of FSFI except pain.**

***Interpretation & conclusions*: A significant proportion of sexually active females with depression currently in remission, receiving escitalopram, reported dysfunction in all domains of sexual function; thus, routine screening for sexual dysfunction during follow up is advisable for early identification and prompt treatment.**

Key words Depression - escitalopram - female - FSFI - remission - sexual dysfunction

The prevalence of female sexual dysfunction (FSD) in general population ranges from 43 to 69 per cent[1]. Factors associated with FSD are increasing age of participant and partner, lower education, and treatment with antidepressants. Women attributed sexual dysfunction to physical illness and substance use in partner, menopause and contraceptive use[2]. Psychiatric disorders and psychological problems have direct association with lower sexual function, especially orgasmic disorders and sexual satisfaction[3-5]. Depression has emerged as an independent risk factor for sexual dysfunction[6,7], and the action is mediated through the

activation of serotonin receptors[8], anti-cholinergic, anti-noradrenergic, anti-histaminergic, anti-dopaminergic actions and elevated prolactin[8,9]. Though the exact mechanism of sexual dysfunction in females due to selective serotonin reuptake inhibitors (SSRIs) is not known, cumulative effect on multiple neurotransmitter systems (serotonergic, noradrenergic, dopaminergic, cholinergic and nitric oxide) has been reported to attribute to anorgasmia, inadequate lubrication, poor arousal and reduced libido[10].

Sexual dysfunction negatively affects quality of life, self-esteem, mood and interpersonal relationships[11] and has potential implications for treatment adherence and outcome. All classes of antidepressants are known to cause sexual dysfunction[12]; sexual dysfunction due to SSRIs has been reported at a rate of 10-80 per cent[13].

Sexual dysfunction attributed to depression as well as treatment-emergent sexual dysfunction (due to antidepressants) has been well studied[13,14]. However, there is a lack of information regarding sexual functioning of female patients with depression currently on antidepressants. SSRIs are recommended as the first-line therapy for depression and escitalopram is considered the first choice among prescribed SSRIs[15]. This study was planned to examine the sexual functioning of females who were in remission phase of depression and were receiving escitalopram, and to compare with sexual functioning of healthy female controls.

Material & Methods

A cross-sectional, observational study was conducted from September 2016 to August 2017 at the department of Psychiatry, King George's Medical University, Lucknow, a tertiary care centre in north India after approval from the Institutional Ethics Committee. Consecutive individuals fulfilling selection criteria were recruited after taking written informed consent.

Selection criteria: Sample in study group A was drawn from sexually active female patients attending Adult Psychiatry Outpatient department (OPD), aged 18-45 yr, already being treated for major depressive disorder as per International Classification of Diseases, 10th Revision ICD-10 DCR[16] (first episode or recurrent) and currently in remission with the current Hamilton Depression Rating Scale (HAM-D) score ≤7[17] with reported normal sexual functioning prior to the onset of depression. Since this was a cross-sectional study, baseline HAM-D scores were not available. The patients had been receiving escitalopram at a dose of 10-20 mg/day since at least the last three months, at the time of inclusion (compliance ensured historically). Those having psychotic symptoms, active suicidal ideation or other diagnosable psychiatric disorders, except tobacco use disorder, dementia and subnormal intelligence were excluded from the study. Pregnant, lactating or menopausal women, those having physical co-morbidities or on concomitant drugs that could affect sexual function, were also excluded. Furthermore, those receiving antidepressants other than escitalopram were also excluded. Individuals, whose partners had significant physical, mental or sexual disorder as per provided history and those reporting significant relationship discord affecting sexual relationship with partners were not included. Only specified daily dosages of sedatives and hypnotics (clonazepam ≤1 mg, lorazepam ≤2 mg, zolpidem ≤10 mg) were permitted in included individuals.

Age-group matched controls (group B) were taken from sexually active healthy females aged 18-45 yr, accompanying patients attending Adult Psychiatry OPD (other than spouses of the individuals and the primary caregiver of the patient), with normal sexual functioning as per self-report. Individuals scoring less than 3 on the General Health Questionnaire (GHQ-12)[18] were included. The exclusion criteria were the same for both the groups. As the study was planned with a pre-specified time frame, convenient sampling technique was followed and a sample size of 50 individuals in each group was calculated after thorough review of outpatient attendance in our centre records over the past two years. First two consecutive patients meeting the selection criteria on specified days of a week were recruited.

Procedure: A sample of 50 women was taken in each group. MINI (Mini-International Neuropsychiatric Interview) v6.0.0[19] augmented with a clinical interview was applied to rule out other psychiatric disorders. Relationship Assessment Scale (RAS)[20,21] was applied to rule out relationship dissatisfaction among females of both groups and those scoring <4 were excluded. Twenty seven (8.8%) of screened population was excluded owing to interpersonal relationship dissatisfaction. Socio-demographic and clinical details were collected on semi-structured proforma. To assess self-report of the current sexual functioning, Brief Sexual Symptom Checklist for Women (BSSC-W)[22,23] was used. For an objective assessment of sexual functioning, a Hindi translated

version of the female sexual function index (FSFI)[24] was applied. FSFI is available in the public domain for free use (*https://www.fsfiquestionnaire.com*). It was translated to Hindi by the investigator and subsequently back-translated and validated. All the tools used in the study were administered with the assistance of clinician(s)/investigator(s).

Assessment tools used

(*i*) RAS[20,21]: 7-item Likert-scale based; respondents answer on a 5-point scale from 1 to 5 for each item. The higher the score, the more satisfied the respondent is with her relationship. An average score of >4.0 likely indicates non-distressed partners.

(*ii*) HAM-D-17 items[17] are used for the assessment of depression severity. It is rated as: 0-7=normal; 8-13=mild depression; 14-18=moderate depression; 19-22=severe depression; ≥23=very severe depression.

(*iii*).BSSC-W[22,23] is a brief screening checklist developed by the International Consultation in Sexual Medicine-5 Committee to facilitate initial identification of a sexual problem. It consists of four simple questions for screening and self- report of sexual functioning.

(*iv*) FSFI[24] is a 19-item questionnaire for the assessment of the key dimensions of sexual functioning in women in previous one month. It measures six domains - sexual desire, arousal, lubrication, orgasm, satisfaction and pain. Total FSFI score below 26.55 is taken as an indicator of FSD.

(*v*) GHQ-12 items[18] is a screening device for identifying minor psychiatric disorders in the general population. It has 12 items and is rated on a Likert-type scoring method, 0=less than usual, 1=no more than usual, 2=rather more than usual and 3=much more than usual. Positive questions (Items 1, 3, 4, 7 and 12) are scored inversely. Any score exceeding 3 is classified as 'psychiatric caseness'.

Statistical analysis: Data collected were analyzed using Statistical Package for the Social Sciences (SPSS) IBM software v16 (IBM Corp., Armonk, NY, USA). Independent samples *t* test and Chi-square test were used to compare continuous and categorical variables, respectively. Pearson's correlation analysis was used to assess linear correlation between continuous variables, where applicable.

Results

Socio-demographic and clinical characteristics: All women were married, in reproductive age group (18-45 yr). Thirty six patients in group A (n=36, 72%) were aged 31-45 yr (mean 34.44±5.66 yr). Controls (group B) (mean 34.34±5.47 yr) were age matched. Majority of the individuals in groups A and B (n=37, 74% and n=40, 80%, respectively) were Hindus, homemakers (n=44, 88% and n=42, 84%) and all of them had comparable mean duration of marriage (13.86±6.83 and 13.84±5.31 yr). Most belonged to nuclear family (n=30, 60% and n=34, 68% in groups A and B) and were educated up to primary school (n=28, 56% and n=26, 52%). Mean years of schooling (7.4±5.91 and 7.5±6.75 yr) and monthly family income were comparable among the groups. Both the groups were homogeneous regarding socio-demographic variables, which could be a chance finding.

In group A, mean duration of the current episode of depression was 11.42±7.18 months. It was the first episode of depression for majority of the individuals (n=39, 78%). However, significant issues with the treatment response (poor response or resistance to treatment), adjustment issues with underlying personality and psychosocial factors were clinically assessed and ruled out. The mean duration of treatment in the current episode was 6.36±4.42 months, mean duration of remission (as per patient report) was 3.3±2.3 months. The mean dose of escitalopram was 10.9±2.8 mg/day. Mean HAM-D score was 5.3±1.40. The mean age at onset of the first episode of depression was 32.34±5.42 yr and family history of depression was positive in five patients (10%).

Distribution of overall sexual dysfunction as assessed on FSFI and BSSC-W: Twenty five of the 50 patients (50%) in group A and five individuals in group B had sexual dysfunction (score <26.55) on FSFI. On direct enquiry on BSSC-W, only 38 per cent individuals (n=19) in group A reported dissatisfaction with their overall sexual function and 12 (24%) were willing to seek medical help for their problems, whereas no individuals in group B reported any sexual problems on the BSSC-W (Table I).

Sexual dysfunction in remitted patients of depression receiving escitalopram (*group A*): Patients in group A had dysfunction in domain of desire (n=45, 90%),

arousal (n=43, 86%), orgasm (n=34, 68%), lubrication (n=27, 54%), pain (n=16, 32%) and satisfaction (n=31, 62%). Patients receiving escitalopram had significantly higher sexual dysfunction as compared to healthy controls ($P<0.001$). Group A had significantly higher sexual dysfunction as compared to group B in mean domain score of desire ($P<0.001$), arousal ($P<0.001$), lubrication ($P<0.01$), orgasm ($P<0.001$) and satisfaction ($P<0.001$). Mean domain score of pain in groups A and B did not differ significantly (Table II).

Table I. Sexual dysfunction as per female sexual function index (FSFI) score, sexual dysfunction as per self-report and need for treatment (n=50)

Sexual functioning	Group A, n (%)	Group B, n (%)
FSFI score <26.55	25 (50)	5 (10)
On self-report	19 (38)	0
Reporting need for treatment	12 (24)	0

Table II. Comparison of groups A and B as per mean domain scores of female sexual function index (FSFI)

FSFI domain (cut-off score)	Groups	
	A (n=50)	B (n=50)
Desire (<4.28)	3.25±1.07***	4.21±0.63
Arousal (<5.08)	3.75±1.10***	4.71±0.70
Lubrication (<5.45)	4.82±1.28**	5.37±0.39
Orgasm (<5.05)	3.87±1.48***	5.03±0.37
Satisfaction (<5.04)	4.32±1.30***	5.43±0.44
Pain (<5.51)	5.50±0.82	5.48±0.71

$P^{**}<0.01$, $^{***}<0.001$ compared to group B

Correlation of socio-demographic and clinical variables with sexual dysfunction in group A: No significant correlation of FSFI total and domain scores with age or family income of patients was found. However, years of schooling were found to have significant correlation with domain score of desire ($r=0.513$, $P<0.01$). No significant correlation was found between FSFI total and domain scores and clinical variables (duration of the current episode, duration of treatment and duration of remission, number of episodes or dose of escitalopram) (Table III).

Discussion

The population characteristics of both groups resembled the socio-demographic characteristics of this geographical area as well as that of previous studies[1,25]. As the remission of depression starts 8-12 wk after starting antidepressants[1,26], a minimum of three months treatment with escitalopram was fixed

Table III. Correlation (Pearson correlation analysis) of socio-demographic and clinical variables with sexual dysfunction in group A (patients with depression currently in remission receiving escitalopram)

Variables	*r*, *P*						
	Desire	Arousal	Lubrication	Orgasm	Satisfaction	Pain	Total FSFI score
Age	0.096, 0.649	0.096, 0.646	−0.096, 0.649	0.167, 0.426	0.167, 0.426	0.167, 0.426	−0.007, 0.974
Years of schooling	0.513, 0.009**	0.125, 0.552	0.294, 0.153	−0.272, 0.188	−0.272, 0.188	−0.272, 0.188	0.118, 0.575
Family income	−0.154, 0.402	−0.332, 0.105	−0.119, 0.572	−0.248, 0.232	−0.248, 0.232	−0.248, 0.232	−0.235, 0.258
Duration of the current episode	0.161, 0.441	−0.099, 0.639	−0.204, 0.327	−0.147, 0.482	−0.147, 0.482	−0.147, 0.482	−0.026, 0.278
Treatment duration of the current episode	0.136, 0.518	−0.080, 0.705	0.098, 0.642	−0.310, 0.132	−0.310, 0.132	−0.310, 0.132	−0.179, 0.391
Duration of remission	0.052, 0.805	−0.149, 0.478	0.058, 0.784	−0.292, 0.156	−0.292, 0.156	−0.292, 0.156	−0.202, 0.332
Number of episode(s)	−0.210, 0.314	−0.261, 0.208	−0.108, 0.607	−0.091, 0.666	−0.091, 0.666	−0.091, 0.666	−0.163, 0.436
Dose of escitalopram	0.112, 0.895	0.210, 0.313	0.328, 0.120	0.027, 0.898	0.027, 0.898	0.027, 0.898	0.338, 0.098

*$P<0.01$, significant. FSFI, female sexual function index

in the study individuals to ensure sufficient treatment length for symptom resolution.

As per total cut-off score of FSFI, 50 per cent patients in group A were found to have sexual dysfunction. This value corroborated with the reported range of treatment-emergent sexual dysfunction in females due to escitalopram (40-70%) in literature[13,27]. Fifty per cent patients receiving escitalopram had sexual dysfunction, while only 38 per cent reported sexual dissatisfaction on BSSC-W screener; and even lesser were willing to seek help. Earlier studies have stated under-reporting of sexual problems and poor help-seeking behaviour in women experiencing sexual problems[3]. Considering individual domains of FSFI in study individuals, dysfunction in domain of desire and arousal was most common. In a study conducted by Grover *et al*[13], 91 per cent of patients on SSRIs had reduced desire and 60 per cent had reduced arousal. Partial or non-remission of sexual symptoms even after remission of depressive symptoms as well as similar neurobiological mechanism being determinants of sexual desire and arousal can explain the comparable values of reduced desire and arousal in our study. SSRIs inhibit the nitric oxide synthesis that hinders vaginal blood-flow and lubrication[7]. Dysfunction in domain of pain could be explained on the basis of desire, arousal and lubrication dysfunction which are determinants of the physical discomfort associated with sexual activity.

Five controls were found to have sexual dysfunction on FSFI. Earlier studies report prevalence of 22-40 per cent dysfunction in domain of desire[3] and arousal problems in 11-48 per cent[28] among healthy females. However, in our study, it was noted that the mean domain FSFI scores of group B (apparently healthy female controls) were marginally less than the cut-off scores of respective FSFI scale domains .This might be explained by the fact that domain cut-off scores of original scale were in keeping with data from Western population and liable to be affected by cultural variations.

No significant correlation was found between total FSFI scores and duration of current episode, treatment and remission, number of episodes or dose of escitalopram. In view of lack of relationship between antidepressant-associated sexual dysfunction and most of the socio-demographic and clinical variables in the present study, it could be inferred that, even after clinical remission of depression, significant amount of sexual dysfunction persisted. This can be an aftermath of depression or antidepressant usage[13].

Our study showed that sexual dysfunctions was present in half of the female patients of depression, receiving escitalopram, manifesting in the form of reduced desire, difficulties in arousal, achieving orgasm and lubrication, along with pain during sexual activity and sexual dissatisfaction. Apparently healthy females, who reported no sexual problems on initial screening, were also detected to have sexual dysfunction. This could be due to unawareness towards sexual problems, fear of stigmatization, low emphasis on female sexual satisfaction or possible cultural variation in application of FSFI.

As the sample size was small and the sample was drawn from treatment-seeking population hence, the results could not be generalized. Another limitation was that the assessment of sexual function prior to illness and duration of remission from depression was based on patient recall only. Similarly, the sexual functioning of the individuals' respective spouses before/after the onset of patient's illness was not a part of our evaluation. The cross-sectional study design did not permit the establishment of complete resolution of depressive psychopathology in all the areas including sexual functioning. Further, it may also be noted that FSFI is not a diagnostic instrument and its use in Indian setting has certain limitations due to individual and cultural variations.

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***Conflicts of Interest*:** None.

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