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Female Sexual Dysfunction in Patients Treated with Antidepressants: A Comparison between Agomelatine and Escitalopram

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Aim: This study aims to determine and compare the prevalence of Female Sexual Dysfunction (FSD) between patients on escitalopram and agomelatine, as well as to investigate possible factors associated with their usage.
Study Design: Cross-sectional.
Place and Duration of Study: Psychiatric Day Care Clinic, Department of Psychological Medicine, University Malaya Medical Centre (UMMC), Malaysia, between November 1, 2020 until February 1, 2021.
Methodology: This study is a cross-sectional study involving 66 women with depression from the outpatient psychiatric clinic of a university hospital; 35 of whom were prescribed with escitalopram and 31 with agomelatine. The subjects were in remission and had no significant signs or symptoms of depression for at least 2 months. The prevalence of FSD between the two groups were compared after adjusting for underlying depression severity.
Results: This study showed that the overall prevalence rate of FSD was 33.3%, with the prevalence being higher for those on escitalopram (42.9%) than those on agomelatine (22.6%), but did not achieve statistical significance (*P*=0.081). Out of the six domains of FSD, multivariate

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analyses revealed that there was a significant reduction of 69% in sexual desire disorder (95% CI:0.110, 0.855), *P*=0.022 for those on agomelatine compared to escitalopram. Controlling for drug dosage and depression severity (as measured using Montgomery-Asberg Depression Rating Scale), the odds for patients on agomelatine developing sexual desire disorder was 0.267 (95% CI:0.091, 0.783), *P*=0.016.

Conclusion: There was no significant difference in FSD risk between patients on agomelatine and those on escitalopram. Patients on agomelatine were however less likely to develop sexual desire disorder, which demonstrates a slightly better sexual acceptability profile of agomelatine in women in this respect compared to escitalopram.

Keywords: Female sexual dysfunction; antidepressant; selective serotonin reuptake inhibitor; escitalopram; agomelatine; major depressive disorder.

1. INTRODUCTION

Depression is a leading cause of disability worldwide and is a major contributor to the overall global burden of disease.The lifetime occurrence of depression in any country is between 8 and 10% [1]. The 12-month prevalence of major depressive disorder (MDD) in the United States has been estimated at 6.7%, with 30.4% of cases classified as serious [2]. Relative to men, the odds ratio for women developing MDD in a 12-month period or during their lifetime is 1.4 and 1.7, respectively (significant at 0.05 level; 2-sided test) [3]. In Malaysia, the prevalence of depression is reported to be between 8-12% [4]. It is projected to affect approximately 2.3 million people in Malaysia, at some point in their lives [1].

While antidepressant drug therapy is the preferred treatment for moderate to severe depression, most come with a series of side effects. Of these, antidepressant-induced sexual dysfunction has been found to prolong depression, compromise treatment outcome and lead to non-compliance [5]. Sexual dysfunction is more common in women (43%) than men (31%) who are on antidepressantswith many reporting a lack of sexual interest, an inability to achieve orgasm, an absence of sexual pleasure, lubrication issues, dyspareunia and performance anxiety [6].

Female sexual dysfunction (FSD) is a multifactorial condition with biological and psychosocial components with a prevalence of 29.6% in Malaysia and a worldwide prevalence of 25% to 63% [7]. Studies have shown that sexual dysfunction is highly prevalent (60–80%) in patients treated with antidepressants, with complaints commonly including loss of sexual desire, impaired arousal and lubrication, delayed orgasm, and anorgasmia[8]. Additionally, sexual side effects have been found to lead to poorer adherence and higher discontinuation of medication in most patients who develop antidepressant-induced sexual dysfunction and are thus believed to be a major factor in the failure of treatment for depression [9].

While the actual mechanism underlying antidepressant-induced sexual dysfunction is currently unknown, it has been tied to the effect of antidepressants on serotonergic and dopaminergic systems [10]. Thus, the prevalence of sexual dysfunction varies depending on the type of antidepressant. Selective serotonin reuptake inhibitors (SSRIs) are one of the most common prescribed antidepressants; the prevalence of sexual dysfunction associated with SSRIs is about 36% to 65% [10].Of these, escitalopram has been found to have the lowest risk of sexual dysfunction (30%) [11]. It is commonly prescribed as the first line drugs along with the relatively newly-marketed agomelatine[12]. Agomelatine is a melatonergic antidepressant with fewer sexual side effects compared to older antidepressants, due in part to its antagonist effects on the 5-HT_{2C} receptor instead of the melatonin [13,14].

Though there is a growing amount of research in this area, there exists a dearth of information surrounding this topic as FSD is often underreported and under-recognized[15]. Given that antidepressant-induced sexual dysfunction isone of the main factors contributing to treatment failure, it is necessary to examine antidepressants in terms of their risk for associated FSD particularly among those most commonly prescribed. For this reason, this study aims to identify and directly compare the prevalence of FSD associated with agomelatine and escitalopram in female patients within a university hospital setting, as well as to investigate possible factors associated with their usage.

2. MATERIALS AND METHODS

2.1 Study Design and Subjects

This is a comparative cross-sectional study that aims to compare and assess the prevalence of FSD associated with escitalopram and agomelatine, as well as to examine the potential risk factors associated with them. Data was collected over a period of three months from November 1, 2020 until February 1, 2021. Participants were female patients prescribed with either escitalopram or agomelatine, who fulfilled the inclusion criteria and attended the Psychiatric Clinic at UMMC during the study period. Subjects were included if they were female outpatients diagnosed with major depressive disorder (MDD) based on the 5th edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-V) by the treating psychiatrists in UMMC, were in full remission (no significant signs or symptoms of disturbance present) and with a score of less than 12 on the Montgomery-Asberg Depression Rating Scale (MADRS), aged between 18-65 years old, with a sexually active partner, able to read and understand the Malay language (the national language), they had given consent for the study. Subjects were excluded if they were suffering from chronic and severe mental illness, are pregnant or were within the 2-month post-partum period, active psychosis or actively suicidal or on poly-pharmacy.

2.2 Sample Size

The sample size estimation on the mean difference between agomelatine and escitalopram is based on Walter fang et al. 2006. Taking into consideration of the effect size of mean difference at 0.88, an approximation of 30 participants per group are needed to achieve study power at 0.9 and alpha value of 0.05.

With the consideration of 20% non-respondent rate, the final sample size required for each arm was 40 participants. The sample size calculation was done using G*power software version 3.1.9.2.

2.3 Data Collection

Participants were identified by their treating psychiatrist at the psychiatric outpatient clinic, UMMC, and written consent was obtained. Depressive symptoms were assessed with MADRS and sexual dysfunction with the Malay version of the Female Sexual Function index (MYFSFI). Basic sociodemographic datawas collected using a predesigned questionnaire.

2.4 Instruments

2.4.1 Sociodemographic data questionnaire

A predesigned questionnaire including components such as race, age, marital status, number of years married, family household income, number of children, frequency of sexual intercourse, use of contraception pills, dysmenorrhea, menopause, use of hormone replacement therapy (HRT), smoking or alcohol use, education status, occupation, as well as dosage and duration of antidepressant usage. Current dosage of antidepressant and duration of antidepressant usage was determined from patient and treatment records. Duration of antidepressant usage further referred to the period from the date of first administration to the date of the interview.

2.4.2 Montgomery-asberg depression rating scale (MADRS)

MADRS is a clinician-rated scale used to measure the severity of depression. MADRS consists of 10 items, which are symptoms of depression rated on a scale of 0 (no abnormality) to 6 (severe). A cutoff score of less than or equal to 10 was determined as remission for depression in agreement with that of the Hamilton Rating Scale for Depression (HAMD).

2.4.3 Malay version of female sexual function index (MVFSFI)

The Female Sexual Function Index is a brief, multidimensional patient-rated questionnaire assessing sexual function. It comprises of 19 items that is further divided into 6 basic domains in FSD (desire, subjective arousal, lubrication, orgasm, satisfaction, pain). Each domain consists of two to four questions with five to six options rated from 0 to 1 (lowest score) to 5 (highest score), selected based on the patient's sexual function within the past four weeks prior to answering the questionnaire.

MVFSFI is a validated and locally accepted questionnaire for use in the assessment of FSD within the Malaysian population. A total sum of 55 serves as the cutoff point to differentiate between those with and without FSD (sensitivity = 99%, specificity=97%). Scores below 55 indicate FSD.

2.5 Statistical Analysis

Data was analyzed using the Statistical Package for Social Science (SPSS) version 23. Skewness and kurtosis was used to assess the normality of continuous variables. Independent *t*-test and Man-Whitney *U*-test were used to compare the differences between normally distributed and non-normally distributed variables respectively while Chi-square test was used to assess associations between categorical variables. Multiple logistic regression analysis was employed to examine associations between the continuous independent variables and categorical dependent variables. All statistical analyses were set at a significance level of $p<0.05$.

3. RESULTS

A total of 66 female outpatients diagnosed with MDD and who fit the abovementioned inclusion criteria were included in the study, with 31 patients on agomelatine and 35 on escitalopram. Table 1 shows the sociodemographic data of the study participants. Participants' mean age was about 30 years old with a majority of participants being of Malay descent (57.6%) followed by Chinese (19.7%) and Indian (9.1%). All participants were sexually active with 54.5% of participants being married and the remaining 45.5% not married, widowed or divorced. More than half of the participants were educated at the tertiary level or above (72.7%). Noticeably more individuals with a monthly household income of more than $ 722 were on agomelatine (67.7%) compared to escitalopram (48.6), though household income was not significantly associated with drug affordability (*P*=0.116).

In terms of frequency of sexual intercourse, most participantsreported a frequency of once a week (66.7%), with this being more common for those in the escitalopram group (71.4%) compared to in the agomelatine group (61.3%). Most participants were not on contraceptives (74.2%) and were not menopausal (89.4%).Half of all participants experienced dysmenorrhea and it was lower in the escitalopram group (42.9%) compared to the agomelatine group (58.1%). A majority of participants did not smoke (75.8%) or consume alcohol (50%). However, there were more participants who smoked in the escitalopram group (31.4%) compared to in the agomelatine group (16.1%).

The mean dosage of agomelatine was 25mg with a mean duration of usage of 9 months while that of escitalopram was 10mg and 12 months respectively. Dosage wise, the dosage of agomelatine was statistically higher compared to escitalopram at 0.01 level of significance but the dosage ratio between these two drugs showed no significance ($p> 0.05$).

Table 2 shows the mean depression severity in terms of their MADRS scores associated with agomelatine and escitalopram usage. Those on escitalopram generally had a greater depression severity with a mean score of 10.3 compared to those on agomelatine with a mean score of 8.0. However, there was no significant difference in depression severity between both groups (*P*=0.079).

Table 3 shows a comparison of overall FSD as well as each FSD domain associated with the usage of agomelatine and escitalopram, based on scores from the MVFSFI. 33.3% of all participants in the study were found to experience FSD (95% CI: 22.2-46.0).No significant difference was found between escitalopram and agomelatine in terms of overall sexual dysfunction (*P*=0.081).Out of the six domains of FSD, only sexual desire showed a significant difference between the two groups (*P*=0.022).There was a reduction of 69% in sexual desire disorder (95% CI: 0.110, 0.855) for those treated with agomelatine compared to escitalopram.There were no significant differences in terms of the other domains between the two drugs.

The results of multivariate logistic regression analysis and adjusted odds ratio (OR) are shown in Table 4. Only clinically relevant factors and sociodemographic variables were included in the analysis; particularly, drug dosage and depression severity (based on MADRS) with p values at the 0.10 level were included given their association to different types of drugs [16].Out of seven models constructed based on female sexual dysfunction total score and its subdomains, only sexual desire disorder remained significant. Agomelatine was able to significantly reduce the likelihood ofindividuals developing sexual desire disorder after controlling for its dosage and depression severity. In detail, the odds of a patient with agomelatine treatment who developed sexual desire disorder was 0.267 (95% CI: 0.091, 0.783), *p*= 0.016 adjusted by dosage and depression status.

Table 1. Socio-demographic and health profiles stratified by different drug usage (n=66)

Variables	Agomelatine (n=31)	Escitalopram (n=35)	Tests	*p*
Age[1]	32.0 (13.0)	29.0 (12.0)	488.500[a]	0.487
Marital status			0.292[b]	0.589
Married	18 (50.0)	18 (50.0)		
Not Married	13 (43.3)	17 (56.7)		
Years of marriage[1]	3.0 (8.0)	1.0 (7.0)	499.500[a]	0.570
Race			0.006[b]	0.940
Malay	18 (47.4)	20 (52.6)		
Non-Malay	13 (46.4)	15 (53.6)		
Family household income			2.473[b]	0.116
≤ $ 722	10 (35.7)	18 (64.3)		
> $ 722	21 (55.3)	17 (44.7)		
Number of Children			0.825[c]	0.616
≤ 3	30 (48.4)	32 (51.6)		
> 3	1 (25.0)	3 (75.0)		
Sexual intercourse frequency			0.383[b]	0.383
Once a week	19 (43.2)	25 (56.8)		
> Once a week	12 (54.5)	10 (45.5)		
Education level			0.063[b]	0.801
Secondary and below	8 (44.4)	10 (55.6)		
Tertiary	23 (47.9)	25 (52.1)		
Employment			0.253[b]	0.615
No	8 (42.1)	11 (57.9)		
Yes	23 (48.9)	24 (51.1)		
Contraception usage			0.000[b]	0.993
No	23 (46.9)	26 (53.1)		
Yes	8 (47.1)	9 (52.9)		
Dysmenorrhea			1.521[b]	0.218
No	13 (39.4)	20 (60.6)		
Yes	18 (54.5)	15 (45.5)		
Menopause			1.064[b]	0.302
No	29 (49.2)	30 (50.8)		
Yes	2 (28.6)	5 (71.4)		
Smoke			2.095[b]	0.148
No	26 (52.0)	24 (48.0)		
Yes	5 (31.3)	11 (68.8)		
Alcohol			0.760[b]	0.383
No	19 (43.2)	14 (56.8)		
Yes	12 (54.5)	10 (45.5)		
Dosage (mg)[1]	50.0 (25.0)	15.0 (10.0)	630.000[a]	< 0.001
Dosage/average dosage (ratio)[1]	2.0 (1.0)	1.5 (1.0)	492.500[a]	0.476
Drug duration (months)[1]	9.0 (6.0)	12.0 (20.0)	481.000[a]	0.423

[a] Mann-Whitney U test; [b] = Pearson Chi-square test; [C] = Fischer's exact test; [1] = Median (IQR) where IQR = Interquartile range.

Table 2. Depression status of the patients stratified by different drug usage (n=66)

Variables	Agomelatine (n=31)	Escitalopram (n=35)	Test	*P*
MADRS (Total)	8.0 (4.3)	10.3 (5.8)	-1.783[$]	0.079

[$] Independent t-test

Table 3. Univariate analysis on a comparison of Agomelatine with Escitalopram as antidepressants in association with female sexual dysfunction and its sub-components (n=66)

Drugs	FSFI (total)		OR (95% CI)	*P*
	FSD	No FSD		
Agomelatine	7 (22.6)	24 (77.4)	0.389 (0.133, 1.140)	0.081
Escitalopram	15 (42.9)	20 (57.1)		
	Sexual desire disorder			
	Yes	No		
Agomelatine	9 (29.0)	22 (71.0)	0.307 (0.110, 0.855)	0.022
Escitalopram	20 (57.1)	15 (42.9)		
	Sexual arousal disorder			
	Yes	No		
Agomelatine	6 (19.4)	25 (80.6)	0.524 (0.167, 1.640)	0.263
Escitalopram	11 (31.4)	24 (68.6)		
	Disorder of lubrication			
	Yes	No		
Agomelatine	6 (19.4)	25 (80.6)	0.360 (0.118, 1.102)	0.069
Escitalopram	14 (40.0)	21 (60.0)		
	Orgasmic disorder			
	Yes	No		
Agomelatine	3 (9.7)	28 (90.3)	0.362 (0.087, 1.509)	0.152
Escitalopram	8 (22.9)	27 (77.1)		
	Sexual dissatisfaction			
	Yes	No		
Agomelatine	13 (41.9)	18 (58.1)	0.608 (0.229, 1.613)	0.316
Escitalopram	19 (54.3)	16 (45.7)		
	Sexual pain disorder			
	Yes	No		
Agomelatine	5 (16.1)	26 (83.9)	0.420 (0.127, 1.385)	0.148
Escitalopram	11 (31.4)	24 (68.6)		

OR = Odds ratio; CI = Confidence interval; Ref = Reference group.

Table 4. Multivariate analysis on the effectiveness of Agomelatine as an antidepressant drug with minimum side-effects on female sexual dysfunction in comparison to Escitalopram

Female sexual dysfunction	Agomelatine versus Escitalopram (Ref)			
	Crude OR (95% CI)	*p*	Adjusted OR (95% CI) [#]	*P*
Overall	0.389 (0.133, 1.140)	0.081	0.406 (0.135, 1.220)	0.108
Desire	0.307 (0.110, 0.855)	0.022	0.267 (0.091, 0.783)	0.016
Arousal	0.524 (0.167, 1.640)	0.263	0.511 (0.159, 1.648)	0.261
Lubrication	0.360 (0.118, 1.102)	0.069	0.341 (0.107, 1.084)	0.068
Orgasmic	0.362 (0.087, 1.509)	0.152	0.362 (0.109, 1.208)	0.099
Satisfaction	0.608 (0.229, 1.613)	0.316	0.460 (0.154, 1.372)	0.164
Pain	0.420 (0.127, 1.385)	0.148	0.437 (0.125, 1.526)	0.194

Ref = Reference; OR = Odds ratio; CI = Confidence interval; [#] Adjusted for drug dosage ratio and depression status rated by Montgomery-Asberg Depression Rating Scale (MADRS)

4. DISCUSSION

The main aim of this study was to compare and determine the prevalence of FSD associated with escitalopram and agomelatine among patients at the Psychiatric Clinic of University of Malaya Medical Centre (UMMC). The overall prevalence rate of FSD for both groups was found to be 33.33%. This side effect is highly prevalent in patients on antidepressants and this finding is comparable to previous studies done in western populations where the incidence of FSD is estimated to range from 24% to 91%[10, 11, 17]. Our findings equally echoes the prevalence of FSD in many Asian countries including Hong Kong, Japan, Korea, Taiwan, Singapore, and Malaysia has also been reported to be around 30% [18].

As this study had found that agomelatine was found to have less sexual dysfunction in desire domain as in comparisons of escitalopram in terms of sexual desire disorder had a significant finding whereby *P*= 0.016. This finding was comparable with a study done previously in Canada whereby it was found that agomelatine was an efficacious antidepressant without affecting sexual response and there was clearly less reduction in desire and orgasm in the agomelatine groups compared to venlafaxine group [13]. This finding is in line with previous studies, which found that SSRIs had the most effect on the sexual desire dysfunction subdomain compared to the others [19]. A key factor in influencing sexual desire utilizes dopamine as an essential neutrotransmitter within the mesolimbic system. As SSRIs, such as escitalopram, selectively and strongly blocks serotonin reuptake, which has been found to decrease dopamine activity through serotonin 2 (5-HTT2) receptors in the mesolimbic system, this suggests a possible mechanism of action for induced dysfunction of sexual desire[19].

In adjusting for dosage and depression severity, those on agomelatine were found to be 18.2% less likely to suffer from FSD compared to those on escitalopram. The prevalence of FSD in patients on escitalopram was 42.9%, almost double that in those on agomelatine (22.6%). Evidences so far have found that serotonergic antidepressants (e.g. SNRIs, clomipramine, SSRIs of which escitalopram falls under) are correlated with high levels of sexual dysfunction without major variations between individual drugs while the lowest rates of sexual dysfunction are correlated with mainly non-serotonergic or melatonergic drugs (e.g. bupropion, mirtazapine, and agomelatine)[20]. Sexual dysfunction and depression has been found to have a bidirectional relationship whereby both influences the other [21]. The novel antidepressant agomelatine, which utilizes the melatonergic MT1MT2 receptor agonist with the serotonin 5-HT2C receptor antagonist, has generally been found to display a higher antidepressant efficacy with a favorable adverse-effect profile that is associated with good patient adherence[22]. Thus, it is possible that agomelatine presents a better outcome for one's depression thus bi-directionally reducing the prevalence of FSD among its users.

With regard to clinical characteristics, it was noted that there were no significant associations between drug dosage and FSD. These findings contrast that of Sidi et al.[23]. which compared escitalopram and fluoxetine, and found a significant association between drug dosage and FSD. This is most probably due to the different drugs used in comparison for the particular study. In the previous study the comparison was with fluoxetine and escitalopram in which fluoxetine was known for its sexual side effects whereas in this current study the comparison is between agomelatine and escitalopram in which agomelatine is known to have no sexual side effects. Thus, due to this most probably the sexual dysfunction association could not be found as there is minimal with agomelatine and agomelatine samples are about more than half of the whole study samples of this study. This is evident base on a previous study done, found that the sexual acceptability of agomelatine 25 or 50 mg is particularly optimal and significantly superior to that of escitalopram 20 mg. The level of SD with agomelatine 25 or 50 mg was low and analogous to that of placebo, with no dose-dependent effect [20].Besides that, another reason that would have led this study to have no significant association between the drug dosage and FSD could be also due to the small sample size.

The main limitation of our study is its small sample size of 66 participants; just about half that of the previous study by Sidi et al [17], which possibly accounts for the lack of significant associations as well as the lack of interpretability of the multivariate analyses. Additionally, as this was a cross-sectional study recruiting from only one site, patient selection was limited to the urban population frequenting UMMC. As such, there possibly existed a selection bias within our sample, particularly in regard to participants' socioeconomic class whereby a large majority was of middle to upper class. This further presents issues of generalizability of our findings.

Another limitation of our study was that we did not manage to include several potentially confounding factors such as the degree of substance use, hormonal changes, interpersonal conflict, medical comorbidities, gynaecology issues, cultural influences, as well as sexual functioning of the participant's husbands. Lastly, the fact that the subjects recruited ultimately reported variability's in their FSD incidence since there was no uniformity in the degree or frequency of sexual activity amongst them based on their differing marital status.These are of special interest and could be included in future study as FSD has been found to be linked with

male sexual dysfunction, issues in relationship intimacy, as well as marital disharmony.

5. CONCLUSION

Our study demonstrated that the overall prevalence of FSD in patients on either escitalopram or agomelatine was 33.33%. Adjusting for dosage and depression severity, agomelatine users were found to be 18.2% less likely to suffer from FSD compared to escitalopram users, with the prevalence of FSD in escitalopram users at 42.9% while that of agomelatine users at 22.6%.

CONSENT

As per international standard or university standard, respondents' written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

Ethical approval was obtained from the Ethics Committee of University Malaya Medical Centre (UMMC) prior to the commencement of the study.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Mukhtar F, Oei TPS. A Review on the Prevalence of Depression in Malaysia. Curr Psychiatry Rev 2011;7(3):234-238.
2. Kessler RC, Wai TC, Demler O, et al. Prevalence, severity, and comorbidity of 12-month DSM-IV disorders in the National Comorbidity Survey Replication. Archives of General Psychiatry 2005;62(6):617-627.
3. Kessler RC, Berglund P, Demler O, et al. The Epidemiology of Major Depressive Disorder: Results from the National Comorbidity Survey Replication (NCS-R). Journal of the American Medical Association 2003;289(23):3095-3105.
4. Ng CG. A review of depression research in Malaysia. Medical Journal of Malaysia 2014;69:42-45.
5. Werneke U, Northey S, Bhugra D. Antidepressants and sexual dysfunction. Acta Psychiatrica Scandinavica 2006; 114(6):384-397.
6. Laumann EO, Paik A, Rosen RC. Sexual dysfunction in the United States: Prevalence and predictors. J Am Med Assoc 1999;281(6):537-544.
7. Sidi H, Puteh SEW, Abdullah N, et al. Epidemilogy: The prevalence of sexual dysfunction and potential risk factors that may impair sexual function in Malaysian women. J Sex Med 2007;4(2):311-321.
8. Osváth P, Fekete S, Vörös V, et al. Sexual dysfunction among patients treated with antidepressants - A Hungarian retrospective study. Eur Psychiatry 2003;18(8):412-414.
9. Ashton AK, Rosen RC. Bupropion as an antidote for serotonin reuptake inhibitor-induced sexual dysfunction. J Clin Psychiatry 1998;59(3).
10. Clayton AH, Pradko JF, Croft HA, et al. Prevalence of sexual dysfunction among newer antidepressants. J Clin Psychiatry 2002;63(4):357-366.
11. Clayton AH, Montejo AL. Major depressive disorder, antidepressants, and sexual dysfunction. J Clin Psychiatry 2006;67:33.
12. Cipriani A, Furukawa TA, Salanti G, et al. Comparative efficacy and acceptability of 21 antidepressant drugs for the acute treatment of adults with major depressive disorder: A systematic review and network meta-analysis. Focus 2018; 16(4):420-429.
13. Kennedy SH, Rizvi S, Fulton K, et al. A double-blind comparison of sexual functioning, antidepressant efficacy, and tolerability between agomelatine and venlafaxine XR. J Clin Psychopharmacol 2008;28(3):329-333.
14. Hickie IB, Rogers NL. Novel melatonin-based therapies: Potential advances in the treatment of major depression. The Lancet 2011;378(9791):621-631.
15. Hensley PL, Nurnberg HG. SSRI sexual dysfunction: A female perspective. J Sex Marital Ther 2002;28(sup1):143-153.
16. Ranganathan P, Pramesh C, Aggarwal R. Common pitfalls in statistical analysis: Measures of agreement. Perspect Clin Res 2017;8(4):187.
17. Montejo-Gonzalez AL, Liorca G, Izquierdo JA, et al. SSRI-induced sexual dysfunction: Fluoxetine, paroxetine, sertraline, and fluvoxamine in a prospective, multicenter, and descriptive clinical study of 344 patients. J Sex Marital Ther 1997;23:176-194.

18. Nicolosi A, Glasser DB, Kim SC, et al. Sexual behaviour and dysfunction and help-seeking patterns in adults aged 40-80 years in the urban population of Asian countries. BJU Int 2005;95(4):609-614.
19. Serretti A, Chiesa A. Treatment-emergent sexual dysfunction related to antidepressants: A meta-analysis. J Clin Psychopharmacol 2009;29(3):259-266.
20. Montejo AL, Prieto N, Terleira A, Matias J, Alonso S, Paniagua G, et al. Better sexual acceptability of agomelatine (25 and 50 mg) compared with paroxetine (20 mg) in healthy male volunteers. An 8-week, placebo-controlled study using the PRSEXDQ-SALSEX scale. J Psychopharmacol 2010;24(1):111-120.
21. Balon R. SSRI-Associated Sexual Dysfunction. Am J Psychiatry 2006;163(9):1504-1509.
22. Kennedy SH, Rizvi SJ. Agomelatine in the treatment of major depressive disorder: Potential for clinical effectiveness. CNS Drugs 2010;24(6):479-499.
23. Sidi H, Asmidar D, Hod R, et al. Female Sexual Dysfunction in Patients Treated with Antidepressant-Comparison between Escitalopram and Fluoxetine. J Sex Med 2012;9(5):1392-1399.

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