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Female sexual dysfunction and Escitalopram antidepressant

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Abstract:

Depression is major risk factor for sexual dysfunction (SD),and vice versa. Relative to men, women are at increased risk for depression and anxiety, as well as increased risk of SD**.** Depression may impair sexual well-being by reducing motivation for or reward from engaging in pleasurable activities, interfering with intimate relationship, or increasing the risk of smoking or substance abuse**.** SD associated with depression and SSRIs affects all phase of sexual activity, including desire, arousal, and orgasm. Escitalopram, is an antidepressant of the selective serotonin reuptake inhibitor (SSRI) group . Escitalopram is principally used to treat major depressive disorder or generalized anxiety disorder . Escitalopram, like other SSRIs, can provoke various types of sexual dysfunction such as anorgasmia, decreased libido, genital numbness, and sexual anhedonia , pleasureless orgasm. **Conclusion:** Although escitalopram is associated with FSD , yet , females with mild to moderate depression disorder should be treated with it otherwise they will suffer from SD.

Key words: major depressive disorder; drug naïve females; escitalopram; sexual function**.**

1- Introduction

Depression is a major risk factor for sexual dysfunction (SD) and vice versa (1). Relative to men, women are at increased risk for depression and anxiety, as well as increased risk of SD (2,3). Depression may impair sexual well-being by reducing motivation for or reward from engaging in pleasurable activities, interfering with intimate relationship (4) or increasing the risk of

smoking or substance abuse (5). SD is also a common adverse effect of many antidepressant drugs, especially selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs) (6). SD is also frequently cited as a cause for treatment discontinuation leading to relapse of depression although there is limited evidence supporting this claim (7). SD associated with depression and SSRIs affects all phases of sexual activity including desire, arousal, and orgasm (8).

Escitalopram is a widely used SSRI generally associated with moderate rates of SD according to previous meta-analyses (9-10). However, one analysis found it to be associated with significantly higher rates than some other second-generation antidepressants(11). The study aimed to evaluate the difference in rates and patterns of SD among drug naïve women with mild to moderate depressive disorder (MDD) compared to those receiving escitalopram.

2- Assessment and management of female sexual dysfunction in the context of depression

Depression is related with a 50–70% increased risk of SD, while SD increases the liability of depression by 130–200% (12-13). Further difficult diagnosis of SD in depressed patients, treatment-emergent sexual dysfunction (TESD), involving both the worsening of pre-existing dysfunction and the growth of new dysfunction in previously untroubled patients (14), is a frequent side effect of many antidepressants, often resulting in noncompliant or canceled drug treatment (8).

Table 1. Recommended protocol for clinical assessment of sexual dysfunction.

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Box A. Medical history[2,3,6]	Box B. Psychological factors[3,6]	Box C. Laboratory investigation[2]
• Past sexual dysfunction • Chronic medical conditions, e.g. o Hypertension o Diabetes mellitus o Brain/spinal cord injury • Cancer (past or present), including history of chemotherapy or radiation • Past surgical procedures, e.g. o Pelvic surgery o Prostatectomy • Current medications, e.g. o Antihypertensive medications o Propranolol o Spironolactone o Opioids • Alcohol/drug use • Menopause	• Depression • Social phobia • Anxiety • Obsessive-compulsive disorder • Attention-deficit/ hyperactivity disorder • Distraction • Performance anxiety • Body image • Sexual trauma/abuse • Relationship issues/divorce • Sexual skills	Suggestive blood work: HSDD: • fasting glucose • lipids • testosterone & free testosterone • luteinizing hormone ED: • testosterone & free testosterone • prolactin • glucose • lipids • urinalysis • blood count (anaemia) • TSH • serum creatinine • PSA

ED, erectile dysfunction; HSDD, hypoactive sexual desire disorder; PSA, prostate-specific antigen; TSH, thyroid-stimulating hormone.

3- Management:

Female SD is a common problem with an important effect on well-being (15)**,** with women most often citing problems with arousal (13-16)**.** Psychological interventions are believed to have two principal advantages over pharmacological agents: there are no known unfavorable side effects and they precipitate a broader approach, beyond simply lowering target symptoms (17)**.** Mindfulness therapy has been beneficial in increasing desire, arousal, lubrication, satisfaction, and general functioning in otherwise healthy women who wanted treatment for low sexual desire and arousal (18)**.** Pharmacological interventions involve flibanserin, a nonhormonal oral treatment used to treat hypoactive sexual desire disorder in premenopausal females , which is thought to hinder sexual inhibition effects while helping dopaminergic sexual excitement effects (19-20-21-22). Instead, the antidepressant and smoking cessation help bupropion has been demonstrated to increase desire in non-depressed females and treat SSRI-induced SD in women with MDD (23),and the local (intravaginal) use of dehydroepiandrosterone (DHEA) has shown possibility in treating multiple domains of SD, including reduced libido (15). In addition, testosterone treatment is a long-standing off-label treatment for low libido, particularly for postmenopausal women, though its long-term impacts have not been well studied (24-23).

Table2. Treating MDD while managing SD: Summary of antidepressants and augmentation agents (with lowest effective dose for adults with MDD).

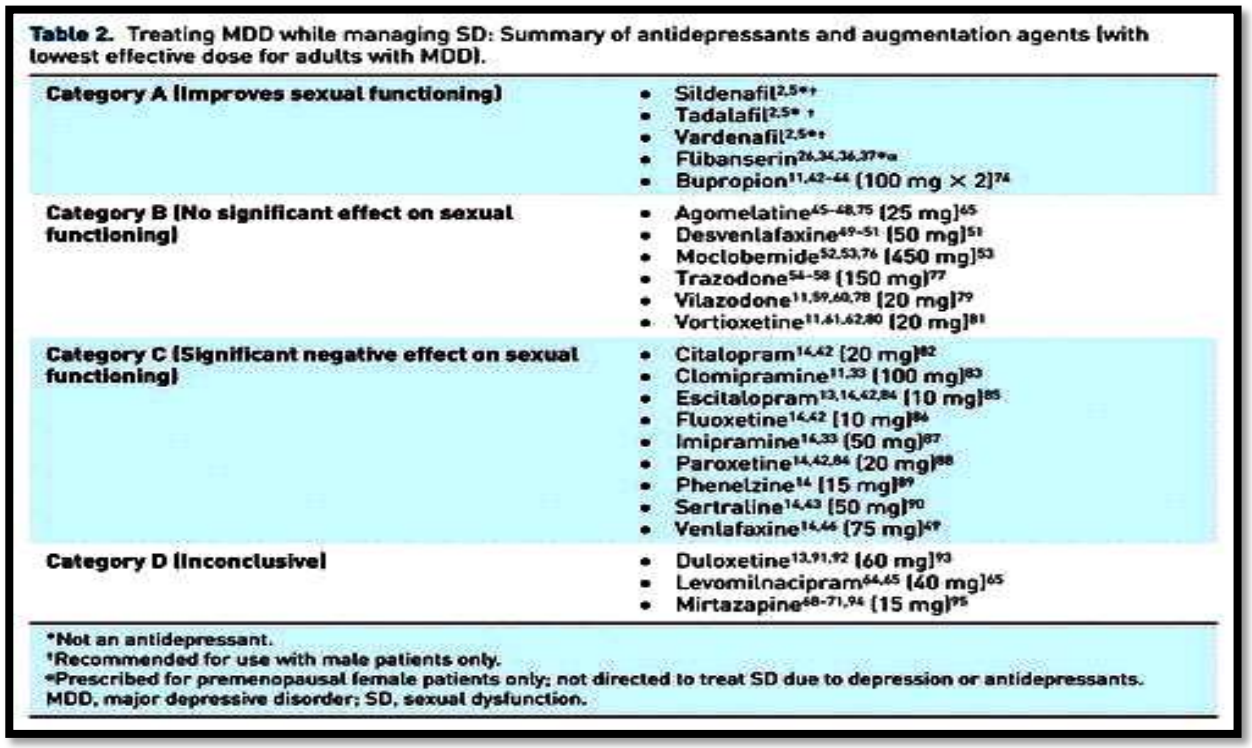

Table 2. Treating MDD while managing SD: Summary of antidepressants and augmentation agents (with lowest effective dose for adults with MDD).

Category A (Improves sexual functioning)	• Sildenafil[2,5*†] • Tadalafil[2,5* †] • Vardenafil[2,5*†] • Flibanserin[26,34,36,37*a] • Bupropion[11,42–44] (100 mg × 2)[74]
Category B (No significant effect on sexual functioning)	• Agomelatine[45–48,75] (25 mg)[45] • Desvenlafaxine[49–51] (50 mg)[51] • Moclobemide[52,53,76] (450 mg)[53] • Trazodone[54–58] (150 mg)[77] • Vilazodone[11,59,60,78] (20 mg)[79] • Vortioxetine[11,61,62,80] (20 mg)[81]
Category C (Significant negative effect on sexual functioning)	• Citalopram[14,42] (20 mg)[82] • Clomipramine[11,33] (100 mg)[83] • Escitalopram[13,14,42,84] (10 mg)[85] • Fluoxetine[14,42] (10 mg)[86] • Imipramine[14,33] (50 mg)[87] • Paroxetine[14,42,84] (20 mg)[88] • Phenelzine[14] (15 mg)[89] • Sertraline[14,43] (50 mg)[90] • Venlafaxine[14,44] (75 mg)[49]
Category D (Inconclusive)	• Duloxetine[13,91,92] (60 mg)[93] • Levomilnacipram[64,65] (40 mg)[65] • Mirtazapine[68–71,94] (15 mg)[95]

*Not an antidepressant.
†Recommended for use with male patients only.
aPrescribed for premenopausal female patients only; not directed to treat SD due to depression or antidepressants.
MDD, major depressive disorder; SD, sexual dysfunction.

In the event of treatment emergent sexual desire, we advise against drug holidays (e.g. leaving medication on weekends) as these can evoke symptoms of medication withdrawal, the reemergence of depressive symptoms, or assist treatment noncompliance (25-13). Instead, physicians might consider switching drugs , increasing an augmentation agent or antidote, or lowering the dose, albeit with cautious monitoring for reduced efficacy (25-13-26-14). When prescribing antidepressants for patients who believe sexual functioning vital , we advise clinicians first consider agomelatine, desvenlafaxine, moclobemide, trazodone, vilazodone, and vortioxetine, as these drugs are least likely to hinder sexual functioning. In some cases, lifestyle alters such as diet, exercise, and smoking arrest , as well as psychotherapy, containing sex therapy, mindfulness therapy, and cognitive behavioral therapy, can also be effective (27).

4- Conclusion and Recommendations:

Although SSRIs are associated with FSD, yet, females with mild to moderate depressive disorder should be treated with SSRIs otherwise they will suffer from SD.

5- References:

1- Bonierbale M., Tignol J.(2003) The ELIXIR study: Evaluation of sexual dysfunction in 4 557 depressed patients in France.

2- Laumann E, Paik A, Rosen R. (1999) Sexual dysfunction in the United States prevalence and predictors. JAMA; 281: 537–544.

3- Lorenz T,Rullo J,Faubion S(2016). Antidepressant-Induced Female Sexual Dysfunction. In Mayo Clinic Proceeding (Vol.91,No.9,pp. 1280-1286).Elsevier.

4- Althof SE, Leiblum SR, Chevret-Measson M, Hartmann U, Levine SB, McCabe M et al (2005).Psychological and interpersonal dimensions of sexual function and dysfunction. J Sex Med;2:793–800.

5- Shifren JL, Monz BU, Russo PA, Segreti A, Johannes CB (2008).Sexual problems and distressin United States women: Prevalence and correlates. Obstet Gynecol.112(5):970-978.

6- Clayton AH, Montejo AL (2006).Major depressive disorder, antidepressants, and sexual dysfunction. J Clin Psychiatry 67(suppl 6):33-7.

7- Jacobsen PL, Mahableshwarkar AR, Chen Y, Chrones L, Clayton AH (2015).Effect of Vortioxetine vs. Escitalopram on Sexual Functionning in Adults with Well-Treated Major Depressive Disorder Experiencing SSRI-Induced Sexual Dysfunction. The journal of sexual medicine 1;12(10):2036-48.

8- Clayton A, Kornstein S, Prakash A, Mallinckrodt C, Wohlreich M. (2007) Changes in sexual functioning associated with duloxetine, escitalopram, and placebo in the treatment of patients with major depressive disorder. J Sex Med; 4 : 917–929.

9- Serretti A, Chiesa A (2009). Treatment-emergent sexual dysfunction related to antidepressants: A meta-analysis. J Clin Psychopharmacol.29:259-66.

10- Gartlehner G, Hansen RA, Morgan LC, Thaler K, Lux L, Van Noord M, Mager U, Thieda P, Gaynes BN, Wilkins T, Strobelberger M, Lloyd S, Reichenpfader U, Lohr KN (2011). "Comparative benefits and harms of second-generation antidepressants for treating major depressive disorder: an updated meta-analysis". Annals of Internal Medicine. 155 (11): 772–85.

11- Reichenpfader U, Gartlehner G, Morgan LC, Greenblatt A, Nussbaumer B, Hansen RA, Van Noord M, Lux L, Gaynes BN (2014). Sexual dysfunction associated with second –generation antidepressants in patients with major depressive disorder: Results from a systematic review with network meta-analysis. Drug Saf 37:19-31.

12- Atlantis, E, Sullivan, T. Bidirectional association between depression and sexual dysfunction (2012) a systematic review and meta-analysis. J Sex Med; 9: 1497–1507.

13- Clayton, AH, ElHaddad, S, Iluonakhamhe, JP.(2014) Sexual dysfunction associated with major depressive disorder and antidepressant treatment. Expert Opin Drug Saf; 13: 1361–1374.

14- Baldwin, DS, Manson, C, Nowak, M. (2015) Impact of antidepressant drugs on sexual function and satisfaction. CNS Drugs**;** 29: 905–913.

15- Nappi, RE, Cucinella, L.(2015). Advances in pharmacotherapy for treating female sexual dysfunction .Expert Opin-Pharmacother 216:875-887.

16- Bijlsma, EY, Chan, JSW, Olivier, B. (2014) Sexual side effects of serotonergic antidepressants: mediated by inhibition of serotonin on central dopamine release? Pharmacol Biochem Behav; 121: 88–101.

17- Fruhauf, S, Gerger, H, Schmidt, HM. (2003) Efficacy of psychological interventions for sexual dysfunction: a systematic review and meta-analysis. Arch Sex Behav; 42: 915–933.

18- Brotto, LA, Basson, R.(2014) Group mindfulness-based therapy significantly improves sexual desire in women. Behav Res Ther; 57: 43–54.

19- Thorp, J, Palacios, S, Symons, J. (2014) Improving prospects for treating hypoactive sexual desire disorder (HSDD): development status of flibanserin. BJOG; 121: 1328–1332.

20- Gao, Z, Yang, D, Yu, L. (2015) Efficacy and safety of flibanserin in women and hypoactive sexual desire disorder: a systematic review and meta-analysis. J Sex Med; 12: 2095–2104.

21- Balon, R. (2016) Flibanserin for hypoactive sexual desire disorder in premenopausal women. Curr Psychiatry**;** 15: 61–64.

22- Vallejos, X, Wu, C. (2017) Flibanserin**:** a novel, nonhormonal agent for the treatment of hypoactive sexual desire disorder in

premenopausal women. J Pharm Pract; 30: 256–260.

23- Kingsberg, SA, Woodard, T. (2015) Female sexual dysfunction**:** focus on low desire. Obstet Gynecol; 125: 477–486.

24- Diaz, VA, Close, JD. (2010) Male sexual dysfunction. Prim Care Clin Office Pract; 37: 473–489.

25- Schweitzer, I, Maguire, K, Ng, C. (2009) Sexual side-effects of contemporary antidepressants: review. Aust N Z J Psychiatry; 43: 795–808.

26- Clayton, AH, Alkis, AR, Parikh, NB. (2016) Sexual dysfunction due to psychotropic medications. Psychiatr Clin North Am; 39: 427–463.

27- Pratap R.,Chokka and Jeffrey R. ,Hankey (2017) : Assessment and management of female sexual dysfunction in the context of depression. Journal of Therapeutic Advances in Psychopharmacology.2045125317720642 doi:10.1177