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Antidepressants, Antipsychotics & Sexual Dysfunction

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Abstract: Sexual dysfunction is a frequent and often underrecognized adverse effect associated with both antipsychotic and antidepressant medications, significantly impacting patients' quality of life, relationships, and adherence to treatment. Antidepressants, particularly those with serotonergic activity such as selective serotonin reuptake inhibitors (SSRIs), are linked to high rates of sexual dysfunction, including decreased libido, arousal difficulties, and delayed or absent orgasm, with prevalence estimates ranging from 30% to over 60% depending on the agent and assessment method. While noradrenergic, dopaminergic, or melatonergic antidepressants tend to have a lower risk, the clinical context often dictates their use. Antipsychotics, especially first-generation agents and those that strongly block dopamine receptors or elevate prolactin levels (e.g., risperidone, haloperidol), are also associated with substantial rates of sexual dysfunction such as erectile, ejaculatory, and orgasmic difficulties. Second-generation antipsychotics like aripiprazole and quetiapine generally have a lower risk, but sexual side effects remain a concern for many patients. These adverse effects are a major cause of treatment nonadherence, particularly among younger patients and those with previously satisfactory sexual function. Effective management requires proactive discussion, individualized risk assessment, and consideration of strategies such as switching to agents with lower sexual side-effect profiles, dose adjustments, or adjunctive therapies. Greater awareness and routine monitoring of sexual function are essential to optimize treatment outcomes and support patient well-being.

Key words: Antipsychotics, antidepressants, sexual dysfunction.

1. Introduction

Sexual Dysfunction (SD) is defined as any reduction in desire or libido, diminished arousal, a decline in the frequency of intercourse, or an undesirable delay in or inability to achieve orgasm. In whole life cycle, women has > 40% prevalence of some form of SD but men do have 30%. Moreover, as the cause of SD, low sexual desire comprises of 22-34% in women & 15% in men, 21% of this male population have premature ejaculation [1].

According to Diagnostic and Statistical Manual of Mental Disorders 5th Edition (DSM-5), male & female sexual dysfunction has been categorized into 4 problems: sexual interest/arousal disorder, erectile disorder, delayed ejaculation and pain disorder [1, 2].

2. Sexual Dysfunction and Psychiatric Disorders

SD is a frequent problem in the population and is often an underrecognized. Its prevalence in psychiatric disorders itself varies. In depressive disorders, SD is present in 45-93% population, in anxiety disorders 33-75%, in Obsessive-compulsive Disorder (OCD) 25-81% and in schizophrenia is around 25%. It significantly impacts Quality of Life, Self Esteem & Intimate relationships of this population, which is also associated with lower treatment adherence that can further exacerbate psychiatric symptoms, creating a cyclical relationship between mental & sexual health [2-4].

Multiple factors have been identified as a risk factor or causes of SD in these populations such as direct effects of psychopathology (as symptoms of depression

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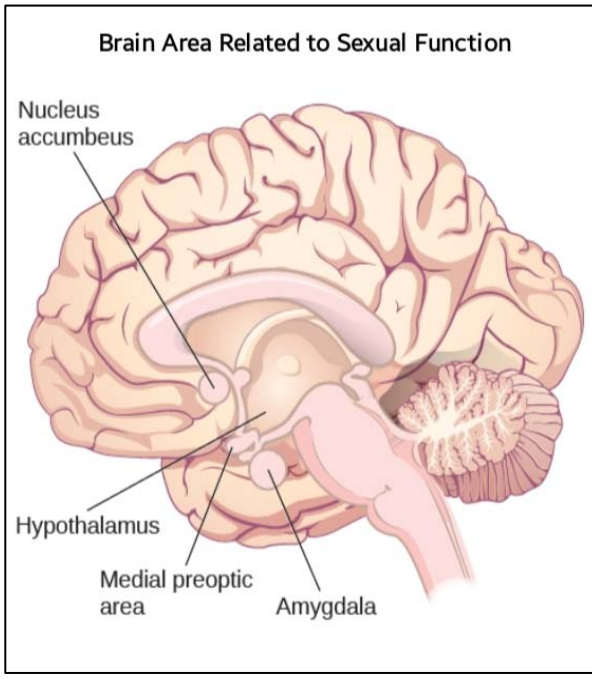
or anxiety), medication side effects (adverse effect associated with both antipsychotic and antidepressant medications), coexisting somatic illnesses, substance use and social & relational factors (trauma, stigma & cultural influences) [4, 5].



Brain area	Sex-related function
Reward system	Triggers sexual motivation Mate choice
Thalamus	Relays erotic stimuli incoming from the spinal cord
Hypothalamus	Coordinates autonomic events in sexual behavior Mate choice Mate choice
Amygdala	Gives emotional significance to incoming erotic stimuli Mate choice Modulates sexual drive
Septal region	Modulates sexual drive
Prefrontal cortex	Blunts the initiation of sexual behavior Modulates sexual drive
Cingulate cortex	Processing sexual stimuli in conflictuary contexts Modules sexual drive
Insula	Awareness of tumescence of erectile organs Modulates sexual drive

Fig. 1 Brain area related to sexual function.

Table 1 How to Differentiate Between Medication-Induced Sexual Dysfunction and Ilness-Induced Sexual Dysfunction.

Medication Induced Sexual Dysfunction	Illness Induced Sexual Dysfunction
• Emerges after starting psychotropic drugs and may persist or worsen with continued use • Symptom Profile ✤ Antidepressants (SSRIs/SNRIs): Delayed orgasm, anorgasmia, erectile dysfunction. ✤ Antipsychotics: Hyperprolactinemia-related symptoms (e.g., amenorrhea, erectile dysfunction, reduced lubrication) or anticholinergic effects (e.g., dry mucosa) • May resolve with dose reduction, switching to lower-risk agents • Clinical Clues ✤ correlates with drug half-life	• Often precedes medication initiation or correlates with acute psychiatric symptoms. • Symptom Profile ✤ Depression: Reduced libido, anhedonia, fatigue. ✤ Psychosis: Social withdrawal, paranoia, or disorganized thinking impairing intimacy • Improves with psychiatric symptom remission • Clinical Clues ✤ aligns with untreated psychiatric symptoms

Antipsychotics, especially first-generation agents and those that strongly block dopamine receptors or elevate prolactin levels (e.g., risperidone, haloperidol), are also associated with substantial rates of sexual dysfunction such as erectile, ejaculatory, and orgasmic difficulties. Second-generation antipsychotics like

aripiprazole and quetiapine generally have a lower risk, but sexual side effects remain a concern for many patients. These adverse effects are a major cause of treatment nonadherence, particularly among younger patients and those with previously satisfactory sexual function [6, 7].

3. Antipsychotics & Sexual Dysfunction

38-86% of patients on antipsychotics will develop SD. There are 3 mechanisms of drugs causing SD: dopamine D2 receptor blockade (causes hyperprolactinemia), anticholinergic & alpha-adrenergic effects and histaminergic & hormonal changes [5]. Its clinical mafestations are decreased libido, erectile/ejaculatory dysfunction, anorgasmia & priapism. There are 2 types of drugs interfering with prolactin which causes SD: prolactin-elevating (haloperidol, risperidone, amisulpride) and Prolactin-sparing (aripiprazole, brepiprazole, quetiapine, olanzapine, ziprasidone) [6, 7].

Psychotropic-Related Sexual Dysfunction Questionnaire.
(PRSexDQ-SALSEX).

The following questions refer to the possible appearance of sexual dysfunction after initiating treatment with psychotropic agents.

A. - Have you observed any type of change in your sexual activity (desire, excitation, erection, ejaculation or orgasm) since you began taking the treatment?
☐ YES ☐ NO

B. - Has the patient spontaneously reported this alteration or was it necessary to expressly question him or her to discover the sexual dysfunction?
☐ YES *It was spontaneously reported* ☐ NO *It was not spontaneously reported.*

1. - Have you observed any decrease in your desire for sexual activity or in your interest in sex?
0. - *No problem*
1. - Mild decrease. Somewhat less interest.
2. - Moderate decrease. Much less interest.
3. - Severe decrease. Almost none or no interest.

2.- Have you observed any delay in ejaculation/orgasm?
0.- *No delay*
1.- Mild delay or hardly noticeable
2.- Moderate delay or clearly noticeable.
3. - Intense delay, even sometimes orgasm is not possible.

3. - Have you observed that you are unable to ejaculate/or to have an orgasm once you begin sexual relations?
0. - *None.*
1. - Sometimes: less than 25% of the time.
2. - Often: 25-75% of the time.
3. - Always or almost always: more than 75% of the time.

4. - Have you experienced any difficult obtaining an erection or maintaining it once you have initiated sexual activity? (vaginal lubrication in women)
0. - *Never.*
1. - Sometimes: less than 25% of the time.
2. - Often: 25-75% of the time.
3. - Always or almost always: more than 75% of the time.

5. – How well have you tolerated these changes in your sexual relations?
0.- *No sexual Dysfunction*
1.- Well. No problem due to this reason
2.- Fair. The dysfunction bothers him or her although he or she has not considered discontinuing the treatment for this reason. It interferes with the couple's relationship.
3.- Poor. The dysfunction presents an important problem. He or she has considered discontinuing treatment because of it or it seriously interferes with the couple's relationship.

TOTAL SCORE:

MILD. 0-5 (with no item >1); MODERATE: 6-10 (OR any item =2, with no item =3); SEVERE: 11-15 (OR any item =3)

PRSexDQ-SALSEX questionnaire [6].

4. Antidepressants & Sexual Dysfunction

27-65% of women & 26-57% of men receiving SSRIs/SNRIs reported that they experience SD. It is caused by SSRIs/SNRIs serotonergic modulation and its dopaminergic & noradrenergic effects. SD is manifested as decreased libido, anorgasmia, erectile dysfunction & delayed ejaculation. Antidepressants categorized as high risk to cause SD are paroxetine, sertraline & fluoxetine, lower risk drugs are fluvoxamine, escitalopram, agomelatine, bupropion, mirtazapine & Vrotioxetine [6, 8].

5. Management

Effective management requires proactive discussion, individualized risk assessment, and consideration of strategies such as switching to agents with lower sexual side-effect profiles, dose adjustments, or adjunctive therapies. Greater awareness and routine monitoring of sexual function are essential to optimize treatment outcomes and support patient well-being.

To assess Medication Induced SD clinicians are encouraged to use routine inquiry (which are often underreported) & to use structured questionnaires & clinical interview. Generally, clinicians should address reversible cause (medical & psychological), educate patients and shared-decision making is chosen. 1 questionnaire can be widely & easily used is Psychotropic-Related Sexual Dysfunction Questionnaire (PRESexDQ-SALSEX). It comprised of 5 points with score of 0 to 3. The total score is interpreted as mild (0-5, with no item > 1), moderate (6-10 Or any item = 2, with no item = 3), severe (11-15, or any item = 3) [6, 8].

In Antipsychotic-Induced SD, prolactin-sparing antipsychotics (aripiprazole, brexpiprazolem ziprasidone) is chosen, with lower dose preferred. Adjunctiove treatments such as PDE-5 (for erectile dysfunction) & hormonal theray (estrogen/testosterone) in selected cases can be used [7-9].

In antidepressant-induced SD, switching to lower risk agents such as agomelatine, bupropion, mirtazapine, vortioxetine and the use of strategies such as dose reduction or drug holidays (with caution). Several adjunct therapies can be used such as bupropion, PDE-5 inhibitors & Vaginal lubricants [7-9].

After all efforts, monitoring and follow up will increase likelihood of success to solve this problem.

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