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Sexual Dysfunction in Schizophenia Patients

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ABSTRACT

Sexual dysfunction (SD) is a significant but often overlooked complication among patients with schizophrenia, with a global prevalence of 56.4%—55.7% in men and 60.0% in women. SD in this population is generally caused by both the symptoms of schizophrenia and the side effects of antipsychotic treatment, leading to diminished motivation for intimacy and potential disruption of marital relationships. Despite its impact on quality of life, SD remains underdiagnosed and stigmatized in clinical practice. This literature review aims to explore the general aspects of sexual dysfunction, its various types in patients with schizophrenia, and potential treatment strategies based on current clinical guidelines and considerations. The review was conducted using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) method. Findings show that the global incidence of sexual dysfunction among schizophrenia patients increased by over 65% between 1990 and 2019, affecting an estimated 941,000 to 1.3 million individuals, primarily due to antipsychotic use. Management strategies include reducing antipsychotic dosages or switching to prolactin-sparing medications, with aripiprazole being the most frequently recommended option.

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INTRODUCTION

Schizophrenia is a serious psychiatric disorder that affects approximately 1% of the world's population. In addition to core symptoms such as hallucinations and delusions, schizophrenia patients often experience various side effects as a result of antipsychotic treatment. One of the less understood but significant side effects is Sexual Dysfunction (SD). Sexual dysfunction includes a variety of disorders, such as decreased sexual desire, erectile dysfunction, premature ejaculation, and orgasm problems, which can reduce a patient's quality of life (Montejo et al., 2021)

The results of a systematic review and meta-analysis conducted by Theo Korchia et al, showed that SD occurs more frequently in schizophrenia than in schizoaffective disorder without marked improvement over time or better tolerance (Korchia et al., 2023).

From 1990 to 2019, the initial prevalence of schizophrenia (14.2 to 23.6 million), the incidence of SD was estimated at 941,000 to 1.3 million, in that span of years each increased by more than 65%, while age-standardized estimates remained globally roughly stable (Solmi et al., 2023). Although patients consider sexual problems to be highly relevant, patients and doctors do not easily discuss these problems spontaneously, leading to an underestimation of their prevalence and contributing to a decrease in adherence to treatment (Solmi et al., 2023).

Experts think that patients with schizophrenia may have difficulty managing their sexual lives and are reluctant to discuss sexual problems with their treating doctors. In this literature review, the author is interested in writing about SD in schizophrenic patients with the hope of increasing awareness in considering the choice of antipsychotic and monitoring clinical symptoms during antipsychotic administration, so that it can support the effectiveness of antipsychotic therapy given and try minimize the occurrence of these side effects, then provide management considerations.

Literature review

Guidelines for Diagnostic Classification of Mental Disorders III (PPDGJ III) defined schizophrenia as a syndrome with a wide variety of causes and disease courses, which are caused by genetic, physical, and socio-cultural factors. Schizophrenia is characterized by fundamental and characteristic deviations of thought and perception, as well as unnatural or blunted affect (Maslim, 2013).

The prevalence of schizophrenia is 1 in 300 people (0.32%) or around 24 million people worldwide suffer from schizophrenia (World Health Organization [WHO], 2024). In Indonesia, the prevalence of schizophrenia or psychosis is 7 per 1000 households. with the highest prevalence in Bali province at 11 per 1000 people, Yogyakarta 10 per 1000 people while the lowest in the Riau Islands province at 3 per 1000 people (Kementerian Kesehatan RI, 2018).

Schizophrenia patients show different clinical presentations, response to therapy and disease course. Schizophrenia is caused by many factors, one of which is the diathesis-stress model which is often used. This model explains that a person has a biological vulnerability that is triggered by stress which can cause symptoms of schizophrenia. Diathesis or stress can be biological stress (for example infection), genetic, psychological (for example a stressful family situation or the death of a close relative), environmental or both (Sadock & Sadock, 2004).

Several studies suggest that there is a pathophysiological role for certain brain areas, namely the limbic system, frontal cortex, cerebellum and basal ganglia. These four areas are interconnected so that dysfunction in one place gives rise to pathological processes in other places (Yudhantara & Istiqomah, 2018). A series of studies suggest a genetic component in the inheritance of schizophrenia. A person has a tendency to suffer from schizophrenia if there are family members who suffer from this disorder and a person has a tendency to suffer from schizophrenia as well. Sigmund Freud stated that schizophrenia was caused by growth fixation in childhood, this linked the existence of ego defects which played a role in the emergence of schizophrenia. Another theory states that schizophrenic patients have difficulty releasing energy, mentally and emotionally due to frustration and conflict with other people (Sadock & Sadock, 2004). Infection in early childhood also causes an inflammatory process that affects the brain development of infants and children, making them vulnerable to the emergence of schizophrenia and other mental disorders in the future (Yudhantara & Istiqomah, 2018).

The diagnosis of schizophrenia is made by meeting several criterias such as thought of echo, thought of insertion, or thought of broadcasting; delusion of control, delusion of influence, or delusion of passivity; auditory hallucinations; and other persisting delusions.

Therapy for schizophrenia includes pharmacological and non-pharmacological therapy. Non-pharmacological therapy can be in the form of family-based intervention, cognitive behavioral therapy, or neuromodulation therapy (Yudhantara & Istiqomah, 2018). Administration of antipsychotics is still a mainstay in the management of schizophrenia. About 70 percent of patients treated with antipsychotics achieve remission or improve (Sadock & Sadock, 2004).

Sexual dysfunction (SD) is a difficulty experienced by individuals or couples during each stage of sexual activity which includes desire, excitement, vaginal lubrication for women, erection/ejaculation, orgasm for men. SD has a major impact on a person's perceived quality of life (Dumontaud et al., 2020).

In the journal Systematic Review and Meta-Analysis involving 72 studies from 33 countries on 6 continents published from 1982 to June 2022 with a total of 21,076 participants with schizophrenia, the global prevalence of SD obtained was 56.4%, with a prevalence of 55.7% for men and 60.0% women. The most common SD is erectile dysfunction in men, followed by loss of libido in men, ejaculation dysfunction in men, orgasm dysfunction in women 28%. In another study, it was said that in men with schizophrenia, the prevalence of SD was estimated at 55.7%. Another 44.0% were estimated to have erectile dysfunction, and 38.6% had ejaculatory dysfunction. Among women

with schizophrenia, SD is even greater—estimated at 60.0%. A quarter (25.1%) were estimated to experience amenorrhea and 7.7% galactorrhea (Korchia et al., 2023). SD in schizophrenic patients can be caused by various things, and often arises from the interaction of various complex factors, although there is no definite cause (Montejo et al., 2021).

Several factors contribute to the high incidence of DS in schizophrenia patients, including age, gender, the patient's marital status, psychotic symptoms, employment status, and the treatment received by the patient.

Sexual dysfunction will increase with age in normal patients, as well as in schizophrenic patients. It was found that as the age of schizophrenic patients increases, the SD rate is higher than in normal patients of the same age. This applies to both male and female patients (Dumontaud et al., 2020). Schizophrenia in women is known to have a peak attack after the age of 40 years, which is also the perimenopause period which is characterized by a rapid decline in estrogen levels in women. The most common interpretation of age differences is that it reflects the estrogen hypothesis, which postulates that estrogen plays a protective role against schizophrenia (Lodha & Sousa, 2020).

In several studies, it was found that female schizophrenia patients are more at risk of developing SD (Düring et al., 2019; Kirino, 2017; Martín et al., 2018). It is known that in the first half of life, the incidence of SD in male patients with schizophrenia is higher than in women, while in the second half of life (age of menopause), the incidence of SD in female patients with schizophrenia is higher[15]. Female patients most often experience loss of libido and arousal disorders, while in male patients, erectile dysfunction and loss of libido are the most frequently occurring SD (Dumontaud et al., 2020).

Schizophrenia patients will be more at risk of developing SD if the symptoms of the disease appear more frequently or recur (Dumontaud et al., 2020). It is known that the more serious the patient's disease, the worse the patient's sexual function (Vargas-Cáceres et al., 2021). In a qualitative study in the Netherlands involving 28 patients with psychotic disorders, 18% of patients felt shame after experiencing psychotic symptoms, which affected their sexual expression (Barker & Vigod, 2020).

Patients with schizophrenia who do not have a job tend to experience higher levels of SD compared to patients with schizophrenia who have a job (Dumontaud et al., 2020). One of the causes of this may be the decrease in self-confidence in schizophrenia patients, which causes SD (Olisah, Sheikh, Abah, & Mahmud-Ajeigbe, 2016).

The tuberoinfundibular pathway originates from the hypothalamus to the anterior pituitary gland. This pathway is responsible for controlling prolactin secretion. The central neurotransmitter dopamine functions to inhibit prolactin secretion. If this function is disrupted as a result of antipsychotic drugs blocking the ptuitary D2 receptor, then prolactin levels in the blood will increase (Patel, Cherian, Gohil, & Atkinson, 2014). Hyperprolactinemia can cause many effects related to SD and fertility in patients such as galactorrhea and menstrual cycle disorders (Basson & Gilks, 2018). Hyperprolactinemia is also thought to be related to low testosterone levels in male patients who receive antipsychotic drugs, causing symptoms in the breasts (gynecomastia, discharge from the nipples) and in the penis, namely difficulty achieving an erection, reduced nighttime erections, difficulty achieving ejaculation (Redman, Kitchen, Johnson, Bezwada, & Kelly, 2021). In a systematic review, it was discovered that first generation or typical antipsychotics were the antipsychotic drugs that most often caused DS side effects in schizophrenia patients (Dumontaud et al., 2020).

Antipsychotics are grouped into prolactine rising, for example risperidone, and prolactine-sparing, for example, clozapinem, Quetiapinem, Olanzapine, Ziprasidone and Aripiprazole. Prolactine-sparing is an antipsychotic that has a lower likelihood of hyperprolactinemia (Anwar & Khairina, 2023).

Haloperidol can increase serum prolactin levels to 20-40 ng/mL at therapeutic doses, which can cause libido disorders, amenorrhea, gynecomastia, and erectile dysfunction (Mathur & Uniyal, 2019). From evidence from a large prospective cohort study, 71.1% of men and women taking haloperidol for 12 months complained of SD consisting of libido disorders, amenorrhea, gynecomastia, erectile dysfunction, and galactorrhea. The prevalence rate of decreased libido was 60.0%, erectile dysfunction was 52.3%, and amenorrhea was 53.8% (Dossenbach et al., 2006). In another study in India, haloperidol was administered to female patients, about 24% of patients

complained of decreased libido, while 9.4% complained of impaired arousal and arousal. As many as 8.1% complained of vaginal dryness (Lodha & Sousa, 2020).

Risperidone is an atypical antipsychotic that has a high potential for increasing serum prolactin levels. A small study reported the occurrence of gynecomastia, galactorrhea, and priapism in male patients. Meanwhile, female patients were reported to experience amenorrhea and galactorrhea with routine consumption of risperidone (Mathur & Uniyal, 2019). Based on clinical trials and cross-sectional studies, risperidone increases serum prolactin to 30~60 ng/ml when used at therapeutic doses. A 5-year prospective observational study evaluating 128 men and 90 women reported that risperidone induced a greater increase in prolactin than other atypical antipsychotics (Eberhard, Lindström, Holstad, & Levander, 2007). Evidence from another large prospective observational study showed that 67.8% of men and women receiving risperidone for more than 1 year experienced SD. Decreased libido was the most frequently reported disorder (described by 60.0% of patients), while 46.0% of patients reported erectile dysfunction (Dossenbach et al., 2006). Another study showed that the relative impact of antipsychotics on SD linked risperidone to high rates of SD (Lodha & Sousa, 2020).

Clozapine is known to rarely increase serum prolactin levels (Dumontaud et al., 2020). Although the incidence is small, when clozapine causes hyperprolactinemia, it can cause decreased libido and impaired arousal (Mathur & Uniyal, 2019). A retrospective study investigated through medical record review reported a significantly lower proportion of patients with SD in the clozapine group compared with the haloperidol and risperidone groups. However, SD is associated with anti-adrenergic and anticholinergic effects, erection and ejaculation problems and priapism may occur with clozapine (Cutler AJ, 2004).

Olanzapine is an atypical antipsychotic that works by binding to 5-HT2A/2C, D1-D4, H1, and adrenergic receptors. High levels of prolactin can reduce pituitary gonadotropin secretion, thereby inhibiting the patient's reproductive function (Mathur & Uniyal, 2019). In a study in Taiwan, it was found that more than 50% of subjects who received olanzapine experienced hyperprolactinemia, and the higher the prolactin level, the more severe the SD experienced by the patient (Wu et al., 2021). In an open-label randomized comparison of the impact of olanzapine versus risperidone on sexual function, fewer SD occurred in the olanzapine-treated group (n=20) than in the risperidone group (n=19), with a large significant difference in erections. erectile dysfunction (erectile dysfunction: 0% in the olanzapine group vs. 31.6% in the risperidone group) (Knegtering et al., 2006).

In a study comparing the administration of brexpiprazole and risperidone in patients with depression and schizophrenia. Patients given brexpiprazole showed a slight increase in prolactin (mean increase, 0.95 ng/mL) when compared with patients given risperidone and paliperidone showed a very high increase in prolactin (37.98 and 48.51 ng/mL) thus confirmed that brexpiprazole had little impact on prolactin levels in patients with depression or schizophrenia (Clayton et al., 2020). Another study conducted research on two groups of schizophrenia patients with prolactin levels that exceeded baseline. Prolactin levels in patients with schizophrenia who were given brexiprazole tended to decrease over time, regardless of previous treatment, when compared with patients given placebo (Ivkovic et al., 2019).

In large population studies, quetiapine was not associated with increases in prolactin levels when used in therapeutic doses (Kelly & Conley, 2004). Patients with schizophrenia or other psychotic illnesses were randomly assigned to receive quetiapine (200~1200 mg/day) or risperidone (1~6 mg/day) for 6 weeks. SD was lower in patients treated with Quetiapine than in patients treated with risperidone. In particular, there is a significant difference in decreased libido and arousal disorders (Knegtering et al., 2006).

Aripiprazole is used as a treatment for schizophrenia and bipolar disorder. It is a partial dopamine agonist that also has affinity with 5-HT2A receptors (Mathur & Uniyal, 2019). Due to its 5-HT1A agonism and partial 5-HT2A antagonism properties, aripiprazole is associated with no increase in prolactin levels (Kirino, 2017). A study argues that aripiprazole provides a smaller SD effect than risperidone, olanzapine, or quetiapine (Montejo et al., 2021). In fact, in several small studies, it was found that when used together with other antipsychotics, aripiprazole could reduce initially high serum prolactin levels (Balon, 2019).

There are findings in studies that suggest that measuring serum prolactin and thyroid-stimulating hormone can be used as a tool to assess schizophrenic patients who suffer from SD.

Regarding specific symptoms, especially in women there is decreased arousal at the beginning of diagnosis and galactorrhea after treatment. Other studies suggest DS may be present in patients with schizophrenia before starting antipsychotic treatment and patients, especially those who are women, become predisposed to hyperprolactinemia after antipsychotic treatment (Edinoff et al., 2021). SD can also be confirmed using various validated instruments such as the Arizona Sexual Experience Scale, Sexual Behavior Questionnaire or other available questionnaires (Zhao et al., 2020).

A number of studies have concentrated on treatment methods that can reduce DS in schizophrenic patients given antipsychotics. The first strategy is to assess whether DS is caused by psychological or somatic factors because treatment must be given first. If no psychological or somatic factors are found or have been resolved, then the first treatment option is to reduce the dose of the antipsychotic the patient is taking or switch to an antipsychotic that does not really interfere with sexual function such as aripiprazole, or use additional therapy such as phosphodiesterase-5-inhibitors (PDE- 5-inhibitor). All patients should be evaluated to determine whether treatment alternatives increase their risk of psychiatric symptoms. However, most studies state that there is rarely an increase in psychotic symptoms when switching to an antipsychotic strategy or adding a dopamine agonist (de Boer et al., 2015).

Another study in Japan looked at the adjuvant use of aripiprazole to treat hyperprolactinemia. This study found that prolactin levels at week 4 and after were significantly lower than at the start of the study, SD also increased significantly, as measured by erectile dysfunction in men and menstrual irregularities (Edinoff et al., 2021).

Open-label studies suggest that adjuvant therapy with aripiprazole, vardenafil, peony-glycyrrhiza herb, carbegoline, amantadine, shakuyaku-kanzo-to, and imipramine may improve return of sexual function. Another study showed that switching from antipsychotics that often cause elevated prolactin levels to aripiprazole, ziprasidone, olanzapine, and quetiapine (prolactin-sparing antipsychotics) improved sexual function. Of the antipsychotic treatment options, the most studied is the switch to aripiprazole (de Boer et al., 2015).

When treatment selection is made, the potential for increased psychiatric symptoms should be explained to the family although no studies have reported on patient psychiatric symptoms after antipsychotic switching. A limited number of studies have focused on treatment strategies to reduce DS in patients treated with antipsychotics including reducing the dose or switching to an antipsychotic with less detrimental effects on sexual function with dopamine agonists, aripiprazole or phosphodiesterase-5-inhibitors (PDE-5-inhibitors) is the main treatment option (de Boer et al., 2015). The following treatment guidelines for SD in schizophrenia can be seen in Figure 1.

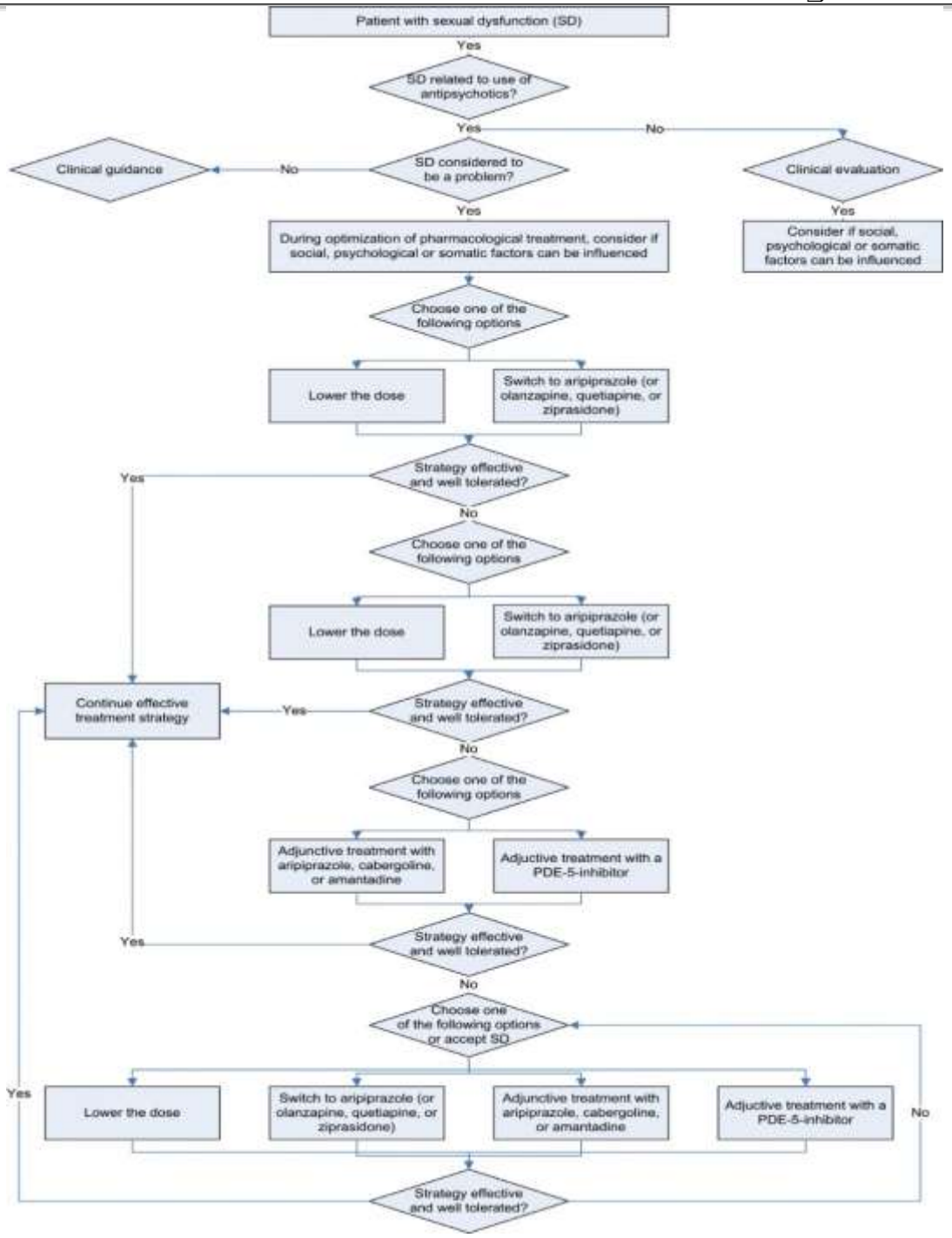

Figure 1. Sexual dysfunction management guideline in schizophrenia

METHODOLOGY

This study was conducted using a literature review approach based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Relevant articles and publications were systematically identified and reviewed to gather comprehensive insights into sexual dysfunction (SD) in patients with schizophrenia. The sources analyzed include global and regional studies, meta-analyses, cohort studies, and clinical trials published between 1982 and 2022, involving data from various countries across six continents. The review focused on the prevalence, types, contributing factors, and treatment strategies for SD related to antipsychotic use in schizophrenic populations.

RESULTS

The global prevalence of sexual dysfunction among patients with schizophrenia was found to be 56.4%, with 55.7% in males and 60.0% in females. The most common sexual dysfunctions in men include erectile dysfunction, decreased libido, and ejaculatory issues, whereas women frequently report orgasmic disorders, amenorrhea, and galactorrhea. The incidence of SD has increased significantly over the last few decades, with an estimated 941,000 to 1.3 million cases globally between 1990 and 2019, representing a more than 65% increase. One of the main contributors to SD in schizophrenia patients is the use of antipsychotic medications, particularly those associated with elevated serum prolactin levels. Risperidone and haloperidol are frequently reported to cause hyperprolactinemia and subsequent sexual side effects.

In contrast, antipsychotics such as aripiprazole, quetiapine, olanzapine, and clozapine are considered prolactin-sparing and are associated with a lower incidence of SD. Clinical strategies to address SD include reducing the dosage of antipsychotics, switching to prolactin-sparing antipsychotics, or adding adjuvant therapies such as phosphodiesterase-5 inhibitors or aripiprazole. Several open-label and observational studies support the effectiveness of these approaches in improving sexual function without significantly increasing psychotic symptoms.

DISCUSSION

Sexual dysfunction (SD) in schizophrenia patients is a complex condition influenced by biological, psychological, and social factors. The primary biological cause is the use of antipsychotic medications, particularly those associated with increased prolactin levels, such as risperidone and haloperidol, which can disrupt the hypothalamic-pituitary-gonadal axis [Montejo et al., 2021]. Nonetheless, the underlying pathology of schizophrenia itself—characterized by negative symptoms such as anhedonia, social withdrawal, and motivational impairments—also contributes to diminished sexual drive and performance independent of pharmacological treatment [Solmi, 2019]. Therefore, distinguishing between medication-induced SD and disease-related factors is crucial when determining the most appropriate management strategies.

The psychological and social implications of SD are significant. Patients experiencing SD often report feelings of shame, frustration, and lowered self-esteem, which can negatively affect their intimate relationships and overall quality of life [Mathur & Uniyal, 2019]. Furthermore, untreated SD may reduce adherence to antipsychotic therapy, as patients might associate the side effects with reduced life satisfaction. Social stigma surrounding mental illness and sexual health often prevents open discussions during consultations, resulting in underdiagnosis and undertreatment of this problem [Montejo et al., 2021]. It is essential for mental health professionals to proactively address sexual health concerns to improve both treatment adherence and psychosocial outcomes.

From a pharmacological standpoint, switching to antipsychotics with lower prolactin impact—such as aripiprazole, quetiapine, or clozapine—has been associated with improved sexual function without compromising psychiatric symptom control [Solmi, 2019]. Aripiprazole, in particular, has been widely recommended due to its unique partial dopamine agonist properties, which not only help stabilize psychotic symptoms but also reduce hyperprolactinemia [Mathur & Uniyal, 2019]. Adjunctive use of aripiprazole alongside other antipsychotics has been reported to lower prolactin levels and improve erectile function in men and menstrual regularity in women [Montejo et al., 2021]. However, medication adjustments must be carefully monitored to prevent relapse or destabilization of psychiatric symptoms.

Non-pharmacological strategies can also play an important role in improving sexual health. Interventions such as psychoeducation, cognitive behavioral therapy (CBT), and sexual counseling have been shown to reduce anxiety and misconceptions surrounding sexuality among patients with schizophrenia [Author, Year]. Partner-focused therapy is particularly beneficial in addressing relationship strains caused by SD and helping couples develop healthier communication. Combining these approaches with pharmacological interventions creates a more comprehensive care model that addresses both the physical and psychological aspects of sexual health.

In summary, sexual dysfunction should be recognized as a vital aspect of holistic schizophrenia care. Regular assessments of sexual health, open patient-doctor communication, and the integration of both pharmacological and non-pharmacological interventions are crucial in improving treatment outcomes and quality of life [Montejo et al., 2021]. Future studies should

explore personalized treatment algorithms and cultural factors influencing sexual health in patients with schizophrenia, particularly in under-researched populations

CONCLUSION

Patients who experience sexual dysfunction are advised to reduce the dose of antipsychotics, or replace them with prolactin-sparing antipsychotics. Aripiprazole is the antipsychotic most commonly recommended for cases of sexual dysfunction in schizophrenia. In clinical consultations, psychological, social, symptomatic and treatment elements related to sexual activity should be routinely evaluated at each patient's follow-up. Additionally, understanding how sexuality affects an individual's overall quality of life is critical to determining whether a patient's treatment adjustments are necessary. Providing an explanation to the patient about all possible factors and alternative treatment options that can be offered to the patient if there is a decrease in sexual function or SD.

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