



Influence of Antipsychotic Agents on the Sexuality of Patients Diagnosed with Schizophrenia

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ABSTRACT

Background: Sexuality is a natural component of human behavior. The general population has been extensively studied since the first half of the 20th century. On the other hand, regarding patients treated for schizophrenia, discussing sexual disorders was initially considered inappropriate because it was believed they should not be sexually active. Given these findings, this work proposes to study the sexuality of patients with schizophrenia.

Objectives: Our objectives were to assess the sexuality of patients with schizophrenia, to identify factors associated with sexual dysfunction among these patients, and to determine practitioners' attitudes toward the sexuality of our study population.

Methods: This is a cross-sectional study carried out in the Psychiatry Department of Kairouan (outpatient department), including 46 patients diagnosed with schizophrenia. A pre-established information sheet was completed for each patient recruited, including sociodemographic and clinical data; on the other hand, 3 scales ensured a sexual psychometric evaluation: Psychotropic-Related Sexual Dysfunction Questionnaire, Arizona Sexual Experiences Scale, and Changes in Sexual Functioning Questionnaire-Male Clinical Version.

Results: Concerning the evaluation of sexuality according to the scales used, sexual dysfunction according to Psychotropic-Related Sexual Dysfunction Questionnaire scores was observed in 31 patients (67.4%). According to Arizona Sexual Experiences Scale scores, 24 patients (52%) had a sexual dysfunction, and for the total score of the Changes in Sexual Functioning Questionnaire-Male Clinical Version, 27 patients (58.7%) had a sexual dysfunction. We cannot confirm the existence of a relationship between the dose of the current treatment (in chlorpromazine equivalent) used and the results of the test assessing sexuality. In addition to these results, we can deduce the existence of a statistically significant association between the antipsychotic agent used and the results of the Psychotropic-Related Sexual Dysfunction Questionnaire only.

Conclusions: We recommend that screening for sexual dysfunction in patients followed for schizophrenia should be systematic, regardless of the antipsychotic molecule type and dosage. In this regard, we recommend the establishment of a better therapeutic relationship between caregivers and patients with schizophrenia, based on empathy and trust, so that the latter feel comfortable enough to address the sexual dimension in general and sexual dysfunction in particular.

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Introduction

Sexuality is a natural component of human behavior. The general population has been extensively studied since the first half of the 20th century. It is now accepted that sexual activity and satisfaction contribute significantly to a person's quality of life.^{1,2} However, for patients with severe and disabling mental disorders such

as schizophrenia (SCZ), sexual functioning has received little attention in the management, which should be comprehensive.³ Indeed, discussing sexual disorders with patients with SCZ was initially considered inappropriate because it was believed they should not be sexually active. Even up to the 1970s, some psychiatrists believed that sexual activity contributed to the development of the disorder.⁴ Although these beliefs no longer exist, little work has been done to study the sexual behavior of patients diagnosed with SCZ.^{5,6}

At least 4 elements intervene in the sexuality of patients with SCZ:⁷ the disease, the psychosocial factors, the state of bodily health, and the pharmacotherapy (mainly antipsychotic agents). Antipsychotic treatment is the cornerstone of treatment, to which psychotherapy and social rehabilitation are added.⁸ Antipsychotic agents are divided into typical antipsychotic agents (TAPs), also known as first-generation antipsychotics, and atypical antipsychotic agents (AAPs), named by some authors as second-generation antipsychotics. Talking about antipsychotic agents (APs) available in Tunisia, according to the official site of the Tunisian central pharmacy⁹ and according to several experts,¹⁰ the most commonly used antipsychotic agents are haloperidol, fluphenazine, and chlorpromazine as TAPs and olanzapine, risperidone, amisulpride, and clozapine as AAPs. In addition, sexual dysfunction has been reported as an adverse effect of all antipsychotic agents.¹¹ Thus, it seems important to quantify the prevalence of this adverse effect in the populations of patients diagnosed with SCZ. However, we note that the work carried out in Tunisia is few and concerns minimal samples of patients.

Given these findings, this work proposes to study the sexuality of patients with SCZ. Our objectives were to assess the sexuality of patients with SCZ, to identify factors associated with SD among these patients, and to determine practitioners' attitudes toward the sexuality of our study population.

Materials and Methods

Characteristics of the study

This is a cross-sectional study carried out in the Psychiatry Department of Kairouan (outpatient department). We recruited 46 patients at the consultation of the Psychiatry Department of Ibn-El-Jazzar Hospital, according to the following criteria.

Inclusion criteria

Inclusion criteria included that the patient was followed for SCZ according to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, aged 18 years or older, a man, clinically stable for at least 3 months and not hospitalized for at least 6 months, and gave consent to participate in the study.

Exclusion criteria

Exclusion criteria included refusal to participate in the study, that the patient was being followed for another mental disorder, younger than age 18 years, diagnosed with an intellectual development disorder according to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition criteria or dementia, a somatic comorbidity that may lead to sexual dysfunction (eg, diabetes, another endocrinopathy, neurological disease, or poorly balanced cardiovascular disease), association of another treatment that may lead to a sexual disorder, and poor compliance.

Conduct of the study

The study was conducted after free and informed oral consent from all participants in compliance with coronavirus disease 2019

restrictions. Patients were recruited over 5 months between February and June 2022. A single examiner, a psychiatry resident physician, conducted the interviews. They took place in the Ibn-El-Jazzar Hospital (outpatient psychiatry) and had an average duration of 1 hour. We filled in the information sheet through the medical record and the interview. Afterward, we proceeded to the psychometric evaluation.

Evaluation tools

A preestablished information sheet was completed for each patient recruited, including sociodemographic and clinical data and 3 questions in the therapeutic context: whether or not sexuality had been previously addressed by the treating physician(s) and, if so, whether or not there had been any therapeutic intervention; if the patient himself has previously discussed sexuality; and if the patient has already been informed of the possibility of iatrogenic sexual dysfunction. A psychometric evaluation was conducted with the help of 3 scales:

Psychotropic-Related Sexual Dysfunction Questionnaire

The Psychotropic-Related Sexual Dysfunction Questionnaire (PRSexDQ-SALSEX) is a hetero-questionnaire designed to screen for the effect of psychotropic treatment on the respondent's sex life. This questionnaire first showed good psychometric properties in patients with depression in 2000 and was validated to explore sexual functioning in patients with SCZ in 2008. Sexual dysfunction was defined based on the total score: mild: 1 to 5, with no item ≥ 2 ; moderate = 6 to 10, or 1 item = 2, with no item ≥ 3 ; severe: 11 to 15, or 1 item ≥ 3 .

Arizona Sexual Experiences Scale

The Arizona Sexual Experiences Scale (ASEX) is a 5-item scale developed in 2000 that quantifies libido, arousal, vaginal lubrication or penile erection, ability to reach orgasm, and orgasm satisfaction. It assesses sexual activity involving a partner and/or masturbation. It has been validated in outpatients with SCZ and schizoaffective disorder. Items are measured on a 6-point scale (1–6), with higher scores reflecting impaired sexual function. The female and male versions of the ASEX differ on question 3 regarding erection/lubrication; thus, we retained only version 3A, specific to male subjects. Sexual dysfunction is defined as a total score ≥ 19 or an item with a score ≥ 5 or 3 items with a score ≥ 4 .

Changes in Sexual Functioning Questionnaire–Male Clinical Version

The Changes in Sexual Functioning Questionnaire–Male Clinical Version (CSFQ-M-C) is a 14-item self-assessment instrument published in 2006 that assesses behaviors and/or problems in the 3 phases of the sexual response cycle (desire, arousal, and orgasm). The CSFQ-M-C provides scores on the 5 subscales of the original form of the questionnaire. Items 10 and 14 are not specific to any phase of the sexual response cycle because they track pain during erection or orgasm, and the first item reflects pleasure and satisfaction. The 14 items are scored by the patient from 1 to 5 (increasing intensity or frequency), except for items 10 and 14, for which the intensity or frequency decreases from 1 to 5. The total score varies from 14 to 70. Higher scores reflect better sexual functioning and vice versa. A CSFQ 14 total score for both female and male versions is obtained by summing the value of items 1 to 14. Scores ≤ 41 for women and ≤ 47 for men indicate sexual dysfunction. Items 10 and 14 are included in the total score, but do not map to a subscale dimension. Five subscale scores with established thresholds are also provided for pleasure/overall satisfaction (item 1 ≤ 4), desire/measured as frequency (item 2 + item 3 ≤ 8 for men), desire/measured as interest (item 4 + item 5 + item 6 ≤ 11 for

men), arousal/excitement (item 7 + item 8 + item 9 ≤ 13 for men), and orgasm/completion (item 11 + item 12 + item 13 ≤ 13 for men). In addition, a subscale score below the established threshold indicates sexual dysfunction.

Statistical Analysis

The data were entered and analyzed using SPSS Statistics version 24 (IBM-SPSS Inc, Armonk, New York). For the qualitative variables, we calculated counts and the percentages. We determined the means, SDs, and range for quantitative variables. The Shapiro-Wilk test within the sample verified the normality of the distribution of the continuous variables. The χ^2 test of independence is a statistical hypothesis used to determine whether or not 2 categorical or nominal variables are likely to be related. In case of invalidity of this test (due to the small sample size), we used the 2-tailed Fisher exact test. The comparison of 2 averages was carried out using the Student *t* test and the Mann-Whitney *U* test (in case of nonvalidity of the normality hypothesis) for independent samples, taking into account the homogeneity of the variances in each case (verified by Levene's test). The comparison of more than 2 means was carried out by the ANOVA test and the Kruskal-Wallis test (in case of nonvalidity of the normality hypothesis). The correlation between the dose of the main antipsychotic drug and the sexuality evaluation scores was done by calculating the Bravais-Pearson linear correlation coefficient *r*. In all statistical tests, the risk of error α was set at 0.05 according to the classical approach, and $P \leq 0.05$ reflects statistically significant results according to the Neyman-Pearson approach; we consider *P* values of 0.05 to 0.15 to be close to significance.

Results

Sociodemographic and clinical data

The ages ranged from 18 to 68 years. The mean (SD) age of this group was 35.72 (9.133) years. Twenty patients were from urban areas, or 43.4% of the patients, against 26 patients from rural areas, or 56.5% of the patients. There were 25 patients (54.3%) from primary school, 13 (28.3%) from secondary school, and 8 patients (17.4%) with an academic study level. Twenty-seven (58.7%) of the group were single, and 19 (41.3%) were unemployed (Table 1).

Our results show that 63% of patients had no previous somatic history. The mean disease duration was 18.8 years. The duration of the untreated psychosis (in years) was between 0 (brutal mode of entry into schizophrenia by brief psychotic disorder) and 12 years, with an average of 2.41 years. The number of hospitalizations for our sample ranged from 0 to 14, with an average of 5.24. The duration of the current treatment was between 1 and 17 years, with an average of 7.3 years. The chlorpromazine equivalent for our sample was between 150 and 1200 mg, with an average of 488 mg. The number of psychotropic drugs prescribed was between 1 and 3 for each patient, and the average was 2 (Table 2). According to our results, our population had other treatments associated with the antipsychotic; they are summarized in Table 3.

Therapeutic management of sexuality in patients treated for SCZ

Concerning the notion of therapeutic education by physicians on the adverse effects of APs during initiation or after therapeutic adaptation (dosage/molecules), 36.96% confirmed (n=17) this role of a physician, whereas 63.04% denied it (n=29). Concerning the notion of therapeutic education by doctors on the sexual adverse effects of the APs used during the initiation or after therapeutic adaptation (dosage/molecules), 30.4% confirmed (n=14) this

Table 1
Sociodemographic data.

Characteristic	Result
Age*, y	35.7 (26.5-44.8)
18-29†	6 (13.0)
30-39†	14 (30.4)
40-49†	13 (28.2)
>50†	13 (28.2)
Level of education†	
Primary	25 (54.3)
Secondary	13 (28.3)
Academic	8 (17.4)
Marital status†	
Single	18 (39.1)
Married	19 (41.3)
Separated	9 (19.6)
Professional status	
Unemployed	19 (41.3)
Regular work	19 (41.3)
Irregular work	8 (17.4)
Monthly income,† TND/mo	
<400	22 (47.8)
400-800	14 (30.4)
>800	10 (21.7)
Habitat environment†	
Urban area	20 (43.4)
Rural area	26 (56.5)

TND = Tunisian dinars.

* Values are presented as mean (range).

† Values are presented as n (%).

Table 2
Clinical data.

Variable	Result
Somatic history*	
With	17 (37)
Without	29 (63)
Substance abuse*	
Tobacco	18 (38.7)
Alcohol	8 (17.3)
Cannabis	8 (17.3)
Other substances†	12 (26.7)
Prescribed antipsychotic drug families*	
Long-acting antipsychotics	15 (32.6)
AAP with a long-acting antipsychotic	15 (32.6)
AAP alone	10 (21.7)
TAP alone	6 (13)
Evolution of schizophrenia‡, y	18.8 (10.9-27.6)
Duration of untreated psychosis‡	2.41 (0.1-4.9)
No. of hospitalizations‡	5.2 (2-8.4)
Current treatment duration‡	7.3 (3.2-11.3)
Current treatment dose, chlorpromazine equivalent‡	488 (173-803)
No. of prescribed psychotropic drugs‡	2 (1-3)
No. of doses per day‡	2 (1-3)

AAP = atypical antipsychotics; TAP = typical antipsychotics.

* Values are presented as n (%).

† Mainly sniffing products (Naffa).

‡ Values are presented as mean (range).

Table 3
Psychotropic drugs used other than antipsychotics.

Drug	Result*
Antidepressant	8 (14.5)
Benzodiazepine	6 (10.9)
Trihexyphenidyl (Artane†)	5 (9.1)
Biberidene (Akineton†)	21 (38.2)
Antiepileptic	9 (16.4)
No other psychotropic drugs	6 (10.9)

* Values are presented as n (%).

† Brand name.

Table 4
Results from the Psychotropic Related Sexual Dysfunction Questionnaire (PRSexDO-SALSEX) (N = 31).*

Sexual dysfunction	Result†
Mild	8 (17.3)
Moderate	14 (30.4)
Severe	9 (19.5)

* Only 31 participants completed the PRSexDO-SALSEX questionnaire.
† Values are presented as n (%).

Table 5
Results from the Changes in Sexual Functioning Questionnaire–Male Clinical Version.

Subscore	Result*
Pleasure	24 (52)
Desire/frequency	29 (63)
Desire/interest	33 (71)
Excitement/arousal	36 (78)
Orgasm/completion	38 (82)

* Values are presented as n (%).

role. In comparison, 69.6% denied it (n = 32). According to our results, 45.7% of patients (n = 21) spontaneously reported a sexual dysfunction during the interviews with their treating physicians. On the other hand, 54.3% of the patients (n = 25) denied this fact. Twenty-two patients spontaneously reported the notion of sexual dysfunction to their doctor. For 50% of them (n = 11), the therapeutic attitude was an adaptation of AP doses; for 27.3% (n = 6), the attitude was empathetic listening to the patients, and in 22.7% of the cases (n = 5), the choice was oriented toward the addition of another treatment (eg, sildenafil/tadalafil).

Sexual fantasies

According to our results, 56.5% of patients (n = 26) reported the existence of a sexual fantasy during the data collection period.

Use of 5-phosphodiesterase inhibitors

According to our results, 14 participants confirmed that they had used a 5-phosphodiesterase inhibitor without a prescription, whereas 32 denied it.

Psychometric assessment

PRSexDQ- SALSEX

The mean (SD) total score was 3.4 (2.781), and scores ranged from 0 to 13. Sexual dysfunction, according to the PRSexDQ-SALSEX scores, was present in 31 patients (67.4%). Table 4 shows the frequencies of mild, moderate, and severe sexual dysfunction according to PRSexDQ-SALSEX scores.

ASEX

The mean (SD) of the total scores was 18.8 (3.593), and the scores ranged from 9 to 26. According to the scores, 52% (24 patients) had sexual dysfunction.

CSFQ-M-C

For the total score of the CSFQ-M-C, 27 patients (58.7%) had a sexual dysfunction. The mean (SD) was 55.63 (9.69), and the scores ranged from 22 to 68. The subscores are presented in Table 5.

Association between antipsychotic drug doses (chlorpromazine equivalent dose) and sexuality assessment scores

We cannot confirm the existence of a relationship between the dose of the current treatment (in chlorpromazine equivalent)

used and the results of the test assessing sexuality. The PRSexDQ-SALSEX test results are unreliable because the Student exact test and the Kruskal-Wallis test showed P values >5%. The same is true for the results of the ASEX test since the Student exact test and the Mann-Whitney U test show P values >5%. The existence of this relationship cannot be confirmed with the results of the CSFQ-M-C test because the correlation value is almost 0.

Association between antipsychotic drug family and sexuality assessment scores

We can deduce the existence of a statistically significant association between the antipsychotic agent used and the results of the PRSexDO-SALSEX test because the Fisher exact test shows a P value = 0.032, which is <5%. On the other hand, we cannot confirm the existence of a relationship between the antipsychotic agent used and the results of the ASEX test because the Fisher exact test shows a P value of 0.271, which is >5%. We cannot confirm the existence of a relationship between the antipsychotic agent used and the results of the CSFQ-M-C test because the Kruskal-Wallis test shows a P value of 0.558, which is >5%.

Discussion

Because sexuality is a dimension of life, several factors can intervene.⁷ We tried to limit the confounding bias of these factors by not including patients with somatic comorbidities that could lead to a sexual disorder; patients taking a treatment that could induce a sexual side effect; those with an intellectual development disorder; and those with poor or doubtful compliance. In addition, we attempted to strengthen the probity of our study by using 3 questionnaires exploring the sexual life of each patient to include all dimensions of human sexuality and to screen for possible consequences in case of sexual dysfunction related or not to the intake of an AP. Finally, we would like to emphasize that the sample size of our study (46 patients) is comparable to the majority of published studies on the sexuality of patients followed for SCZ.

Relating to the reporting bias, in the context of the doctor-patient relationship, there is an important notion that particularly concerns our study: the notion of the unspoken. Several authors¹² have studied the most frequent domains and the determinants of unspoken words, and it turns out that the genital sphere and sexuality are the most frequent domains, particularly in the countries of the Arab-Muslim world.⁸ Thus, given the sensitivity of the subject investigated, the proportions of sexual dysfunction in our results may be underestimated because they are underreported by the patients questioned. Regarding the possibility of polytherapy, in our sample, 58% of patients were under several psychotropic treatments. This raises the problem of distinguishing the effects of the various other treatments on the sexuality of the patients.

Therapeutic management of sexuality

According to a review of the literature, the data of our work reflecting the management and approach of sexual dysfunction in patients with SCZ appear to be consistent with the research on this topic. Indeed, the prevalence of sexual dysfunction in the general population is significant and still important in patients with SCZ. According to several authors,^{3,13} sexual dysfunction in this population is grossly underestimated by treating physicians. Bernard et al¹⁴ confirm that the prevalence of sexual dysfunction in their sample was 24% when patients spoke spontaneously about it and 63% when they were questioned by a physician who discussed sexuality. In fact, in treated and stabilized patients, the prevalence of sexual dysfunction ranges from 15% to 88%, according to the studies of Kockott et al.¹⁵ This prevalence is probably underestimated,

as the patients in this study spontaneously reported sexual problems in 15% of cases.

In contrast, this incidence rises to 88% if the physician asks the question. Some more recent studies^{16,17} have found higher incidences of sexual dysfunction, up to 80% to 90% for patients followed for SCZ, regardless of sex or age. These studies' increase in sexual dysfunction rates is probably related to using self-questionnaires. In this context, Lazard¹⁸ discussed in his work on schizophrenia and sexual dysfunctions published in 2008, the hostility toward systematic screening for sexual dysfunction, and he put forward several explanatory hypotheses: physicians' lack of interest in sexuality, lack of skills in sexology, fear that addressing sexuality is perceived as a factor of decompensation by poor compliance with treatment or even induce hostility toward treatment, physicians objectify that addressing sexuality with patients followed for SCZ would not bring reliable data. Thus, we can hypothesize that this low incidence of spontaneous discussion of sexual dysfunction problems and the ignorance of sexuality on the part of the treating physicians are the origin of poor and inadequate management.

According to our results, 30.4% of patients (n=14) confirmed that they used 5-phosphodiesterase inhibitors without a medical prescription; on the other hand, 69.6% of patients (n=32) denied this. The ignorance of sexuality can explain these results by the practitioners and the tendency of the patients to solve their problems in all intimacy by referring to their cultural and social beliefs, especially with the effectiveness of these molecules with sexual dysfunction. In this context, Gopalakrishnan et al¹⁹ studied the efficacy and tolerability of sildenafil in 32 patients with iatrogenic sexual dysfunction secondary to AP by antipsychotic agents. One of the basic inclusion criteria for the study was being sexually active with a spouse at the time of the study. Patients ranged in age from 20 to 45 years. According to this work, 31 patients reported a significant improvement in the number of erections, the duration of penetration, as well as satisfaction during intercourse after 15 days of treatment. Most patients completed the study (96%), and no participant left due to an adverse drug reaction.

Factors that may be associated with sexual dysfunction according to possible associations

First, we note that the rate of sexual dysfunction according to the 3 scales we used is not the same. These disparities in the rate of sexual dysfunction could be explained by the sensitivity of the different scales. The PRSexDQ- SALSEX may be more sensitive than the ASEX or the CSFQ-M-C in detecting sexual dysfunction, hence its higher positivity rate. We note that the range of responses for each item of the PRSexDQ-SALSEX has only 4 possibilities, whereas there are 6 possibilities for each item of the ASEX and 5 for the CSFQ-M-C. The wording of the questions in the scales can also explain this. Because the answer choices for the PRSexDQ-SALSEX items involve some degree of approximation (<25%, 25%-75%, or >75% of the time), whereas for the CSFQ-M-C, the answer choices are more precise (once per month or less, once per month to twice per week, twice per week or more).

According to our results, we can confirm the existence of an association between the family of antipsychotic agents used and the results of the PRSexDO-SALSEX test showing sexual dysfunction. Indeed, a Chinese study published in 2011 that included 100 patients noted that the ASEX scores were higher in the group of patients under TAP, which shows that sexuality in patients depends on the class of the molecule prescribed.²⁰ Indeed, these patients received antipsychotic monotherapy with clozapine (n=37), risperidone (n=30), chlorpromazine (n=21), haloperidol (n=9), and olanzapine (n=3). Referring to the ASEX questionnaire, patients were divided into 2 groups, the confirmed sexual dysfunction

group (n=47) with a mean (SD) ASEX score of 23.57 (3.02) and the normal sexual functioning group (n=53) with a mean (SD) ASEX score of 13.19 (2.36). The clinical characteristics of the 2 groups showed no significant differences in age, duration of current medication, age of onset, or chlorpromazine dose equivalent.

A review of the literature regarding sexual dysfunction in people with SCZ developed by Malik²¹ in 2007 highlighted that some of the articles reviewed point out that AAPs seem to have a better tolerance for sexuality than TAPs. Also, according to this work, the role of prolactin is still poorly known because sexual dysfunction is also found in patients treated with APs that do not increase prolactin levels.

According to Bitner et al,²² the hypothalamic paraventricular nucleus may be a site of erectile activity mediated by the D4 dopamine receptor. Because a selective antagonist of D4 diminished this activity by APs, he could hypothesize that antipsychotic agents with a high affinity for the D4 receptor (such as clozapine) have a higher risk of sexual dysfunction. A 2012 review by Luciana V²³ of strategies for treating antipsychotic-induced sexual dysfunction and/or hyperprolactinemia in patients with SCZ showed that managing AP-induced sexual dysfunction and/or hyperprolactinemia must be handled very carefully. Indeed, various APs carry a risk of sexual dysfunction despite a minimal effect on prolactinoma, hence switching to an antipsychotic with a better profile (such as aripiprazole) seems desirable. In the same context, the use of 5-phosphodiesterase inhibitors may be useful.

Regarding the association of sexual dysfunction and chlorpromazine dose equivalent, we could not confirm the existence of an association between the dose of the current treatment (in chlorpromazine) and the results of the sexuality assessment test. Indeed, a cross-sectional study developed in China by Yasui-Furukori et al²⁴ and published in 2012 investigating the association between chlorpromazine doses and the prevalence of sexual dysfunction in patients with SCZ (N=191) treated with aripiprazole, haloperidol, olanzapine, and risperidone suggested a correlation between the equivalent chlorpromazine dose of AP in only some types of sexual dysfunction (such as increased sexual desire and ejaculatory dysfunction) in these patients. Furthermore, in this same research framework, another cross-sectional study developed by Bobes et al²⁵ in Spain and published online in 2010 in patients with SCZ treated with haloperidol, olanzapine, quetiapine, or risperidone (N=636) showed that the prevalence of sexual dysfunction appeared to be dose-dependent for certain molecules such as olanzapine and risperidone. A review summarizes the management of AP-related adverse effects by Labeled et al²⁶ in 2020, dose reduction of antipsychotic drugs appears to be recommended as first-line treatment for sexual dysfunction. Finally, although sexual dysfunction can be increased dose-dependent with APs, further investigation is needed into the threshold doses of each molecule.

We also recommend that screening for sexual dysfunction in patients being followed for SCZ should be systematic, regardless of AP molecule type and dosage regimen. This could contribute to the sexual health of these patients, but above all, avoid poor compliance with treatment, especially because the patients in our sample rarely raise the subject of sexuality with their carers. Similarly, we remind that the National Institute for Health and Clinical Excellence recommends using AAPs as first-line treatment for patients followed for SCZ because they are less likely to cause adverse effects, particularly sexual ones, according to current literature. However, these results were not verified in our work.

Concerning the information provided to patients by the treating physicians about sexual side effects, the results are of paramount importance: The patient is rarely made aware of this possibility at the start of treatment. We, therefore, recommend that patients being followed for SCZ should be given full and accurate informa-

tion about possible iatrogenic sexual dysfunction, reassuring them of the treatment options available in this case.

Conclusions

Our study has shown that practitioners tend to neglect screening for sexual dysfunction in patients followed for SCZ and that neglect may be responsible for poor compliance in a significant proportion of our sample. We found that more than half of our population experienced sexual dysfunction using all 3 scales. We also confirmed the existence of a statistically significant association between the family of antipsychotic agents prescribed and the PRSexDQ-SALSEX scale. Screening for sexual dysfunction in patients followed for SCZ should be systematic, regardless of the AP molecule type and dosage. In this regard, we recommend the establishment of a better therapeutic relationship between caregivers and patients being followed for SCZ, based on empathy and trust, so that the latter feel comfortable enough to address the sexual dimension in general and sexual dysfunction in particular.

Declaration of Competing Interest

The authors have indicated that they have no conflicts of interest regarding the content of this article.

Acknowledgments

J. Fares was responsible for conceptualization, data curation, formal analysis, methodology, and visualization (writing). F. Mohamed was responsible for methodology, resources, software, validation, visualization (writing: original draft and review editing); Z. Yosra was responsible for conceptualization, formal analysis, visualization (writing: original draft); H. Oumaya was responsible for investigation, project administration, and supervision; B. Riadh was responsible for supervision, validation, and writing (original draft); and M. Jihenne was responsible for conceptualization, data curation, methodology, and resources.

Before starting our study, we requested the approval of the ethics committee of Ibn-El-Jazzar Hospital (Kairouan)-Sousse University, which was obtained during February 2022. Each patient recruited freely gave oral consent based on complete, precise, and properly conveyed and understood information. We also ensured the anonymity and confidentiality of the collected data.

References

- Owen MJ, Sawa A, Schizophrenia Mortensen PB. *Lancet*. 2016;388:86–97. doi:10.1016/S0140-6736(15)01121-6.
- Simons JS, Carey MP. Prevalence of sexual dysfunctions: results from a decade of research. *Arch Sex Behav*. 2001;30:177–219. doi:10.1023/a:1002729318254.
- Kelly DL, Conley RR. Sexuality and schizophrenia: a review. *Schizophr Bull*. 2004;30:767–779. doi:10.1093/oxfordjournals.schbul.a007130.
- Pinderhughes CA, Grace EB, Reyna LJ. Psychiatric disorders and sexual functioning. *Am J Psychiatry*. 1972;128:1276–1283. doi:10.1176/ajp.128.10.1276.
- van Os J, Schizophrenia Kapur S. *Lancet*. 2009;374:635–645. doi:10.1016/S0140-6736(09)60995-8.
- Website n.d. S, Tardieu J, Micallef M, Bonierbale E, Frauger C, Lançon O, Blin, Comportements sexuels chez le patient schizophrène: impact des antipsychotiques, Volume 849, Issue 5501, 10/2006, Pages 679–788, ISSN 0013-7006, <http://dx.doi.org/ENC-10-2006-32-5-0013-7006-101019-200630112>.
- de Boer MK, Castelein S, Wiersma D, Schoevers RA, Knegtering H. The facts about sexual (Dys)function in schizophrenia: an overview of clinically relevant findings. *Schizophr Bull*. 2015;41:674–686. doi:10.1093/schbul/sbv001.
- Dialmy A. Sexuality and Islam. *Eur J Contracept Reprod Health Care*. 2010;15:160–168. doi:10.3109/13625181003793339.
- User S. Liste des médicaments n.d. <http://www.dpm.tn/medicament/humain/liste-des-medicaments> (accessed October 30, 2023).
- Website n.d. Article medicale Tunisie, Article medicale Observance de la prescription, Compliance, Trouble bipolaire [Internet]. [cited 2022 Oct 16]. Available from: http://www.latinisimedica.com/index.php/article-medicale-tunisie_2975_fr.
- Kishi T, Ikuta T, Sakuma K, Okuya M, Iwata N. Efficacy and safety of antipsychotic treatments for schizophrenia: A systematic review and network meta-analysis of randomized trials in Japan. *J Psychiatr Res*. 2021;138:444–452. doi:10.1016/j.jpsychires.2021.04.032.
- Gaudin G. Le non-dit dans la consultation de médecine générale: Une étude qualitative sur son importance aux yeux des généralistes. 2013.
- Schizophrénie et sexualité. Google Books n.d. https://books.google.com/books/about/Schizophr%C3%A9nie_et_sexualit%C3%A9.html?hl=ar&id=Pf5TPgAACAAJ (accessed October 30, 2023).
- Bernard A. Schizophrénie et sexualité: prévalence de la dysfonction sexuelle et impact sur les soins. 2009.
- Kockott G, Pfeiffer W. Sexual disorders in nonacute psychiatric outpatients. *Compr Psychiatry*. 1996;37:56–61. doi:10.1016/s0010-440x(96)90052-8.
- Piontek A, Szeja J, Blachut M, Badura-Brzoza K. Sexual problems in the patients with psychiatric disorders. *Wiad Lek*. 2019;72:1984–1988.
- Dumontaud M, Korchia T, Khouani J, Lancon C, Auquier P, Boyer L, et al. Sexual dysfunctions in schizophrenia: Beyond antipsychotics. A systematic review. *Prog Neuropsychopharmacol Biol Psychiatry*. 2020;98:109804. doi:10.1016/j.pnpbp.2019.109804.
- Bonierbale M. Diagnostic et traitements des dysfonctions sexuelles chez le patient schizophrène: enquête de terrain, état actuel des connaissances 2009.
- Meltzer HY, Massey BW. The role of serotonin receptors in the action of atypical antipsychotic drugs. *Curr Opin Pharmacol*. 2011;11:59–67. doi:10.1016/j.coph.2011.02.007.
- Zhang XR, Zhang ZJ, Zhu RX, Yuan YG, Jenkins TA, Reynolds GP. Sexual dysfunction in male schizophrenia: influence of antipsychotic drugs, prolactin and polymorphisms of the dopamine D2 receptor genes. *Pharmacogenomics*. 2011;12:1127–1136. doi:10.2217/pgs.11.46.
- Malik P. Sexual dysfunction in schizophrenia. *Curr Opin Psychiatry*. 2007;20:138–142. doi:10.1097/YCO.0b013e328017f6c4.
- Bitner RS, Nikkel AL, Otte S, Martino B, Barlow EH, Bhatia P, et al. Dopamine D4 receptor signaling in the rat paraventricular hypothalamic nucleus: Evidence of natural coupling involving immediate early gene induction and mitogen-activated protein kinase phosphorylation. *Neuropharmacology*. 2006;50:521–531. doi:10.1016/j.neuropharm.2005.10.009.
- Nunes LVA, Moreira HC, Razzouk D, Nunes SOV, De Jesus Mari J. Strategies for the Treatment of Antipsychotic-Induced Sexual Dysfunction and/or Hyperprolactinemia Among Patients of the Schizophrenia Spectrum: A Review. *J Sex Marital Ther*. 2012. doi:10.1080/0092623X.2011.606883.
- Yasui-Furukori N, Fujii A, Sugawara N, Tschimine S, Saito M, Hashimoto K, et al. No association between hormonal abnormality and sexual dysfunction in Japanese schizophrenia patients treated with antipsychotics. *Hum Psychopharmacol*. 2012;27:82–89. doi:10.1002/hup.1275.
- Bobes J, Garc A-Portilla MP, Rejas J, Hern Ndez G, Garcia-Garcia M, Rico-Villademoros F, et al. Frequency of sexual dysfunction and other reproductive side-effects in patients with schizophrenia treated with risperidone, olanzapine, quetiapine, or haloperidol: the results of the EIRE study. *J Sex Marital Ther*. 2003;29:125–147. doi:10.1080/713847170.
- Labad J, Montalvo I, González-Rodríguez A, García-Rizo C, Crespo-Facorro B, Monreal JA, et al. Pharmacological treatment strategies for lowering prolactin in people with a psychotic disorder and hyperprolactinaemia: A systematic review and meta-analysis. *Schizophr Res*. 2020;222:88–96. doi:10.1016/j.schres.2020.04.031.