Psychotropic medication-induced sexual dysfunction and its interference with patient's daily performance: a cross-sectional study

Jisha M. Lucca[a], Madhan Ramesh[a], Dushad Ram[b], Jintu Kurian[a], Noyal Mathew[a]

[a]Department of Pharmacy Practice, JSS College of Pharmacy, JSS University, [b]Department of Psychiatry, JSS Hospital, Mysore, Karnataka, India

Correspondence to Jisha M. Lucca, M.Pharm, Department of Pharmacy Practice, JSS College of Pharmacy, JSS University, SS Nagara, Mysore 570 015, Karnataka, India
Tel: +91 821 254 8353/+91 821 254 8356; fax: +91 821 425 3628;
e-mail: jishajojo06@yahoo.co.in

Received 18 November 2015
Accepted 22 January 2016

Egyptian Journal of Psychiatry
2016, 37:36–40

Objectives

There are very few studies, especially in the Indian population, addressing the frequency of sexual dysfunction due to psychotropic medications. Therefore, this study aimed to quantify the frequency of sexual dysfunction and its interference in the patients' daily performance in a hospital-based population taking psychotropic medications.

Materials and methods

This cross-sectional study was conducted in the psychiatric unit of a Tertiary Care Teaching Hospital in South India over a period of 2 years. The Udvalg for Kliniske Undersogelser side effect rating scale was used to determine sexual dysfunction. A global assessment of interference in daily performance due to side effects was also evaluated.

Results

The overall incidence of sexual dysfunction was 20.95%. A higher incidence of sexual dysfunction was observed in women [*n* = 56 (70.88%)] and in the age group 18–29 years [*n* = 30 (37.9%)]. Amenorrhea [*n* = 32 (38.5%)] was the most prominently observed sexual dysfunction, followed by galactorrhea [*n* = 15 (18.07%)] and decreased sexual desire [*n* = 14 (16.86%)]. Antipsychotics [*n* = 54 (65.06%)] constituted the most common class of drug implicated in sexual dysfunction, followed by antidepressants [*n* = 25 (30.12%)]. Withdrawal of the drug [*n* = 58 (42%)] was the most common intervention for the management of sexual dysfunction. The majority of reports rated interference in daily performance due to side effects as severe [*n* = 48 (60.75%)], followed by moderate [*n* = 26 (32.91%)].

Conclusion

The incidence rate of sexual dysfunction was 20.95%. Amenorrhea and galactorrhea were the two most prominent sexual dysfunctions affecting the patients with psychotropic medications. Thus it is important for all healthcare professionals to acknowledge and encourage discussion as well as the impact of drugs on sexual function.

Keywords:
amenorrhea, psychotropic drugs, sexual dysfunction

Egypt J Psychiatr 37:36–40

1110-1105

Introduction

Sexual dysfunction includes a wide range of disorders that disturb a person's ability to respond to sexual stimulus, or to experience sexual pleasure (Werneke *et al.*, 2006). It affects 43% of women and 31% of men in the general population and is more common in patients with psychiatric disorders (Laumann *et al.*, 1999). Up to 70% of patients with depression and 50% with schizophrenia may experience sexual dysfunction (Dossenbach *et al.*, 2005). It is difficult to accurately identify treatment-emergent dysfunction, because of confounding factors like mental illness itself, cultural influences, and comorbidity (Montgomery *et al.*, 2002). Sexual dysfunction impairs a patient's quality of life, self-esteem, and interpersonal relationship (Olfson *et al.*, 2005). It can occur secondary to physical or mental disorders, substance abuse, or prescribed drug treatment (Baldwin *et al.*, 1997). It is reported that the sexual side effects of medication are distressing and are as bad as any symptoms of the illness itself (Lambert *et al.*, 2004).

Antihypertensives, antidepressants, antipsychotics, steroids, immunosuppressive drugs, antiepileptics, and antiandrogens are frequently reported to cause sexual dysfunction, but the mechanism is poorly understood (Conaglen and Conaglen, 2013). The prevalence of sexual dysfunction associated with neuroleptics was 60% in men and 30–93% in women (Teusch *et al.*, 1995). Benzodiazepines, lithium, monoamine oxidase inhibitors, neuroleptics, and tricyclic antidepressants are reported to cause sexual dysfunctions like anorgasmia (Ghadirian *et al.*, 1992), unsatisfying or painful

orgasm (Aizenberg *et al.*, 1991), altered libido, erectile failure, priapism (Ziegler and Behar, 1992), menstrual irregularities, delayed or retrograde ejaculation (Segraves, 1992), and altered sexual sensation and sensitivity (Lieberman, 1988).

As it is a nonserious adverse drug reaction, psychotropically induced sexual dysfunction is less often studied and reported. However, it is an important problem for patients, because it affects their quality of life (Michels, 1999) and compliance to drug treatment (Kelly and Conley, 2004). There are very few studies, especially in the Indian population, addressing the frequency of sexual dysfunction due to psychotropic medications. Therefore, this study aimed to quantify the frequency and severity of sexual side effects and its interference in patients' daily performance in a hospital-based population taking psychotropic medications.

Materials and methods

Study design and study period

This cross-sectional study was conducted in the outpatient mental health unit of a Tertiary Care Hospital in South India over a period of 2 years.

Study patients

The study included all patients who presented with psychiatric illness as diagnosed by ICD-10 and who were on regular treatment with psychotropic medications for at least 2 months. Patients aged between 18 and 50 years, living with a sexually active partner, were also included in the study. Patients with comorbid medical conditions, alcohol or substance dependence, or taking other medications known to cause sexual dysfunction were exempted from the study. Patients presenting with sexual dysfunctions as a symptom of their psychiatric disease were also excluded.

Study procedure

All patients who visited the Psychiatric Department were reviewed and those who met the study criteria were enrolled. The participants were recruited by the purposive sampling technique. Patients were intensively monitored by interview and chart review to identify the symptoms of sexual dysfunction. It was brought to the notice of the concerned psychiatrist and the outcome was labeled as a sexual dysfunction only after discussing with the consultant.

The Udvalg for Kliniske Undersogelser side effect rating scale was used to determine sexual dysfunction. The scoring sheet includes 48 items, of which 10 items rate the presence and severity of sexual side effects – namely, menorrhagia, amenorrhea, galactorrhoea, gynecomastia, increased or diminished sexual desire, erectile dysfunction, ejaculatory dysfunction, orgasmic dysfunction, and dry vagina. A global assessment of interference in daily performance from side effects was made by the patient and rated on a scale ranging from 0 (not or doubtfully present) to 3 (side effects that interfere markedly with the patient's performance). The information required for the assessment of sexual dysfunction was gathered from various resources and the collected data, such as patient details, medication details, and type of sexual dysfunction, were documented in a suitably designed data form.

Ethical considerations

The study protocol was reviewed and approved by the Institutional Ethics Committee, and permission was obtained from the hospital authority before the commencement of study.

Results

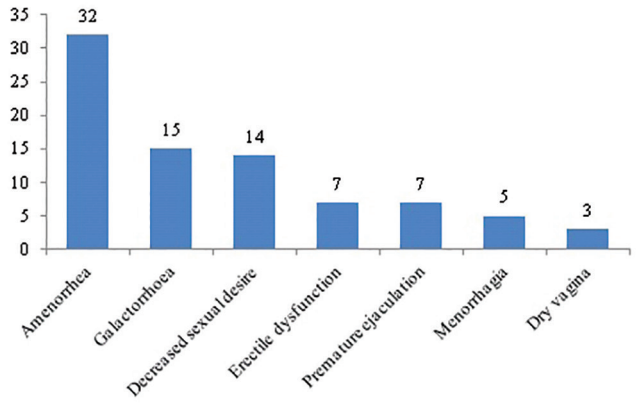
Of the 854 patients reviewed, 377 met the study criteria; 205 (54.3%) were men and 172 (45.6%) were women. The mean age of the patients was 31 (range 18–50) years. Depression (30.3%) was the most common clinical diagnosis among the study patients. A total of 83 sexual dysfunctions were identified from 79 patients. The overall incidence of sexual dysfunction was 20.95%. A higher incidence of sexual dysfunction was observed in women [$n = 56$ (70.88%)] and in the age group 18–29 years [$n = 30$ (37.9%)]. Sociodemographics of the patients are presented in Table 1.

Amenorrhea [$n = 32$ (38.5%)] was the most prominently observed sexual dysfunction, followed by galactorrhea [$n = 15$ (18.07%)] and decreased sexual desire [$n = 14$ (16.86%)]. The type of sexual dysfunction is depicted in Fig. 1

Antipsychotics [$n = 54$ (65.06%)] were the most common class of drug implicated in sexual dysfunction, followed by antidepressants [$n = 25$ (30.12%)], as shown in Fig. 1. Amisulpride [$n = 34$ (40.96%)], risperidone [$n = 14$ (16.86%)], and escitalopram [$n = 11$ (13.25%)] were the top three drugs contributing to sexual dysfunction. The drug class implicated in sexual dysfunction is illustrated in Fig. 2.

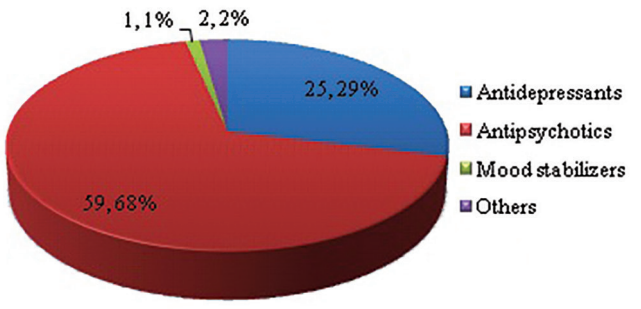
Amenorrhea and galactorrhea were more frequently reported with amisulpride [$n = 34$ (40.96%)], whereas decreased sexual desire and premature ejaculation were associated with escitalopram [$n = 11$ (13.25%)] and amitriptyline [$n = 6$ (7.22%)].

Figure 1



Type of sexual dysfunction.

Figure 2



Drug class implicated in sexual dysfunction (n = 83).

Table 1 Sociodemographics of the patients

Demographic characteristics	Patients with sexual dysfunction (N = 79) [n (%)]	Patients without sexual dysfunction (N = 298) [n (%)]
Sex		
Male	23 (29.1)	182 (61.1)
Female	56 (70.8)	116 (38.9)
Age (years)		
18–29	30 (37.9)	72 (24.1)
30–39	28 (35.4)	128 (42.9)
40–50	21 (26.5)	98 (32.8)
Diagnosis		
Depression	24 (30.3)	123 (41.2)
Bipolar affective disorder	14 (16.5)	61 (20.4)
Schizophrenia	13 (16.4)	39 (13.1)
Psychosis	11 (13.9)	37 (12.4)
Anxiety	10 (12.6)	24 (8.1)
Others[a]	7 (8.8)	14 (4.69)
Duration treatment		
<6 months	12 (15.1)	41 (13.7)
6 months–1 year	49 (62.02)	183 (61.4)
>1 year	18 (22.7)	74 (24.8)
Marital status		
Married	76 (96.2)	289 (96.9)
Unmarried	3 (3.8)	9 (3)
Type of family		
Joint family	33 (41.7)	134 (44.9)
Nuclear family	46 (58.2)	164 (55)
Educational status		
Literate	43 (54.4)	158 (53)
Illiterate	36 (45.5)	140 (46.9)

[a]Sleep disorders (n = 2), somatoform disorders (n = 1), conversion disorders (n = 3), personality disorders (n = 1).

Drugs implicated for each sexual dysfunction are summarized in Table 2.

Withdrawal of the drug [n = 58 (42%)] was the major intervention taken for the management of sexual dysfunction, whereas 35% of the reports required switching to another drug. In 22 (16%) cases, drug dose reduction was instituted, and in seven (5%) cases adjunctive therapy was initiated. Drug holidays of 2–3 days were given in three (2%) of the reports. Management of sexual dysfunction is illustrated in Fig. 3.

The majority of reports rated assessment of interference in daily performance from side effects as severe [n = 48 (60.75%)], followed by moderate [n = 26 (32.91%)]. Assessment results are depicted in Fig. 4.

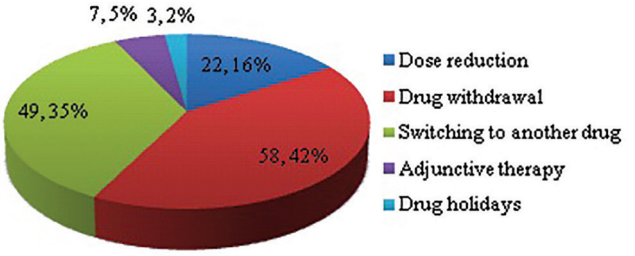
Discussion

Sexual dysfunction affects around half of all patients with psychiatric disorders and impairs their quality of life (Olfson *et al.*, 2005). The overall incidence of sexual dysfunction was 20.95%, which was low compared with other studies (Ernst *et al.*, 1993; Montejo *et al.*, 2001). Rates of sexual dysfunction vary considerably between studies, probably reflecting differences in methodological reasons, study population, the expectation people have about their sexual performance, and types of dysfunction being assessed. Comparative studies indicate higher levels of sexual dysfunction in women (Ernst *et al.*, 1993; Dunn *et al.*, 1998), and the present study showed no discrepancy in this regard. This might be partially due to the decreased willingness of men to discuss problems with the female researcher.

In the present study, ~38% of sexual dysfunctions were observed in the age group 18–29 years, which is consistent with other reports (Ernst *et al.*, 1993; Angst, 1998). Depression (30.08%) was the most common clinical diagnosis among the study patients; this finding correlates with the recent report by Lucca *et al.* (2014). The WHO reports also document that depression is the most common psychiatric diagnosis worldwide.

The duration of antipsychotic exposure is an important factor in impaired sexual functioning. In our study, sexual dysfunction was more common in patients receiving

Figure 3



Management of sexual dysfunction (n = 83).

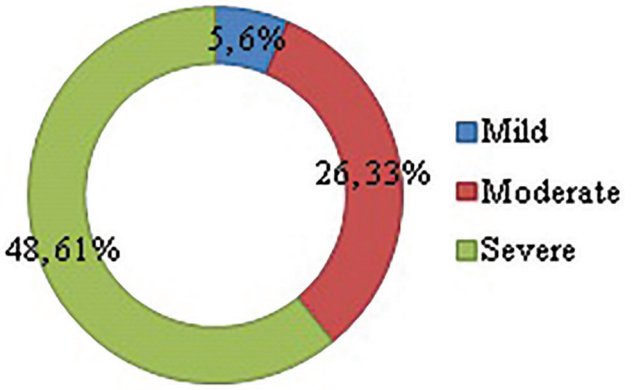
Table 2 Drugs implicated for each sexual dysfunction

Sexual dysfunction	Drugs implicated in sexual dysfunction
Amenorrhea [32 (38.55)]	Amisulpride (20), olanzapine (3), imipramine (1), paroxetine (1), risperidone (4), escitalopram (1), valproic acid (1), desvenlafaxine (1)
Galactorrhea [15 (18.07)]	Amisulpride (12), risperidone (2), haloperidol (1)
Decreased sexual desire [14 (16.86)]	Escitalopram (4), amitriptyline (3), clomipramine (2), risperidone (2), amisulpride (1), paroxetine (1), desvenlafaxine (1)
Erectile dysfunction [7 (8.43)]	Topiramate (1), escitalopram (2), risperidone (2), paroxetine (1), amisulpride (1)
Premature ejaculation [7 (8.43)]	Escitalopram (3), chlordiazepoxide (2), risperidone (2)
Menorrhagia [5 (6.02)]	Amitriptyline (3), olanzapine (1), risperidone (1)
Dry vagina [3 (3.61)]	Escitalopram (1), risperidone (1), haloperidol (1)

psychotropic drugs for a longer duration. This finding is in line with other studies conducted in different settings (Bitter *et al.*, 2005; Dossenbach *et al.*, 2006). The onset of decreased libido, amenorrhea, and erectile dysfunction due to risperidone and haloperidol was observed within 6 months to 1 year. A higher incidence of sexual dysfunction was observed in married patients. It is partially due to more number of married patients and more reliable assessment of sexual functioning with married patients. It might also be due to the social and cultural influences in India.

Amenorrhea and galactorrhea were the most prominent types of sexual dysfunction observed with antipsychotics. The prevalence of amenorrhea in patients with antipsychotics ranges from 15 to 50%, and is 19% for galactorrhea (Windgassen *et al.*, 1996). Antipsychotics block D2 receptors in pituitary lactotroph cells, which leads to an excess of prolactin secretion (hyperprolactenemia) (Bargiota *et al.*, 2013). The time to onset of galactorrhea ranged from 4 to 75 days after the commencement of antipsychotics. This finding is immensely correlated with the finding of the study by Windgassen *et al.* (1996). Galactorrhea was managed by withdrawal of the drug and by switching

Figure 4



Assessment of interference in daily performance from side effects.

to prolactin-sparing agents like aripiprazole but, in two cases, pharmacological interventions like cabergoline and bromocriptine were instituted. None of the male patients presented with galactorrhea.

Approximately 17% of the patients reported decreased sexual desire, which is low compared with the study by Nagaraj *et al.* (2004). Men reported a higher level of decreased libido compared with women. Selective serotonin reuptake inhibitors were most commonly implicated in decreased sexual desire, which is similar to other studies (Montejo *et al.*, 2001; Werneke *et al.*, 2006). It could be due to the blockade of D2 receptors in the tuberoinfundibular pathway. Moreover, in men, decrease in libido has been attributed to limbic fluctuations and to decreased levels of endogenous opioids and testosterone. Only one case of decreased sexual desire was reported in women. Management included switching to another drug, or drug holidays of 1–2 weeks.

Erectile dysfunction and premature ejaculation in the present study was about 8%. Cholinergic receptor antagonism and α-adrenergic receptor antagonism can reduce peripheral vasodilation, resulting in erectile dysfunction. Additionally, abnormal ejaculation is correlated with α I-adrenergic blockade. Sildenafil, a phosphodiesterase-5 inhibitor that enhances nitric-oxide-mediated vasodilatation in the corpus cavernosum by inhibiting breakdown of cGMP, was the first line of management for erectile dysfunction. Dryness of vagina was reported with treatment with haloperidol, escitalopram, and risperidone.

Antipsychotics (65.06%) were the most common class of drug implicated in sexual dysfunction, followed by antidepressants (30.12%). This finding is in line with other studies. The mechanism by which antipsychotic drugs may cause sexual dysfunction includes histamine, dopamine, and cholinergic and α-adrenergic alpha

receptor antagonism. Amisulpride was most frequently associated with amenorrhea and galactorrhea, whereas escitalopram and amitriptyline were associated with decreased sexual desire and premature ejaculation. Among the second-generation antipsychotics, risperidone and amisulpride were reported to cause a marked and sustained increase in serum prolactin levels (Windgassen *et al.*, 1996) and a similar trend was observed in our study also.

The assessment of interference in daily performance from side effects was evaluated. The majority of them were rated as severe by the patients. One of the reasons could be that patients report sexual dysfunction only when it becomes distressing.

Understanding both the impact of a disorder and the effects of its treatment on both the patient and their partner is critical to provide good clinical care. Thus it is important for all healthcare professionals to acknowledge and encourage discussion as well as the impact of drugs on sexual function for efficacious and safe solutions. More attention is warranted in this area as it may provide opportunities for improved quality of life and adherence to treatment for patients.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

References

Aizenberg D, Zemishlany Z, Hermesh H, Karp L, Weizman A (1991) Painful ejaculation associated with antidepressants in four patients. J Clin Psychiatry; 52:461-463.

Angst J (1998). Sexual problems in healthy and depressed patients. Int Clin Psychopharmacol; 13:1–4.

Baldwin DS, Thomas SC, Birtwistle J (1997) Effects of antidepressant drugs on sexual function. Int J Psychiatry Clin Pract; 1:47–58.

Bargiota SI, KS Bonotis, IE Messinis, NV Angelopoulos (2013) The effects of antipsychotics on prolactin levels and women's menstruation. Schizophrenia Res Treat; 1:1–10.

Bitter I, Basson BR, Dossenbach MR (2005) Antipsychotic treatment and sexual functioning in first-time neuroleptic-treated schizophrenic patients. Int Clin Psychopharmacol; 20:19–21.

Conaglen HM, JV Conaglen (2013) Drug-induced sexual dysfunction in men and women. Aust Prescr; 36:42–45.

Dossenbach M, Hodge A, Anders M, Molnár B, Peciukaitiene D, Krupka-Matuszczyk I, *et al.* (2005) Prevalence of sexual dysfunction in patients with schizophrenia: international variation and underestimation. Int J Neuropsychopharmacol; 8:195–201.

Dossenbach M, Dyachkova Y, Pirildar S, Anders M, Khalil A, Araszkiewicz A, *et al.* (2006) Effects of atypical and typical antipsychotic treatments on sexual function in patients with schizophrenia: 12-month results from the Intercontinental Schizophrenia Outpatient Health Outcomes (IC-SOHO) study. Eur Psychiatry; 21:251–258.

Dunn KM, Croft PR, Hackett GI (1998) Sexual problems: a study of the prevalence and need for health care in the general population. Fam Pract; 15:519–524.

Ernst C, Földényi M, Angst J (1993) The Zurich Study: XXI. Sexual dysfunctions and disturbances in young adults. Data of a longitudinal epidemiological study. Eur Arch Psychiatry Clin Neurosci; 243:179–188.

Ghadirian AM, Annable L, Bélanger MC (1992) Lithium, benzodiazepines, and sexual function in bipolar patients. Am J Psychiatry; 149:801-805.

Kelly DL, Conley RR (2004) Sexuality and schizophrenia: a review. Schizophr Bull; 30:767–779.

Lambert M, Conus P, Eide P, Mass R, Karow A, Moritz S, *et al.* (2004) Impact of present and past antipsychotic side effects on attitude toward typical antipsychotic treatment and adherence. Eur Psychiatry; 19:415–422.

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

Lieberman ML (1988) *The sexual pharmacy new american library*. New York, NY: New American Library.

Lucca JM, Kurian J, Ramesh M, Ram D (2014) Appraisal of clinical pharmacy services in mental health unit of a South Indian tertiary care hospital. World J Pharmacy Pharm Sci; 3:780–791.

Michels KB (1999) Problems assessing nonserious adverse drug reactions: antidepressant drug therapy and sexual dysfunction. Pharmacotherapy; 19:424–429.

Montejo AL, Llorca G, Izquierdo JA, Rico-Villademoros F (2001) Incidence of sexual dysfunction associated with antidepressant agents: a prospective multicenter study of 1022 outpatients. Spanish Working Group for the Study of Psychotropic-Related Sexual Dysfunction. J Clin Psychiatry; 62:10–21.

Montgomery SA, Baldwin DS, Riley A (2002)Antidepressant medications: a review of the evidence for drug-induced sexual dysfunction. J Affect Disord; 69:119–140.

Nagaraj AKM, Nizamie SH, Akhtar S, Sinha BNP, Goyal N (2004) A comparative study of sexual dysfunction due to typical and atypical antipsychotics in remitted bipolar 1 disorder. Indian J Psychiatry; 46:261–267.

Olfson M, Uttaro T, Carson WH, Tafesse E (2005) Male sexual dysfunction and quality of life in schizophrenia. J Clin Psychiatry; 66:331–338.

Segraves RT Sexual dysfunction complicating the treatment of depression. J Clin Psychiatry Monograph 1992; 10:75.

Teusch L, Scherbaum N, Böhme H, Bender S, Eschmann-Mehl G, Gastpar M (1995) Different patterns of sexual dysfunctions associated with psychiatric disorders and psychopharmacological treatment. Results of an investigation by semistructured interview of schizophrenic and neurotic patients and methadone-substituted opiate addicts. Pharmacopsychiatry; 28:84–92.

Werneke U, Northey S, Bhugra D (2006)Antidepressants and sexual dysfunction. Acta Psychiatr Scand; 114:384–397.

Windgassen K, Wesselmann U, Schulze Mönking H (1996) Galactorrhea and hyperprolactinemia in schizophrenic patients on neuroleptics: frequency and etiology. Neuropsychobiology; 33:142–146.

Ziegler J, Behar D (1992) Clozapine-induced priapism. Am J Psychiatry; 149:272.