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Psychotropic Drug–Induced Sexual Function Disorders

Diagnosis, Incidence and Management

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Contents

Abstract

The human sexual response can be divided into 3 phases: desire (libido), excitement (arousal) and orgasm. The fourth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) classifies sexual disorders into 4 categories: (i) primary; (ii) general medical condition–related; (iii) substance-induced; and (iv) 'not otherwise specified' sexual dysfunctions. Each of the 4 DSM-IV categories has disorders in all 3 sexual phases.

Substance-induced sexual dysfunctions are caused by the use of either substances of abuse [alcohol (ethanol), amphetamines, cocaine, opioids or sedatives/-hypnotics/anxiolytics], or prescription medications which include psychotropic drugs.

Patients with psychiatric difficulties tend to experience more frequent sexual function disturbances. The literature provides more than anecdotal evidence that psychotropic drugs can induce sexual function disorders in the epidemiologically vulnerable population of psychiatric patients.

Sexual dysfunctions caused by psychotropic drugs can be divided into 2 groups: sexual inhibition (inhibited desire, inhibited arousal and inhibited or-

gasm) and increased sexual function disorders (increased sexual desire, priapism and premature ejaculation).

The diagnosis of psychotropic drug–induced sexual function disorders is easy if the psychiatrist is sensitive to the existence of these adverse effects. This mostly involves careful history taking, although several questionnaires have been developed for reliable and valid quantification of sexual functioning. Diagnosis is usually established if the sexual function disorders develop when the patient is receiving a psychotropic drug and then disappear when the offending drug is discontinued.

The management of psychotropic–drug induced sexual inhibition can be divided into 6 steps: inform the patient about the possibility of sexual inhibition occurring before prescribing a psychotropic agent; wait for remission or tolerance of sexual inhibition; reduce the dosage of the psychotropic drug; switch the medication to one less likely to cause sexual inhibition; if possible, adjust the concomitant nonpsychotropic drugs; and add various pharmacological agents to the existing psychotropic drug to treat the sexual inhibition.

Physicians should take sexual histories as a routine practice when prescribing psychotropic drugs. Through careful management and patience on the part of both the patient and the physician, psychotropic drug–induced sexual function disorders can be improved so that the patient's compliance with medication and quality of life can be optimised.

1. Diagnosis of Psychotropic Drug–Induced Sexual Function Disorders

1.1 Conceptual Evolution of Human Sexual Functioning

In 1966, in St Louis, US, Masters and Johnson described the human sexual response as 4 successive phases: excitement, plateau, orgasm and resolution.[1] Both men and women get excited sexually from the excitement to plateau phase, then go into the orgasm phase, experiencing 'ejaculatory inevitability' and the few seconds of involuntary climax in which tension is relieved in explosive waves of intensive pleasure, often accompanied by myotonia.[1] From this point, sexual response differs physiologically between men and women. During the orgasm phase, orgasm in men is accomplished with ejaculation which is a peripheral sexual response.[1] In other words, orgasm and ejaculation do not always occur simultaneously, and either of them can exist without the other.[2] After ejaculation in the orgasm phase, men enter into the resolution phase, followed by a refractory period, whereas women can enjoy multiple orgasms if stimulation persists in the orgasm and resolution

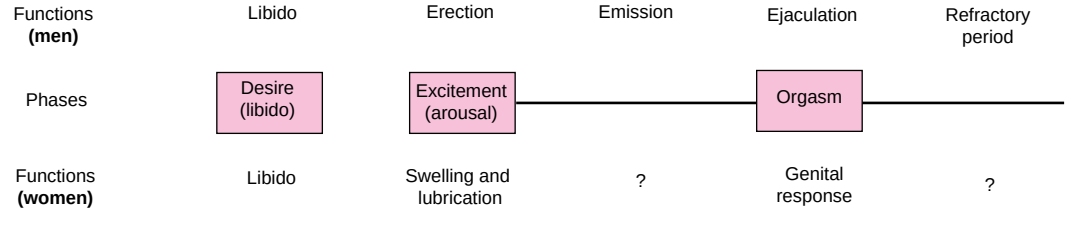

Fig. 1. The clinical classification of male and female sexual phases. The horizontal lines indicate continuous actions in sexual phases (reproduced from Shen et al.,[2] with permission of the Psychiatric Journal of the University of Ottawa).

phases.[1] In their 1970 follow-up publication,[3] Masters and Johnson described the pathology of human sexual functioning and introduced the term 'orgasmic dysfunction' for the first time, to describe the condition of 'frigid women'.[4]

In 1974, Kaplan proposed a clinically oriented biphasic model of sexual functioning.[5] Phase I consists of genital vasocongestion in women or penile responsiveness (erection) in men. Phase II consists of reflex clonic muscular contractions resulting in orgasmic process in both sexes, and ejaculation in men. In 1979, Kaplan incorporated the concept of libido into the original biphasic model and completed the triphasic concept.[6]

In 1984, Shen and associates[2] modified Kaplan's triphasic model by conceptualising the 3 phases into 2 events, separating libido from the other 2 successive sexual phases, as shown in figure 1. Later, in 1987, the American Psychiatric Association adopted these modified concepts into the diagnostic system in describing sexual dysfunction.[7]

1.2 The Diagnostic Classification of Sexual Dysfunction in DSM-IV

In 1994, the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV)[8] modified the classification of sexual disorders to 4 categories: (i) primary; (ii) general medical condition–related; (iii) substance-induced; and (iv) 'not otherwise specified' sexual dysfunctions. All the diagnostic classifications of primary sexual dysfunctions in DSM-IV are listed in table I. Each of the 4 DSM-IV categories has disorders in all 3 sexual phases, including sexual desire, arousal and orgasmic disorders,[8] as shown in figure 1.

Substance-induced sexual dysfunctions are caused by the use of 5 types of substances. These substances are alcohol (ethanol), amphetamines, cocaine, opioids, sedatives/hypnotics/anxiolytics, and prescription medications (including psychotropic drugs).[8] The focus of this review is psychotropic drug–induced sexual dysfunction. The DSM-IV diagnoses of sexual pain disorders (including dyspareunia and vaginismus) and sexual aversion disorder are not included in this review.

Table I. Diagnostic and statistical manual of mental disorders, fourth edition (DSM-IV) classification of sexual dysfunction[8]

1. Sexual desire disorders
Hypoactive sexual desire disorder[a]
Sexual aversion disorder
2. Sexual arousal disorders
Sexual arousal disorder (women)[a]
Erectile disorder (men)[a]
3. Orgasmic disorders
Orgasmic disorder (women)[a]
Orgasmic disorder (men)[a]
Premature ejaculation (men)[b]
4. Sexual pain disorders
Dyspareunia (not due to a general medical condition)
Vaginismus (not due to a general medical condition)

a Implicated as being inhibited by psychotropic medication.
b Not an inhibition.

Previous attempts[9,10] to try to differentiate between sexual dysfunctions in men and women to provide better clinical management have proved to be unnecessary because psychotropic drug–induced sexual dysfunction inhibits sexual phases across both sexes randomly and nonspecifically.[11,12] Management measures (except penile vacuum device for erectile disorders) which are also nonspecific in nature[11,12] are always applicable for all sexual inhibitions, as indicated by the footnote 'a' in table I, of sexual phases in both women and men.

1.3 Scope

In this review, all the sexual dysfunctions designated in table I with the footnote 'a' will be grouped together as 'sexual inhibition'. The opposite of sexual inhibition, other 'disorders' such as enhanced libido, priapism and premature ejaculation, are conceptually understood as 'increased' effects induced by psychotropic drugs. However, these increased effects are not desirable; for example, priapism is painful and is often a medical emergency.

Both psychotropic drug–induced sexual inhibited and increased disorders will be described ac-

cording to classification of psychotropic drugs. However, due to the lack of sufficient data, no attempts are made to include all the classes of psychotropic drugs under the description of increased functioning. The focus is on psychiatric practice in the US and this article is not intended to be exhaustive or to provide a review of the whole body of literature, but its aim is to demonstrate the concepts of diagnosis and magnitude of sexual disorders, as well as principles of management.

Only important representative references have been cited; citations from abstracts of studies presented at meetings or articles in supplement issues of journals which are usually not peer-reviewed, are avoided or minimised, respectively. Effects of psychotropic drugs on fertility and psychotropic drug–induced menstrual irregularity, galactorrhoea and breast engorgement are not listed in DSM-IV,[8] and have not be reviewed. No animal data are discussed and neuropharmacological speculations on sexual function and dysfunction which are attempted elsewhere[2,9,10] have been omitted.

2. Incidence of Psychotropic Drug–Induced Sexual Function Disorder

2.1 Sexual Inhibition

2.1.1 Inhibited Desire

There is a paucity of systematic research on inhibition of desire (libido) induced by psychotropic medication. Libido is difficult to quantify and is influenced by many physiological and social factors besides medications. Decreased desire may be secondary to problems with arousal and/or orgasm. There are also problems with collecting and quantifying reliable data.[13] Face to face interviews report higher levels of dysfunction than written surveys or questionnaires.[11,12,14] Reports from adverse effect surveillance monitoring consistently show lower rates of sexual adverse effects than studies with therapist-patient interviews. A further difficulty is the problem of how to assess premorbid and pretreatment libido. It is often difficult to design a study where this information is obtained prospectively.

In Women

In women, monoamine oxidase inhibitors (MAOIs) have been implicated strongly in causing decreased interest in sex.[15,16] There are numerous case reports that tricyclic antidepressants (TCAs) can decrease female libido, but there is evidence that this decrease in sexual interest may be a consequence of difficulty attaining orgasm.[12] Selective serotonin (5-hydroxytryptamine; 5-HT) reuptake inhibitors (SSRIs) also can cause decreased female libido. The rate of decreased libido can be as high as 40% with a variety of SSRIs[12,17] and there is no evidence that any one SSRI is less prone to cause decreased libido than any other.[12]

The data on antipsychotic drug inhibition of female libido are even more sparse. In the largest study to date,[18] sexual desire decreased in about 37% of antipsychotic-treated women. High dose, low potency antipsychotics were implicated more often.[18,19] Patients aged 60 to 70 years were affected more severely: up to 50% of those patients had decreased libido.[18,19]

About 40% of women with bipolar disorders showed decreased libido while receiving both benzodiazepines and lithium.[20] However, taking lithium alone appears not to cause decreased libido or other sexual inhibitions.[20] Other mood stabilisers [valproic acid (valproate sodium) and carbamazepine] have not been reported to inhibit sexual desire.

In Men

The problems obtaining reliable data on the effect of psychotropic medication on male libido are similar to those mentioned in the previous section on women, although men are thought to be more open to volunteering sexual information.[9,10] Interpretation of the data is also difficult as decreased libido in men is often not a primary adverse effect of medication, but a consequence of decreased ability to get and keep an erection, or to anorgasmia.[14]

Again, MAOIs are the class of antidepressant drug most implicated in decreased libido,[15,16] with phenelzine being the most frequently reported offender. There is evidence that TCAs do not de-

crease libido in men,[17] but this is not the observation from current reviewers' practice. SSRIs decrease libido about as often in men as in women. About 40% of men will admit to decreased libido while taking a variety of SSRIs when questioned.[11]

Information on the effect of antipsychotic medication on the male libido is difficult to obtain. The major problem is the degree of global impairment in the population of men receiving antipsychotic drugs. They often have severely impaired ability to socialise and hence may have largely auto-erotic sex lives. It is difficult to establish the rapport necessary to get reliable information on sex, and the degree of impairment on initial presentation makes obtaining prospective data almost impossible. Sexual desire is severely impaired in the majority of patients with untreated schizophrenia.[19,21] Another difficulty is assuring medication compliance, though this is less of a problem with depot medications. The overall rate of decreased libido with antipsychotic treatment is the same in men as women, about 37%.[18] Again, high dose, low potency medications are more prone to cause decreased libido.[21]

2.1.2 Inhibited Arousal

In Women

Arousal is a subjective feeling, and in women signs of arousal are swelling and lubrication. Anticholinergic effects of medication can cause vaginal dryness, but sexual dysfunction does not correlate to degree of anticholinergic adverse effects.[16] MAOIs, TCAs and SSRIs have not been clearly shown to decrease arousal in women.[14-17] There are no systematic studies of the effects of antipsychotic medications on female arousal.

In Men

By its nature, arousal in men is much easier to study than arousal in women because of obvious anatomical presentation, and this may partially explain the discrepancy in incidence rates between studies of sexual functioning in men and women.[9,10] Regardless, there are few studies which examine sexual arousal in men separately from other phases of sexual functioning.

Nocturnal penile tumescence is one objective measurement of arousal in men. Amitriptyline has been shown to decrease nocturnal penile tumescence in healthy male volunteers.[22] There are numerous case reports but no systematic data about other TCAs, MAOIs, or SSRIs causing erectile difficulties.

Antipsychotic medication is much more frequently associated with inability to attain erection. Thioridazine is most often implicated,[21] but all phenothiazines have been shown to inhibit erection, with rates reported between 20 and 44% of male patients.[21,23]

About 38 to 40% of men with bipolar disorder are found to have difficulty getting and maintaining erections while receiving lithium combined with other drugs.[20] Other mood stabilisers have not been reported to cause inhibition of arousal in men.

2.1.3 Inhibited Orgasm

In Women

Delayed orgasm or anorgasmia is the most frequently reported sexual adverse effect in women induced by psychotropic medications. The list of those psychotropic medications[8,9] should be updated to include the SSRIs fluoxetine,[12,24-29] sertraline,[12,29,30] paroxetine[12,29,30] and fluvoxamine.[31,32] Women receiving newly introduced atypical antipsychotic drugs, especially clozapine and risperidone, are found to have frequent complaints of delayed orgasm or anorgasmia. Other atypical antipsychotic drugs, olanzapine and quetiapine, are new to the US market and cases of inhibited orgasm induced by these agents have not yet been reported.

In Men

Delay of male orgasm is not always viewed negatively by patients or their partners. There is a burgeoning market in prescription of SSRIs to treat premature ejaculation, and this will be discussed in section 3.2.3.

TCAs have been shown to make orgasm more difficult. Imipramine,[15,17,33] amitriptyline,[16] trimipramine,[33] and desipramine[33] have all been implicated as impairing orgasmic functioning. Clomipramine has also been strongly implicated.[14] All SSRIs can delay or prevent male orgasm,[11,29,30] with rates from 13 to 50% of men treated.

Antipsychotic medication is also reported to cause orgasmic dysfunction. Thioridazine is the best-studied medication and is reported to cause retrograde ejaculation into the bladder.[6,21] Almost 50% of patients receiving thioridazine report disturbances in ejaculation.[21] This same study[21] also reported 44% of thioridazine-treated men had difficulty achieving erection, while only 19% of patients with other antipsychotic drugs complained of this adverse effect. Other studies have confirmed these rates.[19,21,23]

2.2 'Increased' Sexual Function Disorders

2.2.1 Increased Sexual Desire in Both Sexes

Testosterone is the substance most widely credited with increasing sexual desire in both sexes.[2,34] The hyperdopaminergic state induced by levodopa (a precursor of dopamine) therapy for patients with Parkinson's disease also makes patients 'hypersexual' and euphoric out of proportion to the improvement of motor activity.[35,36] In contrast, all dopamine antagonists (typical and atypical antipsychotic drugs) cause sexual inhibition.[37] Two of the first 42 patients with schizophrenia enrolled in a recent study became 'hypersexual' and caused management problems on the inpatient ward after they were withdrawn from antipsychotics to prepare for a new drug trial (unpublished observation).

As a rule, all antidepressants except for amfebutamone (bupropion) are implicated in inhibiting sexual functioning. Indeed, with the exception of a single case report,[38] amfebutamone has been least implicated for sexual inhibition.[11,12,15,16,39-41] It is worthwhile noting that the authors' preliminary report of an outpatient study has shown that nefazodone may not cause many inhibitory sexual effects.[42] In our own clinical experience, nefazodone causes less sexual inhibition than SSRIs, but not less than amfebutamone. However, all these claims need further confirmatory reports in peer-reviewed journals. Moclobemide, which is a reversible inhibitor of monoamine oxidase A (RIMA) has been reported to increase sexual desire in some patients,[43,44] although MAOIs are understood to be inhibitory of sexual desire.[11,45]

Lithium as a monotherapeutic agent usually does not change the level of sexual desire.[20] Other mood stabilisers are not clearly reported in the literature to increase or decrease sexual desire.

2.2.2 Priapism

As mentioned in section 1.1 of this article, human sexual phases differ physiologically between men and women. Priapism is an involuntary erection lasting from hours to days. Drug-induced priapism does not give pleasurable sensation, but is often associated with pain. Priapism can lead to fibrosis of the corpora cavernosa and impaired drainage of venous blood resulting in irreversible erectile dysfunction if it is not treated promptly.[46-48] Although 1 case of trazodone-induced clitoral priapism and 5 cases of clitoral enlargement have been reported,[49] most cases of psychotropic drug–induced priapism are understood to be penile priapism.

Besides drug-induced aetiologies, the causes for priapism are prostatitis, trauma, malignancy and sickle cell disease.[46] Of all medication, prazosin, an α_1-receptor antagonist, appears to be most associated with the adverse effect of priapism. Among psychotropic drugs, phenothiazine antipsychotics (chlorpromazine, thioridazine and mesoridazine),[50,51] the atypical antipsychotic drug risperidone,[52,53] as well as the antidepressant trazodone[47-51] have been implicated as the most significant offenders. In a 1987 review article, 57 cases of trazodone-induced priapism were analysed; the median age of patients was 40 years and the median trazodone dosage was 150 mg/day.[49] It is worthwhile noting that in the US, trazodone is often prescribed as a sedative in the dosage level of 50 to 200 mg/day rather than at an antidepressant

dosage level which is much higher, and that trazodone is also highly implicated in causing sexual inhibition, which is far more frequent than priapism.

2.2.3 Premature Ejaculation

In Darwin's evolutionary concept 'survival of the fittest', quicker ejaculation confers a survival advantage because animals can concentrate on avoiding predators. Only after security was established has humanity been able to pursue recreational sex differentiated from reproductive sex. Whether or not male central orgasmic sensation is inhibited, psychotropic drugs more frequently induce ejaculatory inhibition (as described in section 2.1.3) than premature ejaculation. Premature ejaculation is, however, mentioned as an adverse effect of psychotropic drugs in anecdotal reports.

3. Management of Psychotropic Drug–Induced Sexual Function Disorders

3.1 Sexual Inhibition

As reviewed in section 2.1 on incidence, sexual inhibition is the most common form of all sexual dysfunctions induced by psychotropic drugs. As shown in figure 1, inhibition affects every sexual phase randomly and nonspecifically, although clinical experience shows that orgasmic disorder (in the form of delayed orgasm, anorgasmia or delayed ejaculation among male patients)[11] and hypoactive sexual desire disorders (for both women and men)[11,12] appear to be the first psychotropic drug–induced sexual function disorders among all sexual phases.

Suggested management guidelines for psychotropic drug–induced sexual function disorders are listed in table II. The guidelines are applicable to any inhibition in any sexual phase of either sex.

Table II. Guidelines for managing sexual inhibition

1. Explain the possibility of sexual inhibition induced by psychotropic drugs before prescribing them
2. Wait for remission or tolerance of sexual inhibition
3. Reduce the dosage of psychotropic drugs to a lower, but still effective, dosage level
4. Switch the offending medication to one less likely to cause sexual inhibition
5. If possible, adjust the concomitant nonpsychotropic drugs
6. Add various pharmacological agents to the existing psychotropic drug to treat the sexual inhibition[a]

a Sometimes guideline 6 is used before guidelines 4 or 5, if appropriate.

3.1.1 Informing the Patient

Before prescribing any psychotropic drug, the physician must first obtain a baseline history of sexual functioning, then carefully explain the anticipated sexual adverse effects of the particular drug. Patients, especially those receiving psychotropic drugs for the first time, should be warned about the emergence of sexual inhibitions and be assured of the dose-related and reversible nature of these adverse effects. Better knowledge about these adverse effects may improve patients' trust in pharmacotherapy and compliance with respect to taking medications.

3.1.2 Waiting for Remission or Tolerance of Sexual Inhibition

Anorgasmia induced by TCAs has never been reported to remit.[54] However, adverse sexual effects of other classes of drugs, such as MAOIs and SSRIs, have demonstrated remission over time. Once the diagnosis of psychotropic drug–induced sexual inhibition is made, and after the patient reports sexual inhibition temporally related to the use of the psychotropic drug, the patient is informed about the options for management, which can include initially doing nothing. Clinical cases of spontaneous remission or decrease in the severity of sexual inhibition have been described both without[55,56] and with behaviour modification therapy.[57] However, patients may run out of patience because, while they are taking the same medication at the same dosage level, spontaneous remission of adverse effects may only occur after several weeks or months. It takes the patient's confidence and a good physician-patient relationship to await possible remission.

3.1.3 Reducing the Dosage of Psychotropic Drugs

The goal of this approach is to regain pre-medication sexual functioning by reducing the dosage

Table III. A brief list of nonpsychotropic drugs implicated as causing sexual inhibition

Antihypertensive drugs
Diuretics
Reserpine
Methyldopa
Guanethidine
β-Blockers
α_1-Receptor antagonists
α_2-Receptor agonists
Calcium antagonists
Histamine H_2 receptor antagonists
β_2-Receptor agonists
Salbutamol (albuterol)
Orciprenaline (metaproterenol)
Isoprenaline (isoproterenol)
Anticancer drugs
Substances of abuse
Alcohol (ethanol)
Amphetamines
Cocaine
Opioids
Sedatives/hypnotics/anxiolytics

level of psychotropic drugs while maintaining adequate therapeutic efficacy. The relationship between sexual inhibition and dosage level of SSRIs has been described.[11,12,58] Often patients are instructed to miss 1 or 2 doses of SSRIs per week in order to regain their previous level of sexual functioning.[11,12]

Dose reduction in the form of a 'drug holiday'[59] has been suggested to reverse sexual inhibition. This approach requires that the antidepressant be discontinued 2 to 3 days before the anticipated sexual activity. After having sex, the patient can either ignore the skipped medication and carry on with the usual dose or make up all, or part, of the unused medication. Careful planning and a comfortable doctor-patient relationship can make this approach successful and satisfactory. Of available SSRIs, the drug holiday approach is probably less successful with fluoxetine which has a long elimination half-life.[60] This approach is limited and not useful if the patient is involved in frequent sexual activity.

3.1.4 Changing Medication

In antidepressant pharmacotherapy the switch from one TCA to another (such as amoxapine to imipramine,[55] imipramine to desipramine,[56] clomipramine to desipramine,[61] and doxepin to nortriptyline[62]) has been reported to alleviate TCA-induced sexual inhibition. For SSRI-induced sexual inhibition, a switch among SSRIs may be successful,[11,12] but frequently the practice is to change from an SSRI to a non-SSRI antidepressant,[11,12] such as a TCA, or another heterocyclic antidepressant. Usually, MAOI-induced sexual dysfunction is not alleviated if the alteration is from one MAOI to another MAOI.[45]

Although one case has been reported of sexual inhibition induced by amfebutamone,[38] it is generally accepted that amfebutamone has few, if any, sexual adverse effects.[11,12,15,16,39,40] However, amfebutamone is associated with poorer antidepressant efficacy among some patients and is associated with insomnia and irritability; thus, substitution with this agent may not be an option.[11,12] It is thought that venlafaxine, nefazodone and mirtazapine are less likely to induce sexual inhibition than SSRIs or TCAs, but publication of studies in refereed journals substantiating these claims are lacking. In our experience, all 3 of these new drugs have been found to inhibit sexual function.

Of antipsychotics, low potency antipsychotics such as thioridazine and chlorpromazine[63] are often replaced by high potency antipsychotics, such as fluphenazine or haloperidol; however, loxapine has been promoted to be the antipsychotic drug of choice to avoid sexual inhibition. Most cases of fluphenazine-induced sexual dysfunction has successfully been treated by switching to haloperidol in either oral or depot intramuscular formulations. The advent of atypical antipsychotic drugs, such as clozapine, risperidone, olanzapine and quetiapine, in the US is changing psychiatrists' prescription patterns. Most conventional antipsychotic medications have been replaced by atypical antipsychotic drugs. In our experience, all of them have been implicated in causing sexual inhibition. A switch among these atypical antipsychotic drugs is ex-

Table IV. Pharmacological agents used to counteract the sexual inhibition induced by psychotropic drugs

Drug	Directions	Adverse effects	Reference
Bethanechol	30mg 1-2 hours before coitus	Headache, flushing	64
Cyproheptadine	4-12mg 1-2 hours before coitus	Sedation, depression	65-67
Amfebutamone (bupropion)	75-150mg 2 hours before coitus	Restlessness	38
Yohimbine	2.7-5.4mg tid or prn 2-4 hours before coitus	Anxiousness, tremor	68-69
Amantadine	100mg od or bid, or 300mg bid	Nausea, insomnia	70
Buspirone	30mg od or more	Dizziness, headache	71
Dexamphetamine	10-25mg od	Tachycardia, restlessness	72
Pemoline	18.75mg od	Insomnia, anorexia	72
Chlorphenamine (chlorpheniramine)	4mg bid	Sedation	11
Nefazodone	150mg 1 hour before coitus	Sedation	73
Granisetron	1mg 1 hour before coitus	Diarrhoea, constipation	74
Sildenafil	50-100mg 1-4 hours before coitus	Blurred vision	75
Vacuum device		Pain	76

bid = twice daily; **od** = every day; **prn** = according to circumstances; **tid** = 3 times daily.

pected to be the pattern of practice to alleviate sexual inhibition.

3.1.5 Adjusting the Concomitant Nonpsychotropic Drugs if Possible

Some patients who receive other medications for medical disorders develop sexual inhibition after psychotropic drugs are added to their treatment regimen. When these concurrent drugs are taken alone in high dosage, the patients can develop sexual function inhibition. The psychotropic drugs act as 'the straw that breaks the camel's back' to develop sexual inhibition when concurrent medications are in lower dosage. In other words, adding a psychotropic drug increases the likelihood of the patient experiencing a sexual function disorder. If patients continue to complain of sexual adverse effects after having switched from the offending psychotropic drug to one less likely to cause sexual inhibition, the patient's concurrent medications need to be examined and adjusted.

Table III is a brief list of nonpsychotropic drugs that are implicated in causing sexual inhibition. Dose reduction and medication changes of the medications listed in table IV may be necessary to restore sexual function when the psychotropic drug that has been added to the regimen must be continued. A detailed description of sexual function disorders from nonpsychotropic drugs is beyond the scope of this paper. However, it is worth mentioning that among antihypertensives, ACE inhibitors are least likely to cause sexual inhibition and that among antihistamine H_2 receptor antagonists, cimetidine has been most frequently implicated as causing sexual inhibition. The adjustment of nonpsychotropic medication is usually made by referring patients back to their specialist or family practitioners.

3.1.6 Adding Various Pharmacological Agents to Existing Psychotropic Medication

The approach of switching medication to alleviate sexual inhibition is limited when another drug with an equally adequate therapeutic effect cannot be found. Some clinicians believe that it is better to add an adjunct medication before switching from an agent which shows good therapeutic effects. In this case, numerous pharmacological agents have been successfully used as an 'antidote' for psychotropic drugs that cause sexual inhibition.

Table IV is a summary of various agents that are used to alleviate sexual inhibition while the patients continue to receive the offending psychotropic agents.[11,38,64-75] Sildenafil, a phosphodiesterase type V inhibitor was approved for the treatment of erectile dysfunction.[75] We have found that the use of sildenafil is effective for reversing psychotropic drug–induced erectile dys-

function in 5 male clinic patients. For erectile difficulties induced by psychotropic drugs, the use of vacuum devices has been suggested by the US National Institute Consensus Development Panel on Impotence.[76] Often the results from the treatment with these antidotes are not predictable. A couple of methods should be used, as a 'backup'.

3.2 Management of Increased Sexual Function Disorders

3.2.1 Increased Libido

Although increased libido in reasonable and acceptable degree is usually viewed positively by both the clinician and the patient,[77] treatment is needed for increased libido when the patient's behaviours become 'disinhibited' causing social nuisance or a threat to the security of other people. 'Hypersexuality' can cause 'management problems' for both men and women with psychiatric disorders in both outpatient and inpatient settings.[78,79] The latter includes boarding and nursing home environments. The other 'clinical' usage of decreasing libido is in the control of paraphilias.[80,81]

Any chemical which antagonises the effect of testosterone can decrease libido for both women and men.[2,34] Instead of cyproterone acetate which is the preferred choice in Europe, medroxyprogesterone is used as a method of 'chemical castration' in the US.[82] As discussed in a paper,[37] antipsychotic agents as a class cause inhibition or a decrease in sexual functioning in all sexual phases[2] including libido. Phenothiazines and haloperidol have been used to control paraphilia or paraphilia-related behaviours.[83,84] SSRIs such as fluoxetine,[80] sertraline,[81] and paroxetine,[79] have become logical replacements for antipsychotic agents in the treatment of hypersexuality due to their better tolerability and relative lack of permanent non-sexual adverse effects. Due to the long elimination half-life of fluoxetine,[59] a greater dosage of fluoxetine once per week under close supervision might serve the purpose that depot medications, such as medroxyprogesterone, fluphenazine or haloperidol, intend to achieve. However, there are no clinical data to support this contention.

3.2.2 Management of Priapism

Priapism can cause permanent penile tissue damage if not reversed promptly.[45-47] The management of priapism involves surgical drainage of circulating blood in penile cavernous tissue or local injection of chemical into the penile shaft.[45]

Psychiatrists are obligated to educate male patients carefully about the possibility of having priapism induced by phenothiazines,[49,50] risperidone,[51,52] or trazodone.[46] Early detection of 'excessive' penile nocturnal erection is important. Once full-blown priapism develops, immediate referral to a urologist or emergency room physician is mandatory.

3.2.3 Management of Premature Ejaculation

As reviewed in section 2.2.3, the incidence of psychotropic drug–induced premature ejaculation is rare. However, premature ejaculation *per se* is one of the most common sexual complaints, estimated to affect up to 30% of men.[85] Exploiting the adverse effect of inhibiting the male sexual phase of orgasm/ejaculation as shown in figure 1, clinicians have applied psychotropic drugs as therapeutic agents to treat premature ejaculation.

It shows that there is a trend by physicians to abandon the less well tolerated psychiatric drugs (such as thioridazine, MAOIs, clomipramine and lorazepam)[86-95] in favour of SSRIs (such as fluoxetine, paroxetine and sertraline)[77,96-101] because these drugs are more easily tolerated by patients and have less or no potential to cause adverse effects such as tardive dyskinesia or addiction. It is understood that other SSRIs such as fluvoxamine and citalopram can also be used to treat premature ejaculation, although they are not reported as being used as such in the literature; they have, however, been described as offending agents implicated in the adverse effect of sexual inhibition.[66,67]

In clinical experience, ejaculatory delay is often the first SSRI-induced sexual adverse effect in men.[11] It is often dose-related.[11] Furthermore, the total time of delay can be roughly determined by adjusting the dosage level of SSRIs. Instead of

being reported as an adverse effect, some degree of ejaculatory delay is considered as a desirable effect by patients or their sexual partners.

4. Discussion

4.1 Limitations of Clinical Data

The whole body of the literature in psychotropic drug–induced sexual function disorders is plagued by sparsity of data. Except for some controlled studies, most of the reports about incidence and management of psychotropic drug–induced sexual function disorders are based on clinical case reports of single cases or small case series.

Unlike the systematic data reported in the literature about other psychiatric disorders (mood disorders, schizophrenia, etc.), the data on sexual function disorders are 'crude' in nature due to the absence of large samples or systematic reporting. A larger pool of data accumulated from well designed studies is needed in order to advance our understanding and the management of psychotropic drug–induced sexual function disorders.

4.2 Under-Reporting of Sexual Dysfunction in Women

Although about one-fifth of the general US population has a history of recent use of psychotropic drugs,[102,103] investigation of the adverse sexual function effects of psychotropic drugs was only recently started, especially in women.[9,10] For example, thioridazine-induced sexual function disorder in men was first recognised in 1961,[104] several years after the introduction of thioridazine onto the market. It was not until 1982 that it was reported in women,[105] although sexual function disorders induced by psychotropic drugs were briefly mentioned by Wyatt et al.[106] in 1971 and Kotin et al.[21] in 1976. After the introductions of SSRIs onto the US market in 1988, sexual function disorders in women have been better recognised by psychiatrists and primary care physicians. As well as orgasmic disorders, sexual desire disorders in women induced by psychotropic drugs have also been recognised[12] due to better recognition of the ability of SSRIs to decrease libido.

4.3 The Value of Patient Education and Participation

Patients do not have to be denied normal sexual functioning when treated with psychotropic drugs. The key to addressing this issue lies in developing good communication between the physician and the patient. The patient and physician should have a common understanding of the patient's sexual function prior to the initiation of psychopharmacotherapy. Sexual function disorders should be discussed with the patient generally and anticipated adverse effects of particular medication should be outlined. It must be emphasised that active patient interest and participation in alleviating sexual adverse effects induced by psychotropic drugs can predict the successful management of these adverse effects.

5. Conclusion

DSM-IV has defined the diagnostic categories of sexual dysfunctions but has not given the incidence of any of them.[8] Patients with psychiatric difficulties tend to experience more frequent sexual function disturbances.[19,20] The literature reviewed here provides more than anecdotal evidence that psychotropic drugs can induce sexual function disorders in the epidemiologically vulnerable population of psychiatric patients.

The diagnosis of psychotropic drug–induced sexual function disorders is easy if the psychiatrist is sensitive to the existence of these adverse effects. This mostly involves careful history taking, although several questionnaires have been developed for reliable and valid quantification of sexual functioning.[30,41,107] Diagnosis is usually established if the sexual function disorders develop when the patient is receiving a psychotropic drug and then disappear when the offending drug is discontinued.

In spite of the paucity of well-controlled study data, the approaches for management of psy-

chotropic drug–induced sexual inhibition have been developed and are outlined in table II.

Physicians should take sexual histories as a routine practice when prescribing psychotropic drugs. Through careful management and patience on the part of both the patient and the physician, psychotropic drug–induced sexual function disorders can be improved so that the patient's compliance with medication and quality of life can be optimised.

Addendum

After the acceptance of this paper, Ginkgo biloba has been reported to reverse genital anaesthesia, diminished desire and diminished arousal induced by fluoxetine in a female patient.[108]

In the treatment of psychotropic drug–induced sexual dysfunction, sildenafil[75] has been found not only to be effective in men, as shown in table IV, but it may also be effective in women. We have found that the use of sildenafil is effective in reversing reduced arousal and delayed orgasm or anorgasmia induced by fluoxetine, given at a dosage of about 25.7 mg/day, in a 38-year-old woman.[109]

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