

Drug-induced sexual dysfunction in men and women

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SUMMARY

Many medical conditions and their treatments contribute to sexual dysfunction.

Commonly implicated drugs include antihypertensives, antidepressants, antipsychotics and antiandrogens.

Understanding the potential for drug-induced sexual problems and their negative impact on adherence to treatment will enable the clinician to tailor treatments for the patient and his or her partner.

Encouraging a discussion with the patient about sexual function and providing strategies to manage the problem are critical to good clinical care.

Introduction

Several classes of prescription drugs contribute to sexual dysfunction in men and women (Table 1).¹⁻³ Patients who develop drug-induced sexual dysfunction are more likely to be non-adherent. This has been found with antihypertensives⁴ and antipsychotics⁵. The literature has emphasised male sexual problems with less data available on female or couple problems.

Recreational drugs such as alcohol, narcotics, stimulants and hallucinogens also affect sexual function. Short-term use of alcohol affects sexual desire by decreasing inhibitions, but also diminishes performance and delays orgasm and ejaculation. Many substance abusers report better sexual function, but often their partners report the opposite.⁶

Sexual function consists of the phases of sexual desire, arousal and orgasm. Both men and women can experience problems in any of these phases. Low desire, lack of swelling and lubrication in women, erectile dysfunction, premature, retrograde or absent ejaculation, anorgasmia and painful sex not only affect the individual, but also impact on their partner.

Talking to the patient

Whether patients report their sexual problems depends on several factors, including whether the patient is comfortable disclosing these problems, and

whether the clinician is willing to ask about sexual issues and does so in a sensitive way.^{7,8}

Patients on long-term medications may not be aware that their sexual problems have developed as a result of their treatment. Conversely some may blame their drugs for sexual problems which are due to relationship difficulties or other stressors. Some doctors consider that asking patients if they had noticed any sexual adverse effects from their drugs may 'suggest' them to the patient, and possibly result in non-adherence. Patients attributing their sexual problems to their drugs are less likely to continue the treatment even when necessary for their health.⁹ The consultation should include discussion of the patient's sexual issues so these can be considered in treatment decisions.

Treatments for hypertension

Hypertension is associated with sexual dysfunction.¹⁰ Antihypertensives may also contribute to the problem and lead to low treatment adherence.⁴

Men

In an international survey, 20% of men using beta blockers (beta adrenoceptor antagonists) for hypertension had erectile dysfunction.¹¹ Centrally-acting alpha agonists (for example clonidine) and diuretics have also been implicated in impairing sexual function.⁴ The aldosterone receptor blocker spironolactone also blocks the androgen receptor and is associated with erectile dysfunction and gynaecomastia.

Women

Sexual dysfunction is more common in women with hypertension (before treatment) compared to normotensive women (42% vs 19%).¹² Although the sexual effects of antihypertensives have been poorly studied in women, these drugs may have similar adverse effects on the arousal phase as in men, leading to failure of swelling and lubrication. Decreased sexual desire (41% of women) and sexual pleasure (34%) have been reported.¹³ Alpha adrenergic drugs such as clonidine and prazosin also reduce desire (in a small, randomised trial)¹⁴ and arousal¹⁵. The angiotensin II receptor antagonist, valsartan, was associated with improved sexual desire and fantasies when compared with the beta blocker atenolol in women with hypertension.¹⁶

Table 1 Drugs associated with sexual dysfunction¹⁻³

Drug class	Decreased desire	Decreased arousal	Orgasm or ejaculatory difficulties
Antidepressants	amitriptyline	amitriptyline	citalopram
	clomipramine	citalopram	clomipramine
	fluoxetine	clomipramine	doxepin
	imipramine	doxepin	escitalopram
	paroxetine	fluoxetine	fluoxetine*
	phenelzine	imipramine	fluvoxamine
	sertraline	nortriptyline	imipramine
		paroxetine	nortriptyline
		phenelzine	paroxetine*
		sertraline	sertraline*
Other psychotropic drugs	alprazolam	chlorpromazine	alprazolam
		fluphenazine	fluphenazine
	fluphenazine	lithium	haloperidol
	haloperidol	risperidone	risperidone
	lithium		
	risperidone		
Cardiovascular drugs	clonidine	beta blockers	
	digoxin	clonidine	
	hydrochlorothiazide	digoxin	
	methyldopa	hydrochlorothiazide	
	spironolactone	methyldopa	
perhexilene			
spironolactone			
Other drugs	cimetidine	antihistamines	naproxen
		cimetidine	
		cyproterone	
		disulfiram	
		gonadotrophin-releasing hormone agonists	
		propantheline	
		pseudoephedrine	

* common cause of orgasmic difficulty

Psychoactive drugs

Aside from the medicine, it is important to be aware of the effects of psychiatric problems on the patient's relationship and address the psychosocial issues.¹⁷ Up to 70% of patients with depression have sexual dysfunction, which can affect any phase of sexual activity.¹⁸ Reports indicate that 30–80% of women and 45–80% of men with schizophrenia also experience sexual problems.¹⁹ In these patients, it may be difficult to distinguish the effects of the illness on sexual function from the effects of the drugs used for treatment.

Antidepressants

Many antidepressants cause sexual difficulties.^{17,20} Selective serotonin reuptake inhibitors and serotonin noradrenaline reuptake inhibitors inhibit desire, cause erectile dysfunction and decrease vaginal lubrication. They also impair orgasm in 5–71% of patients.^{18,21,22} This adverse effect is used therapeutically to delay premature ejaculation. Tricyclic antidepressants inhibit sexual desire and orgasm.^{23,24} The effects of specific drugs vary depending on their mechanism of action. For example, clomipramine causes orgasmic difficulties in

up to 90% of patients, while nortriptyline causes more erectile dysfunction but has less effect on orgasm.²⁵

Monoamine oxidase inhibitors are also associated with sexual dysfunction. Although moclobemide was reported to increase sexual desire,²⁴ the doses used in that study were considered subtherapeutic.

Other antidepressants such as venlafaxine and mirtazapine have variable negative effects on all aspects of sexual function. Initial reports on agomelatine in both male and female patients with major depressive disorder suggested significant antidepressant efficacy without significant sexual adverse effects. However, more recent reviews of the sexual effects are conflicting.^{26,27}

Antipsychotics

Some antipsychotics may affect sexual function more than others (see Table 2).^{19,28} The only Cochrane review of antipsychotic-induced sexual dysfunction has reported a small number of studies relating to men, but none relating to women.²⁹

Men taking antipsychotics report erectile dysfunction, decreased orgasmic quality with delayed, inhibited or retrograde ejaculation, and diminished interest in sex. Women experience decreased desire, difficulty achieving orgasm, changes in orgasmic quality and anorgasmia. Dyspareunia, secondary to oestrogen deficiency, can result in vaginal atrophy and dryness. Galactorrhea is experienced in both sexes.²⁸

A recent observational study of schizophrenia found that in patients with diminished sexual desire, ziprasidone was preferred over olanzapine.³⁰ The majority of antipsychotics cause sexual dysfunction by dopamine receptor blockade. This causes hyperprolactinaemia with subsequent suppression of the hypothalamic-pituitary-gonadal axis and hypogonadism in both sexes. This decreases sexual desire and impairs arousal and orgasm. It also causes secondary amenorrhoea and loss of ovarian function in women and low testosterone in men.^{31,32} Although

poorly understood, other neurotransmitter pathways including histamine blockade, noradrenergic blockade and anticholinergic effects may also be affected by antipsychotics.

Before commencing dopamine receptor antagonists it is useful to establish a baseline prolactin, as subsequent elevation can then be attributed to the drug. Non-drug induced causes of hyperprolactinaemia such as pituitary tumours should be considered in patients on dopamine receptor antagonists.³³

Antiepileptics

Sexual dysfunction is common in patients on antiepileptic drugs.³⁴ Gabapentin and topiramate have been associated with orgasmic dysfunction in both men and women, and reduced libido in women.³⁵⁻³⁷

Contraceptives

Oral contraceptives decrease circulating free testosterone. It is postulated that this decreases desire in women, although there is little evidence to support this.³⁸ As with other disorders, the impact of social context including the relationship, and fear of pregnancy and sexually transmitted diseases are confounding influences in clinical reports of the impact of oral contraceptives.

Depot medroxyprogesterone acetate, used as a contraceptive in women, can cause weight gain, depression, vaginal atrophy and dyspareunia with decreased libido in up to 15% of women.³⁹⁻⁴¹

Treatments for cancer

The impact of malignancy and its treatment on both the individual and his or her partner can have a significant negative influence on their sexual relationship. Many of the cancer treatments can lead to sexual dysfunction. As common examples, long-acting gonadotrophin-releasing hormone agonists used for prostate and breast cancer result in hypogonadism, with subsequent reduction in sexual desire, erectile dysfunction in men⁴², vaginal atrophy and dyspareunia in women as well as orgasmic dysfunction.³⁴

Drugs for lower urinary tract symptoms and benign prostatic hyperplasia

Men who present with symptomatic benign prostatic hyperplasia and lower urinary tract symptoms have an increased incidence of sexual dysfunction. Overall, 72.2% of men with lower urinary tract symptoms had erectile dysfunction compared with 37.7% in those without lower urinary tract symptoms.⁴³ Although surgery and various therapies can improve lower

Table 2 **The relative impact of antipsychotic drugs on sexual function**^{19,28}

Effect on sexual function	Antipsychotic
Least	aripiprazole
	quetiapine
	clozapine
	olanzapine
	haloperidol
Most	risperidone

urinary tract symptoms, some of these treatments also cause or exacerbate erectile dysfunction and ejaculatory dysfunction.⁴³

Alpha blockers such as doxazosin, tamsulosin, terazosin and alfuzosin for benign prostatic hyperplasia are reported to be no worse than placebo in their effects on sexual function, although tamsulosin was associated with approximately 10% increase in ejaculatory dysfunction in treated men.⁴⁴

Other drugs that cause sexual dysfunction

Antiandrogens such as cyproterone acetate, cimetidine, digoxin and spironolactone block the androgen receptor. This reduces sexual desire in both sexes,⁴⁵ and affects arousal and orgasm.

Steroids such as prednisone used for many chronic inflammatory disorders result in low serum testosterone which reduces sexual desire and causes erectile dysfunction.⁴⁶ Immunosuppressive drugs such as sirolimus and everolimus are widely used in kidney transplantation and can impair gonadal function and cause erectile dysfunction.⁴⁷ Protease inhibitors for HIV have also been implicated in sexual dysfunction and cause erectile problems in over half of men taking them.⁴⁸

Many other drugs including antihistamines, pseudoephedrine, opioids and recreational drugs may cause sexual dysfunction and should be considered when assessing the patient.

Strategies to manage sexual dysfunction

Non-drug approaches include therapy with a clinical psychologist who understands sexual dysfunction. A variety of strategies have been tried to reverse drug-induced sexual dysfunction, including drug switching, dose reduction and drug holidays. Taking a phosphodiesterase type 5 inhibitor in anticipation of intercourse has become the standard of care for men.⁴⁹⁻⁵¹ It improves erections in about 70% of men with hypertension.⁵² However, phosphodiesterase type 5 inhibitors are contraindicated in men using nitrates and should be used with caution in those on

alpha blockers, where postural hypotension can be a problem. In women, sildenafil has shown promise for reversing the inadequate lubrication and delayed orgasm induced by selective serotonin reuptake inhibitors.⁵³

Changing to an alternative drug is recommended for men and women taking antihypertensives. Alpha blockers, ACE inhibitors and calcium channel blockers are not considered to cause erectile dysfunction,⁵⁴ while several studies have suggested that angiotensin II receptor antagonists may even improve sexual function. Beta₁-selective beta blockers such as nebivolol may have potential advantages in these patients.⁵⁵

In patients taking antipsychotics, establish the cause of the hyperprolactinaemia then consider dose reduction or switching to prolactin-sparing drugs. Relationship counselling and addressing patient-specific concerns can be useful.²⁸

In women, oestrogen cream can alleviate local symptoms such as atrophic vaginitis and dyspareunia. If a woman complains of sexual dysfunction while on an injectable progestogen, another form of contraceptive can be considered.³⁴

Suggested solutions to gabapentin-induced anorgasmia include dose reduction, timing of dose away from planned coitus until anorgasmia no longer occurs, substitution with a different medication, and co-administration of other medications.^{35,36}

Conclusion

Understanding both the impact of a disorder and the effects of its treatment on both the patient and their partner are critical to providing good clinical care. It is important for the clinician to acknowledge and encourage discussion regarding sexual function, as well as enquire about the impact of drugs on sexual function. This will ensure patients and their partners understand their sexual difficulties and treatment options. <

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