



Medication Use and Sexual Activity in Older Adults

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9.1 Introduction

Medication prescribed for different conditions can affect sexual activity, especially in older adults. The effects can cause sexual dysfunction or can enhance the sexual function [1]. To establish whether medication use is a cause of sexual dysfunction, one needs to find out if the presence of symptoms was prior to medication commencement, if the persistence had a constant duration even after stopping the intake of the medication and if there are other factors that can explain the dysfunction. Such information can be obtained from medical history, physical examination and laboratory tests. It should also be taken into consideration that the dysfunction can sometimes be directly attributable to the diseases for which the patients are being treated, as in the case of depression, which in itself can negatively modify the sexual response [2]. In this chapter we discuss the main drugs affecting sexual activity or prescribed to enhance the sexual function both in older men and women.

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9.2 Men

9.2.1 Medication Affecting Sexual Function

Several types of drugs can have various consequences on sexuality. Men, on whom most of the studies have been conducted, are mainly affected by decreased libido and erectile dysfunction (ED).

One of the main pathophysiologic mechanisms is related to the increase of prolactin hormone [3]. Hyperprolactinaemia would lead to hypogonadism by inhibitory effect on the hypothalamic-pituitary-gonadal axis. The increase in prolactin secretion can be produced by antipsychotics, tricyclic antidepressants, dopamine receptor blockers, some antihypertensives (alfa-methyl dopa, Reserpine), oestrogens, opioids, calcium channel blockers (Verapamil) anxiolytics and blockers of H2 histamine receptors [3]. If the antipsychotics cause hyperprolactinaemia by dopamine receptor blockade, serotonin reuptake inhibitors, the most common cause of drug-induced hyperprolactinaemia, do not have a clear mechanism and it seems to be caused by the serotonin indirect effect. Before starting antipsychotics, a baseline prolactin level should be measured. The possible consequences are hypogonadism, gynecomastia, galactorrhoea and low levels of serum testosterone, as well as a decrease in libido, infertility and decrease in the sperm volume and quality (oligospermia) [4]. The loss of libido can be caused by a multitude of drugs, including barbiturates, benzodiazepines, lithium, neuroleptics, tricyclic antidepressants, monoamine oxidase inhibitors, lipid lowering agents, serotonin reuptake inhibitors, anticholinergics, antihistamines, progesterone and oestrogen, anorectic agents as fenfluramine and diethylpropion, glucocorticoids and antifungal ketoconazole [5, 6]. Among the antihypertensives, two diuretics have the greatest effects on sexual desire: chlorothiazide, which induces mainly impotence due to its vasodilating action and the alteration of blood pressure in the penis, and spironolactone, which causes a decrease of libido, impotence and gynecomastia [7]. Interestingly, also clonidine, an α_2 -adrenergic receptor agonist, can cause a decrease in desire, but it seems that this is more a consequence of the difficulties in erection and ejaculation, which are the main effects of the substance [8]. Even further, some antihistamine drugs may also decrease libido due to their sedative effect and can also cause ED due to their further action on autonomic nervous system receptors [9].

Antidepressant drugs have real inhibitory effects on sexuality and, in particular, tricyclic derivatives raise prolactin rates while lithium carbonate causes a decrease of sexual desire. Furthermore, MAOIs and “second generation” antidepressants also have negative effects on sexuality, which, however, generally tend to diminish or disappear after the first weeks of treatment [6]. Anti-epileptics can lead to a drop in libido, but it is not clear whether this is a direct effect of the drugs [10]. The adrenergic receptor blockers, which are used as antihypertensives, for some particular heart ailments and for asthma, affect the male sexual response, both with ED and ejaculation disorders [11]. In particular, prazosin can cause impotence and rare cases of priapism [11]. Priapism, a persistent and often painful erection not accompanied by sexual desire, can also be caused by other drugs, such as chlorpromazine,

thiothixene, fluphenazine, clozapine, and thioridazine [12]. Thioridazine, clomipramine and imipramine can also cause painful orgasms [12].

Antipsychotic drugs, due to their antiadrenergic and/or anticholinergic and antidopaminergic effects, can induce both decreases in desire and inhibition of erection and ejaculation: some phenothiazines affect the latter, while thioxanthenes and, in particular, benzamides increase prolactin rates, decreasing libido [13].

ED may also be due to: (a) antihypertensive drugs such as digoxin, which lowers testosterone levels and elevates those of oestrogen causing gynecomastia; (b) metronidazole antibiotic; (c) histamine H2 receptors blockers; (d) natural alkaloids (atropine); (e) other anticholinergics such as bantine, probantine and compounds ammonia; and (f) steroidal anti-inflammatories, which, if used for prolonged treatments together with cortisone derivatives, can cause a libido decrease [14, 15].

Finally, ED may also be determined by barbiturates, benzodiazepines, tricyclic antidepressants, and endocrine drugs, such as progestins, when used in the treatment of benign prostatic hyperplasia, and anti-androgens [15].

9.2.2 Enhancing Sexual Activity

Advanced age often leads to a condition called late-onset hypogonadism (LOH) characterised by low levels of testosterone (T) in men [16]. Low level of T may cause many symptoms including fatigue, loss of energy, depressed mood, decreased libido and ED [17]. Thus, T replacement therapy is able to significantly mitigate these symptoms. Moreover, T treatment may also augment the benefits of lifestyle interventions: T treatment of middle-aged obese men with low T level subjected to a weight loss programme prevented the diet-associated loss of lean mass, while maintaining the loss of body fat [18]. Furthermore, T therapy is associated with multiple benefits highly relevant to the patient including amelioration of sexual function, depressive mood, muscle function, anaemia, vertebral and femoral bone mineral density (BMD), and body composition [19]. Different formulations of T are available, including oral, buccal, nasal, subdermal, transdermal and intramuscular, for replacement therapy to relieve symptoms and signs of androgen deficiency in men with LOH [20].

ED is considered an age-related disease, affecting 20% of men aged >40 years and with prevalence across age groups as follows: 20% before age 30, 25% at age 30–39, 40% at age 40–49, 60% at age 50–59, 80% at age 60–69, and 90% at age 70 or more [21]. Various first-line treatment options are available, including lifestyle modification, testosterone supplementation, psychosexual and couple therapy, phosphodiesterase type 5 inhibitors (PDE5Is), vacuum erection devices and topical or intra-urethral agents (alprostadil) [22]. Lifestyle modification looks at addressing the modifiable risk factors associated with ED: lack of exercise, smoking, diabetes mellitus, dyslipidaemia, obesity and metabolic syndrome. More better quality studies are required to prove the value of this approach. Recent evidence showed that all PDE5Is were superior, when compared to placebo, in treating ED and that lower dosages had comparable effects to higher dosages [22]. Different PDE5Is seem to

have comparable efficacy but they appeared more efficacious when used in combination with alpha blockers or psychological interventions [23]. Despite their high effectiveness, many issues should be considered before their administration including etiologic considerations, performance status, safety, adverse effects, bad experiences with previous treatment, cost and satisfaction [24]. The most common adverse effects of PDE5i are headache, flushing, dyspepsia and upper respiratory tract symptoms [25]. Moreover, especially some clinical conditions should be taken into account before administration. First of all, from a cardiological point of view there are clear cautions and contraindications for PDE5Is in patients with unstable angina, severe congestive heart failure, or uncontrolled hypertension, those at high risk for arrhythmias, and those receiving nitrates or any other form of nitric oxide donors [25]. In addition, PDE5Is undergo extensive tubular reabsorption in the kidney, thus leading to minimal renal clearance and excretion. Thus, in men with chronic renal insufficiency (creatinine clearance <30 mL/min), it is recommended to initiate PDE5I therapy at a lower dose and titrate up as tolerated because of decreased drug clearance [25]. Finally, PDE5Is undergo rapid metabolism and excretion in the liver primarily through the CYP3A, CYP2C9, CYP2C19 and CYP2D6 pathways. Considering that mild and moderate hepatic impairments significantly decrease oral clearance and increase maximum concentration, it is recommended to initiate therapy at lower doses and titrating up as tolerated [25].

Vacuum erection devices might have an efficacy in achieving an erection of 90%, but satisfaction rates are between 27% and 94% and they could be associated with tissue damages [26]. Prostaglandins intracavernous injections can be an option for patients not responding to previously described treatment options. The success rate for achieving an erection can be as high as 85% and, considering the topical action, there are few side effects [26].

9.3 Women

9.3.1 Medication Affecting Sexual Function

As described above for men, the increase in prolactin secretion may affect the sexual health also in women. In fact, it can cause amenorrhea and galactorrhea, with a decrease of libido and it can be produced by tricyclic antidepressants, by some anxiolytics and by drugs blocking the histamine H2 receptors [27, 28]. As reported for men, antidepressant drugs affect sexual activity deeply and, in particular, tricyclic derivatives raise prolactin rates while lithium carbonate causes decrease of sexual desire [29, 30]. Furthermore, as for men, MAOIs and “second generation” antidepressants also have negative effects on sexuality, which, however, generally tend to diminish or disappear after the first weeks of treatment [6]. Anti-epileptics can lead to a drop in libido, but it is not clear whether this is a direct effect of the drugs [10].

In some cases a decreased libido and vaginal dryness have been reported in women taking oral contraceptives: the pill produces a reduction in androgen levels, but these symptoms are not experienced by all women and, therefore, the data cannot be completely generalised [31].

Finally, steroidal anti-inflammatories, especially if used for prolonged treatments together with cortisone derivatives, can cause a libido decrease as described also for men [14, 15, 32].

9.3.2 Medication Enhancing Sexual Activity

Oestrogen treatment in women has been shown to lead to increased frequency of sexual activity and improved sexual interest and arousal. Moreover, they can help also in terms of vaginal dryness or pain during intercourse [33]. Long-term safety, optimal types, doses and routes of therapy, however, remain unclear [34]. Considering that hormone replacement therapy is not without potential risks such as the increased probability of breast cancer and stroke, currently, it is only recommended for short-term use [35].

In addition to these treatments, acute exercise as exercise manipulation improves physical sexual arousal in women taking antidepressants by increasing sympathetic nervous system activity and vaginal sexual arousal [36].

9.4 Conclusions

A wide range of drug categories are well known in affecting sexual activity both in women and men as summarised in Table 9.1. In contrast, efficacious active ingredients are studied and utilised in order to improve the sexual life and, thus, the quality of life especially in older people. In addition to the medicaments reviewed in this chapter, alcohol and nicotine are two widespread substances to consider regarding sexual health. On one side, alcohol, which in small quantities increases desire and decreases inhibitions, when taken for a prolonged period of time and in high doses, can decrease libido, causing ED, poor lubrication, arousal dysfunction and orgasm inhibition. Nicotine, maybe due to its vasoconstricting effects, can induce ED.

To date, studies have focused more on the effects of different substances on men, although many drugs affect the performance and sexual behaviour of both sexes depending on the type of drug, the amount consumed, the length of the period of use, environmental factors and individual expectations.

Regardless of the availability of safe and effective drugs, the first-line treatment of sexual dysfunction should remove the causing conditions such as treating obesity, type 2 diabetes (T2DM) or metabolic syndrome and the promotion of healthy lifestyle and diet.

Table 9.1 Main drugs affecting sexual functioning

Drug category	Active ingredient	Possible effects of active ingredient	Possible effects of drug category
Antihypertensives	Spironolactone digoxin	Gynecomastia	Libido decrease Erectile dysfunction
	Clonidine methyl dopa	Erectile dysfunction, gynecomastia in men Orgasm delay or absence in women	
	Reserpine hydralazine Hydrochlorothiazide Chlorothiazide		
Adrenergic receptor blockers (Alpha-blockers) (Beta-blockers)	Phenoxybenzamine	Dry ejaculation	Libido decrease Erectile dysfunction
	Prazosin	Priapism	
	Propranolol		
Antidepressants (SSRI) (Tricyclics) (MAOIs) ("Second generation")	Sertraline paroxetine		Libido decrease Erectile dysfunction Orgasmic difficulties
	Fluoxetine	Spontaneous erections, priapism, penile and vaginal anaesthesia	
	Amitriptyline, doxepin Isocarboxazid, Phenelzine, tranylcypromine		
	Trazodone	Priapism (including clitoral), spontaneous erections	
Antipsychotics (Phenothiazines) (Thioxanthenes) (Benzamides) (Butyrophenones)	Thioridazine, chlorpromazine	Inhibition of erection and ejaculation, priapism	Libido decrease Orgasmic difficulties
	Chlorprothixene, Sulpiride, Levosulpiride, Sultopride, Tiapride haloperidol	Amenorrhea and galactorrhoea in women; gynecomastia and erectile deficits in men	
Anxiolytics (Benzodiazepines)	Clonazepam, diazepam, Flurazepam, lorazepam, Chlordiazepoxide		Libido decrease Erectile dysfunction Orgasm delay or absence

Legend: *MAOIs* monoamine oxidase inhibitors, *SSRI* selective serotonin reuptake inhibitor

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