Journal of Pharmacy and Pharmaceutics

OMMEGA Publishers

ISSN: 2377-1313
OPEN ACCESS

Research article

DOI: 10.15436/2377-1313.18.1785

Sexual Dysfunction and Treatment Approaches

OumerSada[1*], Kemal Ahmed[2]

[1]Department of Pharmacology and clinical pharmacy, College of health sciences, Addis Ababa University, Addis Ababa, Ethiopia
[2]Department of Public Health College of Medicine and health sciences, Wollo University, Dessie, Ethiopia

Abstract:

Background: Sexual dysfunction is the most common male sexual disorder, and it may have a profound negative impact on a man and his partner's lives. Male sexual dysfunction includes erectile dysfunction, diminished libido, and abnormal ejaculation. Despite this, there is misconception about the management of sexual dysfunction in the general population where they perceive sildenafil is effective against any type of sexual dysfunction. So that the current review is aimed at describing different types of sexual dysfunction and the available treatment approaches.

Methods: The available literatures were reviewed thoroughly and pooled.

Results: The high prevalence of sexual problems was confirmed by data derived from the National Health and Social Life Survey. Even in a cohort of younger men ages 18 to 59, 31 percent suffered from sexual dysfunction. Sexual dysfunction is multi-factorial problem. It may be caused by drugs, psychogenic causes, chronic diseases like diabetes and cardiac problems and trauma. By considering these their diagnosis shouldn't be overlooked by clinicians and the patients should consult their providers about their sexual problem.

Conclusion: The optimal treatment for sexual dysfunction should be individualized, based on a patient's symptoms, expectations, and underlying variant causes.

Keywords: sexual dysfunction; erectile dysfunction; ejaculatory disorders

Introduction

Background: Male sexual dysfunction has long been known to be common. Of late, knowledge of normal male sexual function and the causes of sexual dysfunction have become better understood, and more effective treatments are available.

Male sexual dysfunction includes erectile dysfunction, diminished libido, and abnormal ejaculation.

Epidemiology: A 1994 survey, the Massachusetts Male Aging Study (MMAS), revealed that male sexual dysfunction, presenting as erectile dysfunction, diminished libido, or abnormal ejaculation, first emerges as a common problem for men in their early 40s and increases with advancing age. At age 40, as an example, 40 percent acknowledged some level of impaired sexual function and another 10 percent recognized a waning sexual prowess or interest with each succeeding decade. A nine-year longitudinal follow-up study of this same cohort confirmed the age-associated declines in most domains of sexual function: sexual intercourse, erection frequency, sexual desire, satisfaction with sex, and orgasm[1].

The high prevalence of sexual problems was confirmed by data derived from the National Health and Social Life Survey. Even in a cohort of younger men ages 18 to 59, 31 percent suffered from sexual dysfunction. In this population-representative national survey, comparably - aged women reported a somewhat higher degree of sexual dysfunction (41 percent). The factors responsible for maintaining normal sexual function in the female are less well characterized than in the male. The age-associated increase in the prevalence of sexual dysfunction noted in the MMAS was strongly confirmed by a larger cross-sectional analysis of data from a prospective cohort study of 31,742 men ages 53 to 90 years[2].

Decreased libido: The prevalence of reduced libido is estimated to be 5 to 15 percent in men. It increases with age and it frequently accompanies other sexual disorders. Men with ED may experience loss of libido as a secondary consequence of ED. This usually is ascer-

Received date: January 31, 2018
Accepted date: August 10, 2018
Publish date: August 15, 2018

***Corresponding author:** Oumer Sada, Department of Pharmacology and clinical pharmacy, College of health sciences, Addis Ababa University, Addis Ababa, Ethiopia, Email: Oumer.sada@gmail.com

Citation: Oumer, S., et al. Sexual Dysfunction and Treatment Approaches (2018) J Pharm Pharmaceutics 5(2): 50-56.

tained from a detailed sexual history, including the chronology of the disorder. However, most patients who complain of erectile dysfunction (ED) do not complain of reduced libido or sexual desire.

The causes of low libido include:
• Medications (SSRIs, anti-androgens, 5-alpha reductase inhibitors, opioid analgesics)
• Alcoholism
• Depression
• Fatigue
• Hypoactive sexual disorder
• Recreational drugs
• Relationship problems
• Other sexual dysfunction (fear of humiliation)
• Sexual aversion disorder
• Systemic illness
• Testosterone deficiency

Most of these conditions are potentially treatable, so it is important to take a good medical history, perform a careful examination, and obtain relevant laboratory studies to determine if any of them are present.

Erectile dysfunction: Erectile dysfunction (ED) is defined as the consistent or recurrent inability to acquire or sustain an erection of sufficient rigidity and duration for sexual intercourse.

Prevalence: The frequency of sexual activity decreases with age in both men and women, and sexual problems become more common. In men, the most common sexual problem is erectile dysfunction (ED). A number of cross-sectional and longitudinal studies suggest a high prevalence of ED in the general population[2]. A multinational study of 27,839 men in eight countries (USA, UK, Germany, France, Italy, Spain, Mexico, and Brazil) was conducted with the same survey instrument[3]. The ages ranged from 20 to 75 years, and the overall prevalence of ED was 16 percent. It was 8 percent in men 20 to 30 years of age and 37 percent in men 70 to 75 years of age.

Risk factors: In one study, exercise was associated with a lower risk of ED, while obesity, smoking, watching television, and the presence of comorbid conditions were associated with a higher risk[2]. The lowest prevalence was noted in men without chronic medical problems who engaged in healthy behaviors. In obese men with erectile dysfunction, weight loss and increased physical activity are associated with an improvement in erectile function in about one-third of patients.

Frequency of sexual activity appears to predict the development of ED. This was illustrated in a five-year longitudinal cohort study of 989 men ages 55 to 75 years, who did not have ED at baseline. After adjusting for comorbidities and other major risk factors, men who reported intercourse less than once per week developed ED at twice the rate as men who reported intercourse once per week (79 versus 33/1000 RR 2.2).

In a prospective, cohort study of 570 men followed for approximately 25 years, the presence of risk factors for coronary heart disease (smoking, obesity, dyslipidemia) in midlife (mean age 46 years) were associated with incident ED (mean age 72 years at the time of follow-up).

In addition to age, the best predictors of erectile dysfunction are diabetes mellitus, hypertension, obesity, dyslipidemia, cardiovascular disease, smoking, and medication use[4]. Other diseases associated with erectile dysfunction include systemic sclerosis (scleroderma), Peyronie's disease, and prostate cancer treatment (eg, brachytherapy, prostatectomy).
Association with cardiovascular disease: Erectile dysfunction and cardiovascular disease share many risk factors, and their pathophysiology is mediated through endothelial dysfunction. Cardiovascular disease and its risk factors increase the risk for later ED[4]; on the other hand, erectile dysfunction may be an early warning sign of future cardiovascular events.

This was illustrated in a study of 9457 men aged 55 years or older who were randomized to the placebo group of the Prostate Cancer Prevention Trial.

Based upon these observations, men with ED without an obvious cause (eg, pelvic trauma) and who have no symptoms of coronary or other vascular disease should be screened for cardiovascular disease and its associated risk factors prior to initiating therapy for their sexual dysfunction, since there are potential cardiac risks associated with sexual activity in patients with heart disease[5].

Drugs: A number of drugs or other chemical substances can impede normal sexual functioning. Excessive alcohol consumption is the most common offender. Other recreational substances including marijuana, cocaine, and heroin also can lead to sexual dysfunction. Antihypertensive drugs, including thiazide diuretics, calcium channel blockers, and angiotensin converting enzyme (ACE) inhibitors all have been reported to interfere with normal genital vasocongestion; thiazides are most commonly implicated, while the alpha-adrenergic blockers are least likely to cause erectile dysfunction. It has been thought that beta blockers are an important cause of erectile dysfunction, but a systematic review of randomized, controlled trials found only a small increased risk of sexual dysfunction with beta blocker therapy (5 per 1000 patients treated)[6].

Anticholinergic drugs inhibit normal vaginal transudation (lubrication). Antidepressants, including tricyclics and selective serotonin uptake inhibitors (SSRIs) have been implicated in erectile, ejaculatory, and orgasmic dysfunction, as well as diminished desire. Antiandrogens such as GnRH agonists and 5-alpha-reductase inhibitors also can contribute to erectile dysfunction. Ketoconazole and spironolactone are androgen antagonists that diminish the effect of testosterone peripherally, while H2 blockers (particularly cimetidine) may stimulate prolactin release and secondarily reduce serum testosterone levels.

Psychosocial factors: Depression, stress, or the drugs used to treat depression can result in ED.

Neurological: Neurologic causes of erectile dysfunction include stroke, spinal cord or back injury, multiple sclerosis, or dementia. In addition, pelvic trauma, prostate surgery, or priapism may cause ED.

Bicycling: Less obvious, but of increasing importance, has been the possible (but controversial) association of ED with bicycling. Anything that places prolonged pressure on the pudendal and cavernosal nerves or compromises blood flow to the cav-

ernosal artery can result in penile numbness and impotence. The penile numbness has been attributed to the pressure on the perineal nerves, whereas the ED is thought to be due to a decrease in oxygen pressure in the pudendal arteries (which may be more of a problem with certain bicycle seats)[7]. This is thought to be a potential problem for serious cyclists.

Endocrine disorders: Testosterone deficiency affects peripheral mechanisms that are responsible for penile erections. Testosterone deficient men are still capable of exhibiting some erectile activity during nocturnal penile tumescence studies. However, the penile swelling in this setting usually is not of sufficient rigidity to permit vaginal penetration. This defect is corrected after normalization of testosterone levels, probably due to restoration of intrapenile nitric oxide synthase levels.

The testosterone level associated with ED is uncertain. In a study of 1162 men, serum testosterone levels < 225 ng / dL were associated with an increased frequency of sexual dysfunction. The effects of testosterone on libido are more consistent than on erectile function. Testosterone replacement can restore nocturnal erections in hypogonadal men but the effects are greater when testosterone plus a PDE-5 inhibitor are administered[8].

Other disruptions in hormone secretion, including hyperprolactinemia, hyperthyroidism, and hypothyroidism are commonly associated with ED. Restoration of the normal hormonal state usually results in the return of erectile function.

The recognition that one-third of men with type 2 diabetes mellitus have subnormal testosterone concentrations suggests that this hormone deficiency, and not just diabetic vasculopathy/neuropathy, may play a role in the ED so commonly seen in men with diabetes[9].

Ejaculatory disorders: Ejaculatory disorders are a heterogeneous group of disorders that include premature, delayed, and retrograde ejaculation, and anorgasmia. Painful orgasm may also be included in this category.

Premature ejaculation (PE): Premature ejaculation (PE) is also referred to as rapid or early ejaculation and is defined according to three essential criteria

- Brief ejaculatory latency;
- Loss of control;
- Psychological distress in the patient and/or partner

Ejaculatory latency of about a minute or less may qualify a man for the diagnosis, which should include consistent inability to delay or control ejaculation, and marked distress about the condition. All three components should be present to qualify for the diagnosis. Subtypes of the disorder are symptom-based, including lifelong versus acquired, global versus situational PE, and the co-occurrence of other sexual problems, particularly ED.

About 30 percent of men with PE have concurrent ED, which typically results in early ejaculation without full erection. A wide range of severity is seen, with patients ejaculating on or prior to penetration in the most severe cases. Patients sometimes present for infertility concerns. Normative data on average latency of ejaculation in different age and ethnic groups is limited[10,11].

The etiology of the disorder is uncertain or obscure in most cases. Negative conditioning and penile hypersensitivity may be etiological factors in PE, although neither mechanism has received adequate experimental support to date. Similarly, a genetic basis for the disorder has been proposed but is lacking adequate scientific support. PE is a highly prevalent disorder[10,11]; however, accurate population-based data are not available. Although usually associated with less bother than ED, the disorder may be highly distressing in some instances. It is frequently associated with sexual problems in the partner, particularly an orgasmia or a sexual pain disorder (eg vaginismus). In such cases, couples or sex therapy approaches may be of particular value. These may be combined with pharmacotherapy or behavioral therapy for treatment of PE in the man[4]. Cultural factors are important in determining the degree of distress associated with the disorder.

Delayed ejaculation, an ejaculation, and male anorgasmia: Ejaculatory dysfunction (EjD) includes a spectrum of disorders in men ranging from delayed ejaculation to a complete inability to ejaculate, an ejaculation, and retrograde ejaculation.

Multiple etiological factors have been identified, including organic and psychogenic factors. Any medical disease, drug, or surgical procedure that interferes with either central (including spinal or supraspinal) control of ejaculation or the autonomic innervation to the seminal tract, including the sympathetic innervation to the seminal vesicles, the prostatic urethra, and bladder neck, or sensory innervation to the anatomical structures involved in the ejaculation process, can result in delayed ejaculation, an ejaculation, and anorgasmia.

Retrograde ejaculation commonly occurs following surgery for benign prostatic hyperplasia, whereas an ejaculation is always associated with radical prostatectomy or cystoprostatectomy. Orgasm is typically not impaired with these latter procedures.

Lower urinary tract symptoms in aging men are often associated with ejaculatory disorders. Commonly used drugs such as certain alpha blockers (eg, tamsulosin) and antidepressants, particularly serotonin-uptake inhibitors (eg, paroxetine), have been associated with loss of orgasm or ejaculation.

Little is known about the physiology of the male orgasm. Precise prevalence data for these disorders are not available, although later studies suggest that EjD may be almost as prevalent as erectile dysfunction (ED) in aging men. Loss of ejaculation is often age-related and may be associated with other sexual dysfunction in the male, particularly ED[12].

Treatment of Ed and Ejaculatory Disorders: Management of ED most often will occur concurrently with lifestyle modification and treatment of organic or psycho-sexual dysfunctions. Patients and partners are made aware of efficacy, risks and benefits of appropriate treatments, taking into consideration preferences and expectations.

Phosphodiesterase 5 inhibitors: For men with erectile dysfunction, treatment options now include three phosphodiesterase-5 (PDE-5) inhibitors: sildenafil, vardenafil, and tadalafil. All acts to increase intracavernosal cyclic GMP levels, and each one has been proven to be effective in restoring erectile function, allowing for satisfactory sexual intercourse in many men with erectile dysfunction. However, PDE-5 inhibitors will not work without sufficient environmental and psychological cues that re-

sult in sufficient sexual arousal and stimulation to initiate the physiological changes in the penis.

All three PDE-5 inhibitors: sildenafil, vardenafil and tadalafil work to sustain levels of cyclic GMP within the penile corpora cavernosae to allow men with erectile dysfunction to achieve erections in response to appropriate sexual stimuli.

Duration of action separates one PDE-5 inhibitor from another. Sildenafil and vardenafil are effective as early as 30 minutes and up to four hours after dosing whereas tadalafil is effective as early as 16 minutes after and up to 36 hours after dosing.

Sildenafil and vardenafil must be taken on an empty stomach, while tadalafil can be taken without regard to food.

An important factor in the success of PDE-5 inhibitor therapy is instruction and counseling on proper use and administration. Repeat challenge with proper instruction and counseling of patients labeled as PDE-5 inhibitor failures has been demonstrated to salvage approximately 25 to 30 percent of patients who were apparent initial non-responders to PDE-5 inhibitor therapy[13].

Sildenafil, vardenafil, and tadalafil result in similarly high rates of successful sexual intercourse. Side effect profiles are similar; only rarely do men with erectile dysfunction discontinue treatment because of side effects. Current practice guidelines recommend that the choice of PDE-5 inhibitor should be based upon on the patient's preferences, including cost, ease of use, and adverse effects.

Penile self-injection: Intrapenile injection therapy with alprostadil (prostaglandin E1, Caverject), papaverine, or alprostadil with papaverine and phentolamine (Tri-Mix) have all been used for purposes of inducing erection.

The sympathetic nervous system normally maintains the penis in a flaccid or non-erect state. All of these vaso active drugs, when injected into the corpora cavernosae, inhibit or override sympathetic inhibition to encourage relaxation of the smooth muscle trabeculae within the penile erectile bodies. The ensuing onrush of blood engorges the penile corpora cavernosae sinusoidal spaces with sufficient pressure to compress the emissary veins that normally drain blood from the penis. The combination of accelerated arterial inflow and impeded venous outflow from the corpora cavernosae creates an erection.

Considerable education is required for men to become facile with this form of therapy. Under the guidance of urologists men are trained in sterile methods and the proper technique for inserting an insulin syringe with a 26 gauge needle through the shaft of the penis and injecting the vasoactive agent into one corporeal body. The cross circulation of the penile corpora allows medication injected into one penile corporeal body to diffuse over to the contra-lateral side so that a full, firm erection can be expected within a few minutes after intra-penile installation of the drug[13].

Vacuum-assisted erection devices: Several mechanical devices have been developed which utilize vacuum pressure to encourage increased arterial inflow and occlusive rings to discourage venous egress from the penile corpora cavernosae. A certain amount of mechanical dexterity is required to use these devices effectively, but once men become comfortable with using the vacuum and restraining rings they can create an erection sufficient for vaginal penetration and sexual intercourse. They cannot, however, ejaculate externally because the occlusive rings that prevent venous drainage also compress the penile urethra sufficiently to prevent seminal fluid from reaching and traversing the urethral meatus. A number of devices are available for purchase over the counter.

Vacuum devices successfully create erections in as many as 67 percent of patients. Satisfaction with vacuum-assisted erections has varied between 25 and 49 percent. As an example, one prospective study evaluated 18 men by questionnaire at six months: 16 (89 percent) were able to attain satisfactory erections, and the overall satisfaction rate was 83 percent[14]. Sixteen of the 18 men found the device easy to use.

Penile Prostheses: Enthusiasm for drug and penile injection therapy has greatly reduced reliance on surgical implants of penile prostheses as treatment for men with erectile dysfunction. This form of therapy remains a viable option for those men who do not respond to sildenafil and find penile injection or vacuum erection therapy distasteful. There are two general types of prostheses: malleable rods and inflatable prostheses.

Side effects include those related to the anesthesia, local wound infections, and mechanical failure necessitating surgical removal and reimplantation of a new functioning prosthesis.

Psychotherapy and psychoactive medications: Psychological counseling, including the use of sensate focus exercises by both partners, can be helpful when the man is suffering from performance anxiety. This is usually best accomplished by referral to a certified sexual therapy counselor.

Erectile dysfunction is also a common symptom of depression and potency is usually restored as psychotherapy or antidepressant drugs alleviate the depression. However, many of the newest and most effective antidepressant drugs of the serotonin reuptake inhibitor class (eg, fluoxetine, sertraline, paroxetine) decrease both libido and erectile function. On the other hand, trazodone, imipramine, and desipramine can cause delayed or retarded ejaculation, a "side effect" that may actually be beneficial for men suffering from premature ejaculation.

Yohimbine: By blocking presynaptic alpha-2-adrenergic receptors, yohimbine increases cholinergic and decreases adrenergic tone, changes that should theoretically be effective in men with psychogenic erectile dysfunction. Although a rich folk lore has imbued yohimbine with mystical aphrodisiacal properties, it has limited clinical effectiveness.

Optimal results are achieved when yohimbine use is restricted to men with psychogenic erectile dysfunction. As an example, two double-blind, placebo-controlled studies evaluated 101 men with psychogenic erectile dysfunction. Erectile function and sexual intercourse resumed in 37 percent of men treated with yohimbine (5.4 mg TID) within three days to three weeks of starting therapy; only 15 percent of placebo-treated men had a comparable response.

In contrast, a randomized, double-blind study of 29 men with erectile dysfunction of unclear etiology but no known endocrine or psychologic cause showed no difference between yohimbine and placebo; in both groups almost half improved. A virtual lack of response was also noted in 20 men with erectile

dysfunction due to arterial insufficiency and cavernous venous leakage who were treated with either a combination of yohimbine and isoxsuprine or pentoxifylline.

A meta-analysis reviewed this confused set of data on the efficacy of yohimbine[15]. Seven randomized controlled trials of reasonable quality were found and evaluated; the investigators concluded that there was enough evidence to recommend a trial of yohimbine as initial therapy (odds ratio: 3.9).

In practice, the prompt onset of action in "responders" has encouraged clinicians to consider a trial of yohimbine in men with apparent psychogenic erectile dysfunction. Treatment is continued only in those who respond and also tolerate the drug's side effects, which include dizziness, flushing, nausea, and headache.

Yohimbine should be used with caution in patients with heart disease because of its cardiovascular side effects, including tachycardia and the potential for hypertension.

Androgen replacement therapy: If sexual dysfunction is associated with testosterone deficiency, testosterone therapy to restore normal range testosterone levels can be achieved with transdermal testosterone gels, patches or testosterone injections. Each of these preparations has its own advantages and disadvantages. The different preparations and goals of therapy are discussed in detail elsewhere.

Role of vascular surgery: For an erection to occur blood must flow through a network of arteries all branching from the iliac artery and then on to smaller tributaries ending at the helicine arteries that feed the corpora cavernosae. During moments of sexual excitation blood flows into the corpora cavernosae under such high pressure that if first causes penile swelling (tumescence) and then compresses the emissary veins that normally drain blood form the corpora cavernosae creating a rigid erection? Any condition that compromises arterial flow to the genital area can cause impotence by a "failure to fill" whereas premature egress of venous blood out of the emissary veins would set the stage for a "failure to store" form of erectile dysfunction.

Surgical techniques have been devised to alleviate arterial occlusions and correct "failure to fill" and also shore up sagging veins in men when "failure to store" seemed to be the root cause of their sexual dysfunction. Although these surgical procedures had enjoyed some popularity in the past, long-term sexual outcomes have been quite poor, with the exception of young patients with traumatic arterial lesions.

Melanocortin receptor agonists: Melanocortin receptor agonists, which act on the central nervous system rather than the vascular system, are being developed as a possible new therapy for erectile dysfunction. PT-141, an intranasal preparation, appears to be effective as monotherapy or in combination with PDE-5 inhibitors. However, significant side effects, including flushing and nausea, may limit its clinical utility. This agent is neither approved for use nor commercially available.

Treatment of Premature Ejaculation: No pharmacologic therapy such as the "pause and squeeze" technique has achieved variable success, but drug therapy has proved quite useful.

Several psychoactive drugs can cause delayed or retarded ejaculation, and some have been evaluated for the treatment of premature ejaculation. In one double-blind study, 37 potent men ages 19 to 70 years who complained of premature ejaculation were randomly assigned to receive the selective serotonin reuptake inhibitor (SSRI) sertraline (50 mg/day) or placebo. The mean ejaculatory latency time before treatment in both groups was 0.3 minutes and the mean interval after four weeks of treatment was 0.5 minutes in the placebo group and 3.2 minutes in the sertraline group, a significant difference. In a subsequent open-label phase of the study, 20 of 29 men (67 percent) were able to discontinue the drug after a mean of seven months and maintain a mean ejaculatory latency time greater than four minutes. Other SSRIs also appear to be effective[16].

Intermittent use of SSRIs may be as effective as continuous use. This issue was examined in a study of 26 men with premature ejaculation who were randomly assigned to receive paroxetine (20 mg) or placebo as needed three to four hours before planned intercourse. The mean ejaculatory latency time was significantly greater in the paroxetine group compared with placebo after four weeks (3.2 versus 0.45 minutes). In a second phase of the study involving 42 men, treatment with paroxetine daily for three weeks prior to using it on an as needed basis improved ejaculatory control compared to men who only used the drug only as needed.

An additional SSRI, dapoxetine, also appears to be effective, based upon two randomized trials of nearly 2000 men with premature ejaculation who were randomly assigned to receive placebo or dapoxetine (30 mg or 60 mg/day)[16]. Unlike other SSRIs, which are taken daily, dapoxetine is taken on-demand one to three hours before intercourse. The mean ejaculatory latency time before treatment in all groups was approximately 0.9 minutes, while the mean intervals in the placebo and dapoxetine groups (30 and 60 mg) on treatment were 1.8, 2.8, and 3.3 minutes, respectively. The most common side effect with dapoxetine was nausea (8 and 20 percent with 30 and 60 mg, respectively).

Dapoxetine is not commercially available in all countries.

The tricyclic antidepressant clomipramine is useful and possibly more effective than SSRIs in prolonging the interval from intromission to ejaculation. In one study of 36 men with premature ejaculation, four weeks of treatment with either placebo, fluoxetine, sertraline , or clomipramine resulted in increased ejaculation time from 46 seconds (placebo) to 2.27 minutes (fluoxetine), 4.27 minutes (sertraline), and 5.75 minutes (clomipramine). However, significantly more side effects, most notably dry mouth, occurred in patients treated with clomipramine. One small trial suggested that sildenafil may be superior to clomipramine and SSRIs for premature ejaculation[16], but this has not been confirmed in larger studies.

Safarinejad and Hosseini have published a randomized, controlled trial on the use of tramadol HCL to treat PE[17]. Various research groups have shown tramadol to have some efficacy in treating PE[18], especially as an on-demand medication, although the mechanism is poorly understood[17,18]. However, there is evidence that some cases of secondary PE are seen in men who are withdrawing from opiate addiction. There may therefore be a relation between central opioid receptors and ejaculatory control.

An alternative to oral medication is the use of topical agents to treat one of the supposed causes of PE hypersensitivity of the penis. This approach involves applying local anesthetics

in cream, gel or spray formulations in order to decrease penile sensitivity. Busato and colleagues designed a double-blind, randomized, placebo-controlled study to assess the use of lidocaine-prilocaine solution in 42 men with PE. A significant increase in mean IELT ($P < 0.001$) was reported in the lidocaine-prilocaine group (from 1.49 to 8.45 min) compared with in the placebo group (from 1.67 to 1.95 min). With the use of local anesthetic, formulated as a cream, spray or gel, no systemic adverse effects have been reported; topical adverse effects might include skin burning, numbness, pain and irritation. The occurrence of other sexual problems, such as sexual dysfunction, is rarer[19].

Psychological treatment for PE has been proposed, with the aim of prolonging IELT and thus improving the sexual relationship between the patient and his partner. Several studies of psychotherapies have been reported, but there is a dearth of well-designed and controlled trials. Behavioral training techniques, including the stop-and-start and squeeze methods, are currently used by sexologists. The former was initially described by Masters and Johnson, and begins with manual auto stimulation. After achievement of good arousal control by the man, the partner becomes involved with manual stimulation and then with sexual intercourse. The squeeze technique is similar to the aforementioned approach, except that when the stimulation is stopped, the penis is squeezed with the fingers. Although a good short-term success rate has been reported, behavioral techniques have never been studied in appropriate trials and tend to lose their efficacy over the long term.

Some authors have tried to induce a permanent penile hypoesthesia by surgical selective dorsal nerve neurectomy. This surgical procedure has also been compared with hyaluronic acid gel injection, which can potentially block nerve receptors for tactile stimuli[20]. No significant additive effect has been observed when injections and neurectomy are combined, but both individual treatments significantly prolong postoperative IELT.

Delayed ejaculation and an ejaculation

Men suffering from delayed or inhibited ejaculation, when organic or pharmacologic causes are excluded, can benefit from a psychological approach. Preliminary psychosexual counseling is required before the psychotherapist can choose a therapy. Several approaches have been described: sex education, reduction of goal-oriented anxiety, increased and more genitally focused stimulation, and patient role-playing of an exaggerated ejaculatory response on his own and in front of his partner. In this field the literature is difficult to evaluate, as most authors report only a small series of cases with seemingly exaggerated results.

A variety of drugs have been suggested to induce ejaculation, but no placebo-controlled studies have been published. Cyproheptadine, a serotonin-receptor antagonist, as well as several dopaminergic agents such as amantadine, yohimbine and apomorphine, are a few of the medications proposed but with variable and controversial results.

In order to achieve fertility for a patient who experiences an ejaculation, sperm retrieval is possible via vibrostimulation. Vibrostimulation requires an intact lumbosacral spinal cord segment (above T10); if this method is not successful, electro ejaculation, in which the periprostatic nerves are stimulated by a probe inserted into the rectum (generally under anesthesia), might be of benefit. If ejaculation does not occur using the aforementioned techniques, surgical sperm retrieval is the treatment of choice.

Retrograde ejaculation: Most men do not require treatment for retrograde ejaculation because they are still able to enjoy a healthy sex life and the condition does not have adverse effects on their health. If retrograde ejaculation is caused by using a certain medication then normal ejaculation will usually return once the medication is stopped. When a spinal cord injury, urethral anomalies or drug consumption is excluded, men suffering from retrograde ejaculation can benefit from a pharmacological treatment. For example, imipramine, ephedrine sulfate and desipramine (chlorpheamine and phenylpropanalamine) have been found to improve bladder neck closure[21]. Sperm collection from the urine is considered in cases of drug failure, contraindication for pharmacologic management, spinal cord injuries, or when other medications that induce retrograde ejaculation cannot be suspended. However, if the retrograde ejaculation has been caused by significant muscle or nerve damage, treatment may not be possible.

Conclusion

Sexual dysfunction is common in men and increases with age. There are several kinds of male sexual dysfunction: decreased libido, erectile dysfunction, and ejaculatory disorders. Ejaculatory disorders include premature ejaculation, delayed ejaculation, and an ejaculation. Painful orgasm is also included in this category. The management of sexual dysfunction has to be individualized based on cause and type of disorder because they have different treatment approaches.

Abbreviations

PE: premature ejaculation
SSRIs: selective serotonin reuptake inhibitors

Declarations

Availability of data and materials: The data that support the findings of this study are available from the corresponding author.

Funding: This study was not funded

Consent for publication: Not applicable (the manuscript does not contain any individual person's data in any form).

Consent for publication: Not applicable (the manuscript does not contain any individual person's data in any form).

Competing interests: The authors declare that they have no competing interests

Authors' contributions: OS designed and conducted the study, drafted the manuscript, revises it critically and submitted it.

Acknowledgements: I would like to extend sincere thanks to my colleagues for their extensive support in getting the necessary documents.

References

1. Araujo, A.B., Mohr, B.A., McKinlay, J.B. Changes in sexual function in middle-aged and older men: longitudinal data from the Massachusetts Male Aging Study. (2004) J Am GeriatrSoc52(9): 1502-1509.
   Pubmed| Crossref| Others
2. Bacon, C.G., Mittleman, M.A., Kawachi, I., et al. Sexual function in men older than 50 years of age: results from the health professional's follow-up study. (2003) Ann Intern Med 139(3): 161-168.
   Pubmed| Crossref| Others
3. Rosen, R.C., Fisher, W.A., Eardley, I., et al. The multinational Men's Attitudes to Life Events and Sexuality (MALES) study: I. Prevalence of erectile dysfunction and related health concerns in the general population. (2004) Curr Med Res Opin 20(5): 607-617.
   Pubmed| Crossref| Others
4. Fung, M.M., Bettencourt, R., Barrett-Connor, E. Heart disease risk factors predicts erectile dysfunction 25 years later: the Rancho Bernardo Study. (2004) J Am Coll Cardiol 43(8): 1405-1411.
   Pubmed| Crossref| Others
5. Min, J.K., Williams, K.A., Okwuosa, T.M., et al. Prediction of coronary heart disease by erectile dysfunction in men referred for nuclear stress testing. (2006) Arch Intern Med 166(2): 201-206.
   Pubmed| Crossref| Others
6. Shamloul, R., Ghanem, H. Erectile dysfunction. (2013) Lancet 381(9861): 153-165.
   Pubmed| Crossref| Others
7. KO, D.T., Hebert, P.R., Coffey, C.S., et al. Beta-blocker therapy and symptoms of depression, fatigue, and sexual dysfunction. (2002) JAMA 288(3): 351-357.
   Pubmed| Crossref| Others
8. Marberger, M., Roehrborn, C.G., Marks, L.S., et al. Relationship among serum testosterone, c sexual function, and response to treatment in men receiving dutasteride for benign prostatic hyperplasia. (2006) J Clin Endocrinol Metab 91(4): 1323-1328.
   Pubmed| Crossref| Others
9. Rochira, V., Balestrieri, A., Madeo, B., et al. Sildenafil improves sleep-related erections in hypogonadal men: evidence from a randomized, placebo-controlled, crossover study of a synergic role for both testosterone and sildenafil on penile erections. (2006) J Androl 27(2): 165-175.
   Pubmed| Crossref| Others
10. De Rosa, M., Zarrilli, S., Vitale, G., et al. Six months of treatment with cabergoline restores sexual potency in hyperprolactinemic males: an open longitudinal study monitoring nocturnal penile tumescence. (2004) J Clin Endocrinol Metab 89(2): 621-625.
    Pubmed| Crossref| Others
11. Dhindsa, S., Prabhakar, S., Sethi, M., et al. Frequent occurrence of hypogonadotropichypogonadism in type 2 diabetes. (2004) J Clin Endocrinol Metab 89(11): 5462-5468.
    Pubmed| Crossref| Others
12. Rowland, D.L., Patrick, D.L., Rothman, M., et al. The psychological burden of premature ejaculation. (2007) J Urol 177(3): 1065-1070.
    Pubmed| Crossref| Others
13. Hatzimouratidis, K., Moysidis, K., Bekos, A., et al. Treatment strategy for "non-responders" to tadalafil and vardenafil: a real-life study. (2006) Eur Urol 50(1): 126-132.
    Pubmed| Crossref| Others
14. Gruenwald, I., Shenfeld, O., Chen, J., et al. Positive effect of counseling and dose adjustment in patients with erectile dysfunction who failed treatment with sildenafil. (2006) Eur Urol 50(1): 134-140.
    Pubmed| Crossref| Others
15. Shenfeld, O., Hanani, J., Shalhav, A., et al. Papaverine-phentolamine and prostaglandin E1 versus papaverine-phentolamine alone for intracorporeal injection therapy: a clinical double-blind study. (1995) J Urol 154(3): 1017-1019.
    Pubmed| Crossref| Others
16. Kennedy, S.H., Rizvi, S. Sexual dysfunction, depression, and the impact of antidepressants. (2009)J Clin Psychopharmacol 29(2): 157–164.
    Pubmed| Crossref| Others
17. Safarinejad, M.R., Hosseini, S.Y. Safety and efficacy of tramadol in the treatment of premature ejaculation: a double-blind, placebo-controlled, fixed-dose, randomized study. (2006) J Clin Psychopharmacol 26(1): 27-31.
    Pubmed| Crossref| Others
18. Alghobary, M., El-Bayoumy, Y., Mostafa, Y., et al. Evaluation of tramadol on demand vs. daily paroxetine as a long-term treatment of lifelong premature ejaculation. (2010) J Sexual Med 7(8): 2860–2867.
    Pubmed| Crossref| Others
19. Busato, W., Galindo, C.C. Topical anaesthetic use for treating premature ejaculation: a double-blind, randomized, placebo-controlled study. (2004) BJU Int 93(7): 1018-1021.
    Pubmed| Crossref| Others
20. Kim, J.J., kwak, T.I., Jeon, B.G., et al. Effects of glans penis augmentation using hyaluronic acid gel for premature ejaculation. (2004) Int J Impot Res 16(6): 547-551.
    Pubmed| Crossref| Others
21. Kamischke, A., Nieschlag, E. Update on medical treatment of ejaculatory disorders. (2002) Int J Androl 25(6): 333-344.
    Pubmed| Crossref| Others