Mini review

Contemporary management of erectile dysfunction

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Abstract
Erectile dysfunction (ED) is one of the most common sexual disorders in men, and the existence of an underlying cause should always be considered. It is also commonly and closely associated with age and risk factors for cardiovascular disease. Therefore, all men with ED should be screened for medical problems. Treatment of ED can enhance self-esteem, reduce psychological morbidity, and increase the emotional well-being of both partners. Today, unless contraindicated, user-friendly, effective, and safe therapies offered for the treatment of ED are lifestyle and risk factor modification (e.g., exercise and weight loss) and the use of oral phosphodiesterase type 5 inhibitors, such as sildenafil, tadalafil, or vardenafil. Vacuum erection devices, intracavernous injection therapy, and penile prostheses are other options of treatment when oral medication fails. The following minireview provides a practical approach for the management of ED in outpatient departments.

1. Introduction
Erectile dysfunction (ED) is a common, persistent inability to achieve or maintain an erection of sufficient quality for sexual intercourse. It is a risk factor for other diseases and conditions, and it is a secondary condition brought about by other primary causes, such as certain lifestyles, side effects of drugs, aging, systemic diseases, and neurovascular and psychological disorders. ED commonly occurs, and the incidence increases with age. ED is classified as psychogenic, organic, or mixed psychogenic and organic. The increased amount of study devoted to ED has provided more pathophysiological evidence to support the association of ED with organic causes; hence, 80% of cases are now considered to be organic in origin. Chew et al’s study also showed that ED is not only significantly associated with—but is also strongly predictive of—subsequent atherosclerotic cardiovascular (CV) events. Montorsi et al pointed out that sexual dysfunction in men represents a group of common medical conditions that needs to be managed from a multidisciplinary perspective.

Araujo et al’s findings demonstrated that ED is significantly associated with increased all-cause mortality, primarily through its association with CV disease (CVD) mortality. ED is a common problem among aging men. The factors that increase the risk of ED include older age, depression, diabetes, and CVD risk factors. There are a number of risk factors associated with ED that can be modified: obesity, hypertension, unfavorable lipid levels, alcohol abuse, physical activity, tobacco addiction, diabetes mellitus (DM), depression, anxiety disorders, hypothyroidism, prostate carcinoma, testosterone deficiency, renal, hepatic, and neurologic diseases, and a number of medications. ED may also act as a sentinel symptom for other important underlying diseases, primarily coronary heart disease and depression.

2. Prevalence
ED is currently one of the most common sexual dysfunctions in men worldwide, including Taiwan. Among 15 large-scale prevalence studies undertaken between 1994 and 2004, the prevalence of ED ranged from 10% to 64%. Fatusi et al reported an overall ED prevalence of 43.8% among 355 married men aged 30–70 years. Parazzini et al’s study on more than 2000 individuals aged ≥18 years showed a prevalence of ED of 12.8%, and up to 48.3% for men over 70 years. ED prevalences in the United States, the United Kingdom, Australia, Japan, and Korea were reported to be 52%, 32%, 43%, 26%, and 37%, respectively. The prevalence rate of ED in Taiwan, as defined by the International Index of Erectile Function (IIEF)-5, was 27% among all respondents and 29% among those aged...
Although ED is a common health problem in Taiwan and the prevalence of ED increases with age, affected men lack awareness regarding the presence of erectile problems and the importance of initiating timely and effective treatment. Wu et al. also found that the prevalence of ED among study participants was 17.7%, and the frequency increased with age. Patients with chronic diseases were significantly associated with ED. A significant number of men now know that ED is not just a consequence of advancing age, but also can be a result of chronic illness or radical prostate cancer surgery. Because many chronic diseases are associated with ED and because of its high prevalence, ED has been given increasing attention in recent years.

3. Initial evaluation of ED

3.1. Initial assessment

The initial evaluation should include medical, sexual, and psychosocial histories, as well as laboratory assays to identify possible comorbidities for a well-organized management. The evaluation process should include the patient’s partner, their relationship, and the situation in which their sexual activity occurs or is attempted. A few effective and most commonly used ED-related questionnaires include an abridged, five-item version of the IIEF-5 score, Sexual Health Inventory for Men, and Erection Hardness Grading Scale.

3.2. Medical history

For a well-organized evaluation, a complete medical history should be collected. A detailed description of the problem, including the duration of symptoms and original precipitants, should be obtained. Concurrent medical (especially hypertension, DM, hyperlipidemia, ischemic heart disease, peripheral vascular disease, and cerebrovascular events), and psychiatric and surgical histories (especially urogenital or spinal surgery and trauma) should be asked about, as should the current relationship status (single, married, in a long-term relationship, etc.) and history of previous sexual partners and relationships. Issues of sexual orientation and gender identity should also be noted. Finally, the patient’s use of social and illicit drugs (e.g., tobacco, alcohol, marijuana, and heroin) should be recorded.

3.3. Physical examination

It is important to identify the underlying disease that brought about the sexual difficulty with ED symptoms or that may contribute to the maintenance of the difficulty or influence its treatment. Blood work should be based on the potential underlying conditions listed above plus special concerns raised from the history and physical examination. Data such as weight, height, body mass index, and waist circumference should be recorded to identify metabolic syndrome. A genitai examination is recommended, and is essential if there is a history of rapid onset of pain, deviation of the penis during tumescence, or symptoms of hypogonadism or other urological symptoms (past or present). The blood pressure, heart rate, waist circumference, and weight should be measured.

3.4. Laboratory examination

ED is an independent marker for CV risk and can be the presenting feature of diabetes, so serum lipids and fasting plasma glucose should be measured in all patients. Special examinations, such as Doppler flow studies, nocturnal penile tumescence, and angiography, rarely impact therapy and are therefore rarely indicated. Hypogonadism is a treatable cause of ED that may also make men less responsive; therefore, all men with ED should have serum testosterone measured with a blood sample taken in the morning between 08:00 and 11:00. Serum prostate-specific antigen should be considered if clinically indicated. It should certainly be measured before commencing testosterone and at regular intervals during testosterone therapy. ED in an otherwise asymptomatic man may be a marker for underlying coronary artery disease, so all men with unexplained ED should have a thorough evaluation, and any risk factors for coronary artery disease that are identified should be addressed.

3.5. Management options for ED

For most men, ED is a personal issue that is difficult and embarrassing to admit to their physicians. All treatments are individualized, and it is important to identify the etiology in all cases. In addition to patient difficulties in discussing their personal matters with a specialist, the process of the care model for ED outlines a goal-oriented approach for diagnosis and treatment of ED.

3.6. Objectives of treatment

The primary goal in managing ED is to enable the individual or couple to enjoy a satisfactory sexual experience. This involves: (1) identifying and treating any curable causes of ED; (2) initiating

![Fig. 1. Treatment algorithm for erectile dysfunction. ED = erectile dysfunction; PDE5 = phosphodiesterase type 5.](image-url)
lifestyle changes and risk factor modification; and (3) providing education and counseling to patients and their partners (Fig. 1).

3.7. Reversible causes of ED

3.7.1. Hormone deficiencies and ED
Endocrine disorders may have a significant effect on sexual function. These conditions, including hypogonadism, hyperthyroidism, and hyperprolactinemia, are examples of relevant disorders. The advice of an endocrinologist is necessary when there is doubt about the cause and appropriate management of the disorder. Androgen deficiency in the adult male is more common with increasing age, but its management remains controversial. In addition to sexual dysfunction, androgen deficiency is associated with osteoporosis, dyslipidemia, type 2 diabetes, metabolic syndrome, and depression. Hyperthyroidism may influence erectile function by increasing sex hormone-binding globulin production, thereby reducing free testosterone levels. Effective treatment of hyperthyroidism may resolve the coexisting ED. Hyperprolactinemia is associated with ED, loss of sexual interest, and anorgasmia. It is frequently accompanied by an androgen deficiency, because high prolactin levels suppress luteinizing hormone production, consequently causing hypogonadism. Hyperprolactinemia should be ruled out by blood tests in all men with reduced sexual interest. A moderate elevation of prolactin levels (<1000 mU/L) is unlikely to cause ED.

3.7.2. Drug-induced ED
Many drugs are implicated in ED. In many cases, the evidence for drugs having a direct causal relationship with some form of sexual dysfunction is relatively poor (but patients often blame the drugs).

Drugs may affect sexual response in a number of ways: (1) those that cause sedation may affect sexual motivation and, indirectly, cause ED; (2) those that affect CV function, such as antihypertensive agents, may act centrally and may also affect penile hemodynamic; (3) some drugs affect endocrine parameters (antiandrogens and estrogens may affect both sexual desire and erection); and (4) drugs that cause hyperprolactinemia, such as phenothiazines, may also affect sexual desire and erection.

3.8. Irreversible causes of ED

3.8.1. Diabetes mellitus
Neuropathic ED develops in relation to other diabetic complications and is more likely to be present when there is evidence of both somatic and autonomic neuropathies. It is hypothesized that cavernosal artery insufficiency, corporal veno-occlusive dysfunction, and/or autonomic neuropathy are the major organic pathophysiologic mechanisms leading to persistent erectile impairment in men with DM. It was estimated that 10–19% of organic ED is neurogenic. Once present, neuropathic ED is permanent and irreversible. Its onset is always gradual and slowly progressive over months and years.

3.8.2. Postradical prostatectomy
Penile revascularization involves harvesting of the inferior epigastric artery and Anastomosing it to either the dorsal vein or artery of the penis to increase arterial inflow to the corporal bodies. Bicycle riding for more than 3 h/week was described as an independent risk factor for ED. The mechanism is postulated to be related to the rider's interaction with the saddle. This may produce a neuropathy, which is occasionally persistent, but usually reversible or vascular endothelial injury and vasculogenic ED.

3.8.3. Postradical prostatectomy
The etiology of the development of corporal veno-occlusive dysfunction in postprostatectomy patients has not been fully elucidated, but it is thought to result from a combination of denervation-induced cavernosal smooth muscle dysfunction and collagen deposition resulting from relative ischemia of the corporeal tissues. However, in men who develop persistent ED after surgery, the cavernosal smooth muscle is gradually replaced by collagenous tissue. This change in the cavernosal structure may be what leads to persistent ED in some men, even though they have had nerve-sparing surgery. In these men, there is inadequate healthy cavernosal smooth muscle to create an erection.

3.8.4. Venous leakage syndrome
A venous leak is a leak in the veins of the penis. Because leakage allows blood to leave the penis during an erection, an erection cannot be maintained. Venous leak can occur from damage to the veins in the penis caused by injury or disease.

3.9. Partner sexual problems and ED
Patients with significant psychosocial problems and/or relationship difficulties should be offered sex and/or couple therapy as appropriate. Therapeutic programs include sex education, communication and sexual skills training, sensate focus, systematic desensitization, and cognitive—behavioral therapy.

4. Treatment of ED

4.1. First-line treatment

4.1.1. Oral pharmacotherapy: phosphodiesterase 5 inhibitors
Selective inhibitors of phosphodiesterase 5 (PDE5) are currently the treatments of choice, owing to their general efficacy, safety, convenience, and physiologic mechanism of action. First-line therapy for the majority of patients today is the use of selective PDE5 inhibitors, which are associated with a reasonable efficacy of 60–70%. They have proven efficacy and tolerability in improving erectile function across a wide range of clinical conditions. PDE5 inhibitors include tadalafil (Cialis), vardenafil (Levitra), and sildenafil (Viagra). All three medications work in much the same way. These drugs mainly have an effect on nitric oxide, which is a natural chemical produced by the body that relaxes muscles in the penis. Drugs that inhibit PDE5 increase arterial blood flow, which leads to smooth muscle relaxation, vasodilation, and penile erection; however, PDE5 inhibitors are not initiators of erection—sexual stimulation is still needed.

Overall, the adverse effects of PDE5 inhibitors are mild, transient, and dose-related. These medications may not work or may be dangerous for a person if that person: (1) takes nitrate drugs for angina, such as nitroglycerin (Nitro-Bid and others), isosorbide mononitrate (Imdur), and isosorbide dinitrate (Isordil); (2) takes a blood-thinning medication, which may affect sexual desire and erection; and (3) some drugs affect endocrine parameters (antiandrogens and estrogens may affect both sexual desire and erection) and dose-related.
considerably at 35 trauma, anger resulting from marital discord, depression, and ED include an uncaring partner, which leads to psychological inefficiency, testosterone replacement therapy may be an option to continue to use them in the long term; (5) adverse effects include pressure medications; (3) has heart disease or heart failure; (4) has had a stroke (5) has very low blood pressure (hypotension) or uncontrolled high blood pressure (hypertension); or (6) has uncontrolled diabetes.

Most men who take Viagra, Levitra, and Cialis are not bothered by the side effects. When side effects do occur, they can include headaches, flushing, indigestion, stuffy or runny nose, back pain and muscle aches (with Levitra), and temporary vision changes, including “blue vision” (with Viagra). In a small number of cases, men taking Viagra, Levitra, or Cialis have reported more serious side effects, such as hearing or vision loss and priapism. Taking Viagra, Levitra, or Cialis without treating the original problem may improve sexual performance, but the patient should not ignore an underlying health issue by just taking pills to treat the symptom.

4.2. Hormone replacement therapy

For the small number of men who have a testosterone deficiency, testosterone replacement therapy may be an option to treat ED.

4.3. Other drug therapies

Other drug therapies include the following: Yohimbine, Delaqua mine, Trazodone, L-arginine, red Korean ginseng, oral limaprost, oral phen tolamine, and nitroglycerine; Papaverine and Minoxidil are applied topically, but their effects are limited.

4.3.1. Psychosexual/relationship therapy

Psychosexual causes normally addressed in Taiwanese men with ED include an uncaring partner, which leads to psychological trauma, anger resulting from marital discord, depression, and performance anxiety that may lead to a loss of self-confidence. This option focuses on the patient’s interpersonal difficulties. Psychosexual techniques, including the setting up of realistic goals for a couple, periodic psychosexual therapy follow-up, continual utilization of nonintercourse pleasuring sessions, and initiation of intimacy dates, are advocated as prevention strategies. Some studies showed the benefits of combining pharmacotherapy with sexual counseling or brief sex therapy.

4.3.2. Physiotherapy

The pelvic floor muscles have a role in erection. Contraction of the ischiocavernous muscle facilitates erection. A study showed the benefit of treating ED via pelvic floor exercises. Aegel exercises for men can help prevent or control urinary incontinence and possibly improve sexual performance. Kegel exercises for men can help prevent, treat, or delay some of the symptoms caused by weak pelvic floor muscles, such as urine leakage.

4.4. Second-line treatment

4.4.1. Vacuum erection devices

The vacuum constriction device is a hollow tube with a hand-powered or battery-powered pump, which creates a vacuum that pulls blood into your penis. It is usually used in patients that who do not want to use pharmacotherapy or for whom the drugs are contraindicated. The vacuum constriction device has the following features: (1) it is highly effective in inducing erections regardless of the etiology of the ED; (2) reported satisfaction rates vary considerably at 35–84%; (3) long-term usage of vacuum devices also varies but is considerably higher than for self-injection therapy; (4) most men who are satisfied with vacuum devices continue to use them in the long term; (5) adverse effects include bruising, local pain, failure to ejaculate, and partners sometimes report that the penis feels cold; and (6) serious adverse events are very rare, but skin necrosis was reported.

4.4.2. Intracavernous injection therapy

With intracavernous injection treatment, the patient is taught to inject his penis with a vasoactive drug in a private room. Intracavernous injection therapy is the most effective form of pharmacotherapy for ED and has been used for more than 20 years. However, because of the invasive nature of the procedure, it is unacceptable to some patients and their partners, and this may result in poor long-term compliance among those who do try it. The most frequently used drug is alprostadil; other agents include phentolamine, papaverine, and vasoactive intestinal polypeptide, or a combination of agents. Alprostadil (Caverject, Viridal) was the first and, until recently, the only licensed drug approved for intracavernous ED treatment.

4.5. Third-line treatment

4.5.1. Penile prosthesis

This is a surgical treatment that involves emplacing devices into the two sides of the penis. These implants consist of either inflatable or semirigid rods made from silicone or polyurethane. This invasive treatment can be expensive and is usually not recommended until other methods have been tried first. Penile prostheses are particularly suitable for those with severe organic ED, especially if the cause is Peyronie’s disease or postpriapism. Implanted inflatable penile prostheses have demonstrated the capacity to produce suitable erections and good patient satisfaction in long-term follow-up. The reliability of the implants is excellent, and postoperative morbidity is low. However, infections associated with inflatable penile prostheses are the most disastrous complication. As bacterial infection on the new penile prostheses is one of the major problems, coating the prostheses with rifampin and minocycline reduced bacterial growth; this method was developed and approved in May 2001 by the US Food and Drug Administration. With the InhibiZone (American Medical Systems, Minneapolis, Minnesota, USA) prosthesis, tissue-contacting surfaces are impregnated with quantifiable doses of rifampin and minocycline. The reported incidence rates of infections after 60 days were 0.28% in the treated (InhibiZone) group and 1.59% in the control group (p = 0.0014). After 180 days, the respective infection rates in the treated (InhibiZone) and control groups were 0.68% and 1.61% (p = 0.0047). The use of InhibiZone to target postoperative infections resulted in a statistically significant decrease in penile prosthesis infection rates in original implants.

4.5.2. Penile revascularization surgery

Penile revascularization surgery is microvascular arterial bypass surgery for ED that is similar to a cardiac bypass, but in the penis. The most common causes of ED that can be treated by penile revascularization are blunt trauma to the perineum or bike riding. The aim of penile arterial revascularization surgery is to increase the cavernosal arterial blood supply to the penis in order to produce a natural erection. Patients with systemic arterial disease or atherosclerosis from conditions such as DM, hypertension, smoking, dyslipidemia, and aging should not be considered for penile arterial bypass surgery. This procedure is highly specialized and requires extensive training in microvascular surgery as well as special equipment in the operating room, so patients should be referred only to centers of excellence that run strict protocols that objectively measure success over long intervals. In conclusion, ED affects a significant proportion of the population on a worldwide scale and is associated with a significant
reduction in health-related quality of life, but clinicians must be aware that ED is not a diagnosis, it is a symptom. It represents an underlying cause that should always be considered. Treatment of male ED is associated with enhanced self-esteem, reduced psychological morbidity, and increased emotional well-being for both sexual partners. With the advent of highly effective and widely available pharmacotherapy for ED, physicians are increasingly involved in the diagnosis and treatment of this important quality-of-life issue.

Conflicts of interest statement

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