



European Association of Urology

**GUIDELINES  
ON  
ERECTILE  
DYSFUNCTION**

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Male erectile dysfunction (ED) (impotence) has been defined as the persistent (at least 6 months) inability to attain and maintain an erection sufficient to permit satisfactory sexual performance.

Although erectile dysfunction is a benign disorder, it is related to physical and psychological health and has a significant impact in the quality of life of both sufferers and their family. Recent epidemiological data have shown a high prevalence and incidence of ED. The Massachusetts Male Aging Study reported a combined prevalence of 52% for minimal, moderate, and complete ED in non-institutionalized 40 to 70 years old men in the Boston area. In this study, the individual prevalence were 17.2%, 25.2% and 9.6% for minimal, moderate and complete ED, respectively (1). The same study found that the incidence of ED is 24 new cases for 1000 men.

Erection is a neurovascular phenomenon under hormonal control and includes arterial dilatation, trabecular smooth muscle relaxation and activation of the corporeal veno-occlusive mechanism (2,3). The advances of basic and clinical research during the last 15 years has led to the development of several new treatment options for erectile dysfunction, including new pharmacologic agents for intracavernosal, intraurethral and oral use. The recent advent of medical therapy, and the poor results of long-term follow-up in reconstructive vascular surgery, have significantly modified the medical management of this disorder (4,5,6).

The current availability of an effective and safe oral therapy for ED, the future availability of other oral drugs awaiting final approval, in conjunction with the tremendous media interest for the condition, has resulted in an increasing number of men seeking help for ED. As a consequence, many physicians without background knowledge and clinical experience in diagnosis and treatment of ED, are involved in making decisions about the evaluation and treatment of these men. This has meant that some men with erectile dysfunction may undergo little or no evaluation before treatment is initiated, or that men without erectile dysfunction may seek treatment in order to enhance their sexual performance with anti-ED drugs. In such circumstances, the disease causing the symptom (ED) may remain untreated. Such observations made the development of guidelines for the diagnosis and treatment of ED a necessity. The European Association of Urology formed an expert panel to address the shortcomings and problems associated with the diagnosis and treatment of ED. The overall objective of the project was to develop guidelines for clinical evaluation and treatment, based on the evaluation and review of available scientific information, as well as current research and clinical practice in the field. Moreover, the panel identified critical problems and knowledge gaps, setting priorities for future clinical research.

## DIAGNOSIS

During the first visit, the essential step in the management of erectile dysfunction is the taking of a comprehensive medical and psychological history of the patients and their partner when possible (7,8).

A detailed medical history is critical as many common disorders are associated with erectile dysfunction, including hypertension, diabetes mellitus, myocardial disease, lipidemia, hypercholesterolemia, renal insufficiency, hypogonadism, neurologic and psychiatric disorders, and indeed any chronic illness. Genitourinary and rectal surgery, as well as many drugs, particularly antihypertensive and psychotropic drugs may cause ED. Other drug groups and substance abuses are well-documented causes of ED. The chronic use of alcohol, marijuana, codeine, meperidine, methadone and heroin is associated with a high percentage of ED (9).

The influence of radiation therapy on ED is well known. Evaluation revealed vasculogenic alteration to be the most consistent organic erectile abnormality in radiotherapy (10).

The initial enquiry about medical history allows the establishment of a more relaxing atmosphere and permits the questions about erectile function and other sexual history to be asked more easily, even when men do not volunteer to describe their problem. The sexual history may include information on previous and current sexual relationship, the current emotional status, the onset and the duration of the erectile problem and possible previous consultations and treatments. Detailed description of the quality of both erotic and morning erections, in terms of rigidity and duration, as well as arousal, ejaculation and orgasmic problems should be discussed.

The use of validated questionnaires, such as the International Index for Erectile Function (IIEF) may be helpful in order to objectively assess not only the present status, but also the impact of a specific treatment (11).

A focused physical examination must be performed on every patient with particular emphasis on the genitourinary, endocrine, vascular and neurologic systems (7). The physical examination may reveal unsuspected findings as Peyronie's disease, small testes, prostatic cancer. A rectal examination should be performed in every patient older than 50 years.

Selective laboratory testing (blood glucose and testosterone) is advisable in the majority of the patients and selectivity in other patients when a lipids profile, prolactin and PSA should be considered (12,13,14).

It is important that the physician facilitates communication with the patient and his partner and explains the strategy of the diagnostic and therapeutic approach.

It may not be often possible to involve the partner on the first visit but an effort should be made to involve the

partner during the second visit. On that occasion the physician analyses the results of the blood tests and if any abnormality is observed, further investigation is referred to another specialist may be necessary.

*The discussion considers patient's expectations and needs and should be carried out between the physician, the patient and their partner about the understanding of the disorder, the interpretation of the diagnostic tests and the rational selection of treatment options. Patient and partner education are essential components in the management of erectile dysfunction (15).*

While the majority of patients with erectile dysfunction can be managed within the sexual care setting, some circumstances may dictate the need for specific diagnostic testing:

- The patient with primary erectile disorder because beside the psychogenic cause, it is mandatory to exclude any other organic disease.
- Young patients with a history of pelvic or perineal trauma who could benefit for potentially curative vascular surgery.
- Specific tests may be indicated also at the request of the patient or its partner.
- For medico-legal reasons.

Among the specific tests used are: assessment of nocturnal penile tumescence and rigidity (Rigiscan-NTPR); vascular studies such as intracavernous vasoactive drug injection, duplex ultrasound completed with arteriography or cavernosometry; neurologic studies such as bulbocavernous reflex latency, nerve conduction; endocrinologic studies and specialized psychodiagnostic evaluation. The NPTR should take place for at least 2 nights. Presence of an erectile event of at least 60% rigidity recorded on the tip of the penis, lasting for 10 min or more should be considered as indicative of a functional erectile mechanism (16).

The intracavernosal injection test offers limited information, regarding the vascular status. A positive test is defined as a rigid erectile response (unable to bend the penis), that appears within 10 min after the intracavernosal injection and lasts for 30 min. Such response may be considered associated with normal arterial and veno-occlusive hemodynamics (16).

In all the other cases, the test is inconclusive and a duplex ultrasound of the penile arteries is request. A peak systolic higher than 30 cm/sec and a resistance index higher than 0.8 are generally considered as normal (16). If the duplex examination is normal, the vascular investigation stops. When it is abnormal arteriography and cavernosometry should be performed only for the patients who are considered potential candidates for vascular reconstructive surgery. Patient with psychiatric disorders will be sent to a psychiatrist particularly interested in erectile dysfunction. Patients with penile abnormalities like hypospadias, congenital curvature or Peyronie's disease with preserved rigidity may require surgical correction with very good success.

## TREATMENT

The first objective of every doctor is to cure the medical condition.

Therefore, the primary goal in the management strategy for a patients with ED is to determine the etiology of the disease and treat it when possible and not to treat the symptom.

It is clear that erectile dysfunction may be associated with modifiable or reversible factors including lifestyle or drug-related that may be modified prior to or in conjunction with specific therapeutic operations.

Testosterone deficiency is potentially reversible and is a result of primary testicular failure or secondary to pituitary/hypothalamic causes (12). Patient with hormone abnormalities will take the advice of an endocrinologist.

Testosterone replacement is effective but can only used when another endocrinological disease responsible for the testicular failure is excluded.

Testosterone replacement therapy is contra-indicated in men with an history of prostate carcinoma or with symptoms of prostatism.

Prior to initiating testosterone replacement, a digital rectal examination and serum PSA should be performed. Patients with androgen therapy should be monitored for the clinical response as well as for developing hepatic or prostatic disease (12).

However, it should be mentioned that this treatment is not always effective in the management of erectile dysfunction associated with hypogonadism.

In young patients with pelvic or perineal trauma, a surgical penile revascularization erection procedure is often associated with good results; 60-70% long-term success rate (5). The lesion must be demonstrated by Duplex sound and confirmed by the penile phar-maco-arteriography. A corporeal venoocclusive dysfunction must be excluded by the pharmacocavernosometry.

When no specific therapies for erectile dysfunction are required, a strategy approach should be followed. Again the patient and his partner when it is possible, must be informed by the case of administration, the invasiveness, the cost and the reversibility of the treatment.

In the other cases, in older patient without traumatic lesion or in patients with secondary cavernovenous leakage, vascular surgery is no more recommended anymore due to the poor results at long-term follow-up.

## 1. FIRST LINE THERAPY

### Oral therapy

Sildenafil citrate (Viagra) is currently the only oral drug available in the market with proven efficacy and safety for the treatment of ED. Sildenafil is a potent and selective inhibitor of cyclic GMP (cGMP), specific phosphodiesterase type 5, the predominant isoform of the enzyme found in human penis, resulting in smooth muscle relaxation, vasodilatation and penile erection (4).

Sildenafil is an oral drug, effective after 60 min in the presence of sexual stimulation. The most common side effects include headaches, flushing, dyspepsia, and a nasal congestion. It causes small decreases in systolic and diastolic blood pressures, but clinically significant hypotension is rare.

For that reason, it is formally contra-indicated in patients who take long-action nitrates or who use short-acting, nitrate-containing medications (17).

It may be hazardous to prescribe Sildenafil in patients:

- with active coronary ischemia;
- with congestive heart failure and borderline low blood pressure;
- with borderline low cardiac volume status;
- with a complicated multidrug antihypertensive program and;
- with drugs that can prolong the half-life of Sildenafil.

The dosages are 25, 50 and 100 mg. The starting dose could be 50 mg regardless the etiology of erectile dysfunction and adapted according with the success and the secondary effects. Twenty five mg should be used in patients with liver/renal failure; age > 65 years. **After 24 weeks of treatment in the dose-response study, improved erections are reported by 56, 77 and 84 percent of the men taking 25, 50 and 100 mg of sildenafil, respectively, as compared with 25 percent of those taking placebo.**

It should be emphasized that physician should warn the patient that sexual intercourse is considered as a vigorous physical activity, which increases heart rate as well as cardiac work. Physicians should assess the cardiac fitness of patients prior to treating erectile dysfunction.

New investigational oral agents for erectile dysfunction including sublingual apomorphine (18), oral phentolamine (19) and other phosphodiesterase inhibitors are under investigation.

### Vacuum device

and could be used in patients with stable relationships which it is easily understood due to the mechanism (20). It is also better accepted in older patients.

The device applies a negative pressure to the penis, thus drawing venous blood into the penis. It is then retained by the application of a visible constricting band at the base of the penis. The adverse effects associated with vacuum therapy are penile pain, numbness, and delayed ejaculation.

### Psychosexual therapy

For patients with a significant psychological problem; psychosexual therapy will be applied either alone or in combination with other therapeutic approach. Sexual therapy takes time and has been associated with variable results (21).

## 2. SECOND LINE THERAPY

According with the wish of the patient, intracavernous injection or intraurethral therapy will be used.

### Intracavernosal injection

Several drugs have been proposed to be injected intracavernously alone or in combination (PGE<sub>1</sub>, phentolamine-VIP, phentolamine-papaverine, maxilitrimx) however only two are approved by the F.D.A., alprostadil sterile powder and alprostadil alfadex (22). Patient comfort and education are essential elements of

the practice of intracavernosal injection therapy. The use of an automatic special pen that avoids the needle view can resolve the fear of the penile puncture.

Injection therapy is effective in most cases of erectile dysfunction but it is contra-indicated in men with a history of hypersensitivity to the drug employed and in men at risk for priapism. It is not advised in men with limited manual dexterity but their partner's may be taught the technique.

Intracavernosal therapy is effective in 60-90% of the cases. The erection appears after 5 to 15 minutes and lasts according to the dose injected. Side effects include prolonged erections or priapism, penile pain and fibrosis.

After 4 hours of erection, patients are advised to consult the doctor to avoid any damage to the intracavernous muscle which would provoke permanent impotence.

A 19 gauge needle is used to aspirate blood and therefore to decrease the intracavernous pressure. Most often this simple method is sufficient for the penis to be flaccid. **But if the penis becomes rigid again after this simple method** phenylephrine intracavernous injection in a dose beginning at 200 µg every 5 minutes and increasing to 500 µg if necessary is required. **The risk of having a prolonged erection during the following injections can not be predicted. Most often when this problem occurs, the dose is reduced for the next injection.** The patient must be carefully observed for systemic effects of the treatment used.

### **Intraurethral therapy**

PGE<sub>1</sub> may be administered intraurethrally in the form of a semi-solid pellet. A band placed at the base of the penis seems to improve the result of rigidity. **± 70% of patients have been satisfied or very satisfied.** Even the administrated way seems to be less invasive, side-effects include penile pain, and hypotension and the clinical success rate is lower than intracavernosal therapy (23).

## **3. THIRD LINE THERAPY**

### **Prosthesis**

For patients who fail pharmacologic therapy or who prefer a permanent solution for his problem, surgical implantation of a prosthesis is available. Two types of prosthesis exist: malleable or inflatable. The inflatable penile prosthesis provides not only a more cosmetic erection but a more satisfying one. Penile growth is usually better with inflatable rather than semirigid erection although there is an increased rate of mechanical failure and complications. The price is also different; the inflatable prosthesis is much more expensive.

In several countries, they are reimbursed but an organic cause has to be determined. In that case, the patient has to follow a complete impotence assessment.

Prosthetic infection is the most problematic complication following surgery since the combination of infection and foreign body requires removal of the prosthesis.

The patients most affected with infection problems are the diabetics (24).

Exact intra-operative length measurement is mandatory. If the device is too long postoperative pain and finally prosthesis erosion may result.

In too short device, the "concorde" deformity with leaking of the glans during intercourse may occur and perforation laterally occurs.

## **CONCLUSION**

A great deal of progress has been made in the pharmacological treatment of erectile dysfunction. In the past, the most effectiveness therapy required intracavernosal injections but an increasing number of oral agents have been introduced with very good success rates. Any successful pharmacologic treatment for erectile failures demands a degree of integrity of the penile mechanisms of erectile. Further studies of individual agents and synergistic activity of available substances are underway. The search for the ideal pharmacologic therapy for erectile failure aims at fulfilling the following characteristics: good efficacy, easy to administer, free of toxicity and side effects, with a quick onset and a possible long acting effect.

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