

How to treat erectile dysfunction

M.C. Raynor and W.J.G. Hellstrom

Introduction

Management of erectile dysfunction (ED) may vary considerably depending on the etiology. Following a focused evaluation of the ED patient (Chapter 34), therapy can usually be recommended based on the underlying mechanism. In most men, a thorough history, physical exam, and basic laboratory studies should suffice. Further evaluation with more invasive studies may be indicated for specific patient populations (Peyronie's disease, pelvic injury, endocrine disorders, young males unresponsive to oral agents, etc.).

Non-pharmacologic management

Non-pharmacologic management of ED can be used with success in some men. Lifestyle modifications may be implemented to alter certain risk factors for ED. Obesity and low levels of physical activity are recognized to be significantly associated with ED. Men with higher body mass index (BMI) and a sedentary lifestyle were at most risk for ED. In addition, cigarette use increased the risk of ED in men with other risk factors, such as hypertension or diabetes mellitus. One randomized trial demonstrated that men who lost weight and increased physical activity had significant improvements in erectile function.

Medications can also have a profound effect on sexual function. These effects can range from decreased blood pressure, hormonal alterations, decreased sexual arousal, or central suppressive effects (Chapter 34). Treatment of hypertension is one of the most common causes of medication-induced ED. Non-specific α -adrenergic antagonists and thiazide diuretics are commonly associated with ED. Spironolactone interferes with testosterone synthesis and antidepressants can have a significant impact on sexual function. Monoamine oxidase inhibitors (MAOIs) and selective serotonin reuptake inhibitors operate through central mechanisms and can decrease arousal. Simply altering medications to a different class may be successful. Calcium channel blockers and angiotensin converting enzyme (ACE) inhibitors both have decreased effects on sexual function. Other antidepressant medications, such as bupropion or venlafaxine, may also have decreased inhibitory effects on sexual function.

Psychosexual counseling

Psychological counseling has been used with success in various groups of men with ED. In general, men with psychogenic ED are the main beneficiaries of counseling. These men generally are found to be physiologically normal in terms of erectile function but may suffer some cognitive impairment that affects sexual function. For example, young men with congenital penile chordee or infertility may develop psychogenic ED secondary to dysmorphia or anxiety. Individual and couples counseling can be successful in improving self-confidence and decreasing anxiety surrounding sexual function or body image. Counseling can also be utilized in conjunction with pharmacologic strategies to improve outcomes.

Vacuum erection device

One non-pharmacologic management strategy that aims to physically produce an erection, as opposed to modifying risk factors, is the vacuum erection device (VED). The VED is a vacuum cylinder with a constriction ring that is placed at the base of the penis once the penis is engorged. Advantages of the device include its ability to produce a rigid erection sufficient for intercourse, including engorgement of the glans. Although relatively inexpensive, it can also cause pain at the band site, decreased ejaculate volume or anejaculation, and bruising.

Pharmacologic management for ED

Phosphodiesterase type-5 inhibitors

Pharmacologic management has become the mainstay of treatment for most men with ED following the advent of phosphodiesterase type-5 (PDE-5) inhibitors. Approved in 1998, sildenafil (Viagra, Pfizer, NY, NY) significantly changed the management of ED for most men. Later, vardenafil (Levitra; Bayer, GlaxoSmithKline, Schering-Plough) and tadalafil (Cialis; Lilly) were approved for use. All three medications have similar efficacy and side effect profiles. These medications work by potentiating the effect of nitric oxide on cavernosal smooth muscle. Nitric oxide stimulates guanylyl cyclase and leads to elevated cGMP levels. These second messengers then decrease intracellular calcium levels, which leads to smooth muscle relaxation and penile erection. PDE-5 breaks down cGMP to GMP, thus, inhibition of this enzyme increases cGMP levels (Fig. 1).

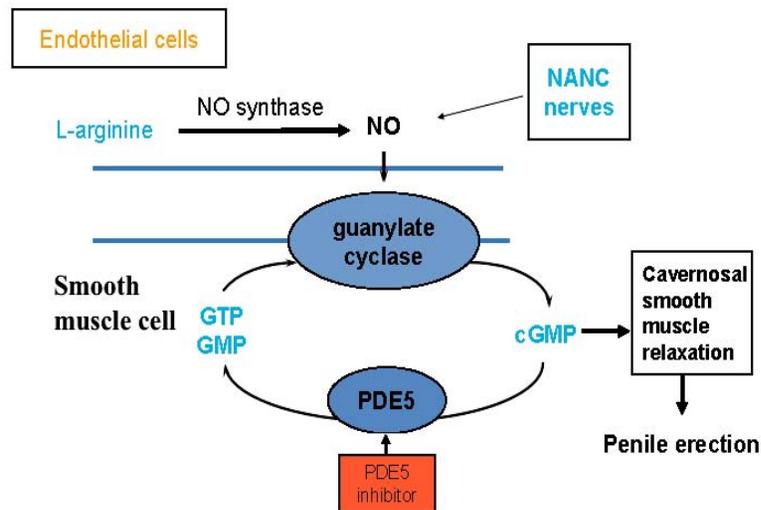


FIG. 1. The role of nitric oxide and cGMP in the physiology of erection.

Side effects include flushing, headache, muscle ache, and visual disturbances. These effects are likely due to cross-reactivity with other phosphodiesterases (usually PDE-6 and 11). There have been isolated reports of vision loss following use of PDE-5 inhibitors, known as non-arteritic anterior ischemic optic neuropathy (NAION). Men with retinal conditions including retinitis pigmentosa should not use these medications. Vardenafil carries an added warning about cardiac conduction defects as it may have an effect on the QT interval, therefore, some men taking anti-arrhythmics should avoid vardenafil. PDE-5 inhibitors are also contraindicated in men taking nitrates because of the risk of an unsafe drop in blood pressure. Men taking α -adrenergic antagonists for BPH should be cautioned regarding the risk of decreased blood pressure with concomitant use. Patients undergoing radical prostatectomy for prostate cancer and men with diabetes mellitus all have shown improvements in erectile function with use. Unless a contraindication for use exists, PDE-5 inhibitors have become first-line therapy in the treatment of ED.

Intracavernosal therapies

If PDE-5 inhibitors fail after proper instruction has been given or if a contraindication for use exists, men may consider alternative medical treatments. Intracavernosal injection (ICI) agents have been around for over 25 years. These vasoactive agents are injected directly into the cavernosal tissue and

produce an erection. Medications include papaverine, phentolamine, and alprostadil. Papaverine is a non-selective PDE inhibitor that increases intracellular cAMP and cGMP levels. Phentolamine is an α -adrenergic antagonist that increases presynaptic norepinephrine levels. Alprostadil works by increasing intracellular cyclic AMP levels and decreasing intracellular calcium. These medications are used alone or in combination for injection. Side effects include painful erection, priapism, and increased incidence of cavernosal fibrosis (mainly with papaverine and phentolamine). Men taking anticoagulants should be advised to apply manual pressure for several minutes following injection to avoid hematoma formation. Alprostadil is also available in a urethral suppository form (MUSE, VIVUS, Mountain View, CA) and has the advantage of not using a needle for delivery.

Testosterone replacement

Studies have shown that hypogonadal ED men show improvement in erectile function with testosterone replacement therapy. In addition, men may have improved responses to PDE-5 inhibitors in combination with testosterone replacement therapy. These men should be cautioned regarding the risks of hormonal replacement, including erythrocytosis and possible effects on the prostate. Men should be monitored while on therapy with yearly digital rectal exams, serum PSA, and complete blood counts. Any elevation in PSA or abnormal DRE should warrant prostate biopsy to rule out underlying prostate cancer. Men with a history of prostate cancer need to be cautioned about the risks of testosterone replacement therapy. Recent studies have shown that testosterone replacement therapy is safe in men with a history of prostate cancer; however, the patient should be well-informed and judicious about follow-up. Testosterone replacement therapy can be provided through injections, transdermal gels, or implantable pellets.

Surgical therapy for ED

Surgical therapy for ED is reserved for patients who fail medical therapy or exhibit an underlying condition that is not amenable to medical therapy. Surgical therapy involves implantation of a penile prosthesis. The prosthesis may consist of inflatable cylinders, or malleable rods. The inflatable devices consist of intracavernosal cylinders with a reservoir and a scrotal pump. In two-piece devices, the scrotal pump and reservoir is self-contained, whereas the three-piece device contains a separate reservoir that is implanted within the pelvis. These devices carry very high patient and partner satisfaction rates. Risks include infection or malfunction of the device that may necessitate removal. In certain men with documented arteriogenic ED resulting from pelvic trauma, penile revascularization surgery may be indicated. The ideal

patients are young men with no risk factors for ED and have documented arteriogenic insufficiency diagnosed with pelvic angiography. Successful revascularization in these patients can result in normal erectile function in the majority of men.

Summary

Currently, most men with ED can be safely started on a trial of PDE-5 inhibitors following history, physical exam, and basic laboratory studies. Patients with a contraindication for PDE-5 inhibitor use, or who have failed PDE-5 inhibitor use, may consider VED, intracavernosal/transurethral therapy, or surgical options.

Suggested reading

- Carson CC 3rd. Phosphodiesterase type 5 inhibitors: state of the therapeutic class. *Urol Clin North Am.* 2007; 34: 507-15.
- Derby CA, Mohr BA, Goldstein I, Feldman HA, Johannes CB, McKinlay JB. Modifiable risk factors and erectile dysfunction: can lifestyle changes modify risk? *Urology.* 2000; 56: 302-6.
- Greenstein A, Mabjeesh NJ, Sofer M, Kaver I, Matzkin H, Chen J. Does sildenafil combined with testosterone gel improve erectile dysfunction in hypogonadal men in whom testosterone supplement therapy alone failed? *J Urol.* 2005; 173: 530-2.
- Khera M, Lipshultz LI. The role of testosterone replacement therapy following radical prostatectomy. *Urol Clin North Am.* 2007; 34: 549-53.
- Marks LS, Mostaghel EA, Nelson PS. Prostate tissue androgens: history and current clinical relevance. *Urology.* 2008; 72: 247-54.
- Melnik T, Soares BG, Nasselo AG. Psychosocial interventions for erectile dysfunction. *Cochrane Database Syst Rev.* 2007; (3):CD004825.
- Hellstrom Varady JC and Place VA. A double-blind, placebo-controlled evaluation of the erectile response to transurethral alprostadil. *Urology.* 1996; 48: 851-56.
- Hellstrom WJ, Montague DK, Moncada I, Carson C, Minhas S, Faria G, Krishnamurti S. Implants, mechanical devices, and vascular surgery for erectile dysfunction. *J Sex Med.* 2010; 7: 501-23.
- Segraves RT. Sexual dysfunction associated with antidepressant therapy. *Urol Clin North Am.* 2007; 34: 575-9.
- Shabsigh R, Kaufman JM, Steidle C, Padma-Nathan H. Randomized study of testosterone gel as adjunctive therapy to sildenafil in hypogonadal men with erectile dysfunction who do not respond to sildenafil alone. *J Urol.* 2004; 172: 658-63.