Erectile dysfunction is defined as the inability to develop and sustain an erection adequate for intercourse on at least 50% of attempts. It occurs commonly and the incidence increases with age.1

What are the implications for primary care physicians?
Only about 10% of an estimated 3 million Canadian men with erectile dysfunction tell a doctor. The problem may be an early symptom of possibly modifiable factors including: tobacco addiction, diabetes mellitus, atherosclerosis (hyperlipidemia and hypertension), depression, anxiety disorders, alcoholism, hypothyroidism, prostate carcinoma, testosterone deficiency, renal, hepatic or neurologic disease, and a number of medications.2 The early detection of these factors could be facilitated, if physicians discussed erectile function in all adult men.

How does one confirm the diagnosis?
A sexual history is necessary to clarify the diagnosis. Have the patient explain the problem in plain terms. Unrealistic expectations, low desire of patient or partner, rapid (premature) ejaculation and anorgasmia impact on sexual functioning; however, none of these constitute erectile dysfunction.

What investigations are appropriate?
The sexual and medical histories are most important. A physical exam should focus on the cardiovascular, genitourinary, endocrine and neurological systems, but abnormal findings are frequently absent. Blood work should be based on the potential underlying conditions listed above plus special concerns raised from the history and physical exam. Special investigations such as Doppler flow studies, nocturnal penile tumescence and angiography rarely impact on therapy and are therefore rarely indicated. Attempting to differentiate organic from psychogenic causes is inappropriate, as elements of both likely co-exist.

What is the role of the partner?
The partner’s perspective often enhances the diagnostic accuracy and improves the overall management. The partner’s health (eg. chronic dysparunia, depression, low desire) may pose a barrier to effective therapy. Since sex serves to reinforce feelings of intimacy between partners, when erections fail, communication and self-esteem are frequently adversely affected in both partners. The physician can help couples to discuss these issues openly and to decide whether erection enhancement is desirable.

What modes of therapy are available?
- Modifying remedial factors: treatment of depression, stopping unnecessary medications, and risk factor modification (tobacco, alcohol, exercise, etc.).
- Encouragement to reinstate sexual intimacy (e.g. counseling in methods of non-intercourse sexual activity).3
- Erection enhancement: These therapies work best in conjunction with the other interventions above.

What are the options for erection enhancement?

LOCALLY ACTING TREATMENTS
Constriction rings with or without a vacuum device. Various makes and models are available and are well tolerated by some men. They are safe for frequent use and the effect is readily reversible. Approximate cost for vacuum device is under $600.

Prostaglandin (PGE1). PGE1 initiates an erection whether stimulation is present or not and acts locally with little or no systemic effects. PGE1 causes tumescence by increasing cavernous blood flow. It produces an erection lasting from 30 to 120 minutes in about 70% of patients. Major side effects: penile pain (37%), penile fibrosis (3%) and priapism (0.4%).
Formulations: intracavernosal injection: (Caverject) $8-35 per use depending on dose. (Bimix) PGE1 combined with phenolamine. Intra-urethral pellet (MUSE) 50-70% effective. Incidence of penile pain is less (10%).

SYSTEMICALLY ACTING TREATMENTS

Yohimbine: Limited effectiveness.

Testosterone: Not indicated as empiric treatment of erectile dysfunction. Even with documented testosterone deficiency, replacement seldom improves erections significantly.4

Sildenafil (Viagra®)

Pharmacology: Sildenafil facilitates erections associated with sexual stimulation. It will not act if the man is not sufficiently mentally aroused or his peripheral autonomic nerves are absent (e.g. radical prostatectomy). It acts by inhibiting phosphodiesterase isoenzyme 5 (PDE5), thus prolonging cyclic guanosine monophosphate (cGMP) activity in erectile tissue, and enhancing the vasodilating actions of nitric oxide, which is released in response to sexual stimulation.5 Sildenafil is rapidly absorbed from the gut peaking 30-120 min. after an oral dose. At peak effect it lowers mean systolic supine blood pressure (8 mmHg) in healthy volunteers. The drug is eliminated by liver metabolism (CYP3A4) with a half-life of 3-5 hours. Half-life is prolonged in patients > 65 years and in patients with renal or hepatic impairment.

Effectiveness: Six randomized, double-blind, clinical trials comparing sildenafil versus placebo were published prior to June, 1999.6-10 Each trial enrolled between 12 and 532 patients over a duration of 2 to 24 weeks. In the best designed trial of 329 patients over 12 weeks, intercourse was reported successful in 59% of patients taking sildenafil as compared to 15% of patients taking placebo (absolute risk increase over placebo, were headache 34%, NNT = 2 to achieve one success).6

Adverse effects: The most common adverse effects, as absolute risk increase over placebo, were headache 14%, flushing 17%, dyspepsia 4%, rhinitis 4% and visual disturbance 1%.7 None of the studies assessed the effects of long-term sildenafil use. Such studies are needed, particularly in patients with a history of retinal and cardiovascular disorders. Serious rare side effects include priapism, severe hypotension, heart attack, stroke and death.

Contraindications: Patients taking or at risk of requiring nitrates in any form. Patients in whom sexual activity is inadvisable because of their cardiovascular status (e.g. MI or CVA within 6 months, heart failure, unstable angina, hypotension, uncontrolled hypertension, aortic stenosis, etc.). Patients with retinitis pigmentosa, anatomical deformities of the penis, conditions predisposing to priapism (e.g. sickle cell anemia, multiple myeloma), or receiving multiple antihypertensive drugs.

Precautions: There is no safety information on patients excluded from the trials (e.g. patients with alcoholism, active peptic ulcer, proliferative diabetic retinopathy, etc.). Inhibitors of CYP3A4 such as erythromycin, ketoconazole, grapefruit juice and others would be expected to increase the magnitude and duration of response to sildenafil.

Dosage and cost: The drug should be taken on an empty stomach 1 hour before intended sexual activity and no more than once daily. Dose range 25-100 mg. As with most drugs start with the lowest dose, 25 mg, and increase only if necessary. Since the cost of each tablet is similar ($10 - $12), prescribing the higher dose tablets and dividing them can substantially reduce the cost.

Conclusions

• Inquire about erectile dysfunction in all adult males as a potential early indicator of modifiable factors.
• The presence of erectile dysfunction is a unique opportunity to motivate a patient to decrease risk factors.
• Partner involvement with the patient and physician facilitates the diagnosis and enhances the treatment.
• Sildenafil is the first-line choice for erection enhancement, provided that the risks of using sildenafil in that patient are minimal.

References

This Letter contains an assessment and synthesis of published (and whenever possible peer-reviewed) publications up to May 30, 1999. We attempt to maintain the accuracy of the information in the Therapeutics Letter by extensive literature searches and verification by both the authors and the editorial board. In addition this Therapeutics Letter was submitted for review to 73 experts and pri-

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