

Clinical Pearls in Men's Health

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Clinical Pearls is a novel presentation format that was introduced at the American College of Physicians' 2001 Annual Meeting. This format was designed with the understanding that physicians enjoy learning from real patient cases, solving problems, and applying useful tips or "pearls" to practice.

Using the Clinical Pearls format, speakers present brief cases followed by multiple choice questions to a general medicine audience. The audience members' answer distributions, obtained using electronic audience response systems, are displayed along with the correct answer. The speaker then discusses teaching points, provides reasons for correct and incorrect answers, and concludes by revealing a clinical pearl.

As a service to its readers, *Mayo Clinic Proceedings* has invited Clinical Pearl presentations to be published in our Concise Review section.

CASE 1

A 67-year-old man presents for a follow-up visit regarding his erectile dysfunction (ED). Three months previously, he was prescribed 25 mg of sildenafil (Viagra) by mouth to be taken as needed before sexual activity but no more frequently than every 24 hours. He was also told that if the 25-mg dose was ineffective, then he could take two 25-mg tablets (50 mg). Despite taking 50-mg doses of sildenafil on several occasions, the patient reports that the medication did not produce erections. He says that he has a satisfying relationship with his wife and that they created ample time for lovemaking before taking the medication. He reports feeling frustrated.

The patient inquires about additional options for treating his ED.

QUESTION

Which *one* of the following is the *next best* step in managing this patient's ED?

- Continue the current dose of sildenafil, educate the patient that sildenafil will not produce erections without sexual arousal, and advise him to take the medication on an empty stomach at least 1 hour before sexual activity
- Increase the sildenafil dose to 100 mg
- Continue the current dose of sildenafil and add penile injection therapy as a second agent
- Discontinue sildenafil and initiate penile injection therapy
- Discontinue sildenafil and refer the patient for psychotherapy

DISCUSSION

Physicians may overlook that patients often take sildenafil and other phosphodiesterase type 5 (PDE-5) inhibitors incorrectly. To be effective, sildenafil must be taken on an empty stomach at least 1 hour before sexual intercourse.¹ Unlike penile injections or intraurethral alprostadil, PDE-5 inhibitors do not cause erections without prior sexual arousal. Research has shown that approximately half of patients in whom sildenafil treatment has failed will have success with this medication once they have been educated how to take it properly.² Although the dose of sildenafil ranges from 25 to 100 mg, the next step would not be to increase the dose until it has been determined that the patient is taking the medication correctly. It would also be incorrect to add injection therapy to existing PDE-5 inhibitor therapy because combining these types of medications may cause adverse reactions. Switching to penile injection therapy would be reasonable only if this patient developed a contraindication to PDE-5 inhibitors or if PDE-5 inhibitor therapy failed even with correct use of the medication.

CLINICAL PEARL

Sildenafil will not produce erections without sexual arousal, and this medication is ineffective unless taken on an empty stomach at least 1 hour before sexual activity. Counseling patients how to take sildenafil correctly often results in success for patients in whom treatment previously failed.

CASE 2

A 70-year-old man reports gradual onset of weak urinary stream, urgency, incomplete bladder emptying, and nocturia that occurs 2 to 3 times nightly. His medical history includes chronic obstructive lung disease, hypertension, hyperlipidemia, osteoarthritis, and symptomatic cataracts. On physical examination, the patient's

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See end of article for correct answers to questions.

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prostate is firm and symmetrically enlarged to about 30 cm³ (normal prostates are about 20 cm³ or roughly the size of a walnut). Findings were normal on a screening prostate-specific antigen (PSA) test performed within the past year. Current urinalysis with microscopy is only remarkable for 2 white blood cells per high-power field (reference ranges provided parenthetically) (1-3 per high-power field), and his serum creatinine level is normal at 1.2 mg/dL (0.8-1.3 mg/dL [to convert to μmol/L, multiply by 88.4]).

The patient inquires about medical therapy for his urinary symptoms.

QUESTION

Which *one* of the following is the *single best* treatment option for this patient?

- Initiate 0.4 mg/d of tamsulosin by mouth
- Initiate 1 mg/d of doxazosin by mouth
- Initiate 5 mg/d of finasteride by mouth
- Refer the patient to a urologist for invasive therapy for benign prostatic hyperplasia (BPH)
- Refer the patient to an ophthalmologist for cataract surgery

DISCUSSION

Although α₁ receptor–blocking medications such as tamsulosin or doxazosin would usually be considered first-line therapy for patients with BPH, this patient's case is complicated by the fact that he has cataracts. Finasteride and other 5-α reductase inhibitors would not be first-line therapy for most patients with BPH. Most patients will choose medical treatment for BPH before considering a urologic consultation for invasive therapy. Nonetheless, physicians should know the indications for immediate invasive therapy, which include moderate to severe symptoms, persistent gross hematuria, urinary retention, renal insufficiency from BPH, bladder calculi, and recurrent urinary tract infections.³

For patients with cataracts, it is important to know about the intraoperative floppy iris syndrome (IFIS), which is a potentially serious pupillary constriction and billowing of the iris during eye surgery. A retrospective cohort study of more than 96,000 patients revealed significant increases in adverse surgical events in patients who were exposed to tamsulosin within 14 days of cataract surgery.⁴ Indeed, all α₁ receptor–blocking medications are associated with IFIS.⁵ Consequently, the American Academy of Ophthalmology recommends that patients with cataracts consider undergoing cataract surgery before initiating long-term α-blocker therapy and report use of such therapy to the ophthalmologist before undergoing any type of eye surgery.⁶

CLINICAL PEARL

Tamsulosin is associated with IFIS. Patients with BPH and cataracts should consider undergoing cataract surgery before initiating long-term α receptor–blocking medications. Patients who are already taking an α receptor blocker should inform their ophthalmologists that they are taking this medication before undergoing any eye surgery.

CASE 3

A 55-year-old man reports sudden onset of ED about 6 months previously. He has been married to his wife for 25 years and reports that their relationship is very good. However, lately he is less interested in sex with his wife and feels guilty because he sometimes dreams of having sex with other women, which produces firm nocturnal erections. His medical history is remarkable for diabetes, hypertension, and hyperlipidemia, which have all been stable for the past 3 years while he was receiving medical therapy with metformin, hydrochlorothiazide, and atorvastatin. On physical examination, the patient is obese (body mass index [calculated as the weight in kilograms divided by height in meters squared], 32 kg/m²), has a normal affect, and has a blood pressure of 130/80 mm Hg. Findings on examination are otherwise unremarkable. Laboratory testing yields normal results for complete blood cell count and for levels of electrolytes, creatinine, and glycated hemoglobin.

QUESTION

Which *one* of the following is the *most likely* cause of this patient's ED?

- Hypogonadism
- Hypothyroidism
- Diabetes
- Mood disorder
- Hydrochlorothiazide

DISCUSSION

Endocrine problems most commonly associated with ED include hypogonadism, thyroid disorders (both hyperthyroidism and hypothyroidism), and prolactinomas.⁷ Although this patient has decreased libido, which is sometimes associated with hypogonadism, there is no other compelling evidence of hormonal dysfunction, and endocrinopathies are not the most common causes of ED. The patient has diabetes, hypertension, and hyperlipidemia, which are all cardiovascular risk factors. Although cardiovascular risk factors are strongly correlated with ED,^{8,9} this patient's risk factors are well managed, and his history suggests a different cause, namely mood disorder. Telltale signs of mood disorder and associated psychogenic ED are sudden symptom onset and the persistence of nocturnal erections,¹

TABLE. The American Urological Association (AUA) Symptom Index for Benign Prostatic Hyperplasia

Each of the AUA symptom index items are scored by patients on the following scale:					
Not at all	Less than 1 time in 5	Less than half the time	About half the time	More than half the time	Almost always
0	1	2	3	4	5
1. Incomplete emptying: During the past month, how often have you had a sensation of not emptying your bladder completely after you finished urinating?					
2. Frequency: During the past month, how often have you had to urinate again less than 2 h after you finished urinating?					
3. Intermittency: During the past month, how often have you found that you stopped and started again several times when you urinated?					
4. Urgency: During the past month, how often have you found it difficult to postpone urination?					
5. Weak stream: During the past month, how often have you had a weak urinary stream?					
6. Straining: During the past month, how often have you had to push or strain to begin urination?					
7. Nocturia: During the past month, how many times did you most typically get up to urinate from the time you went to bed at night until the time you got up in the morning?					
Note: The total AUA symptom score is determined by summing the scores for all 7 items. The total score is interpreted as follows: mild = 0-7; moderate = 8-19; and severe = 20-35					

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which indicates that the patient's physiologic and anatomic mechanisms for erection are intact. Educating patients on this fact and that the situation is often temporary can provide great reassurance. However, erectile function in these patients may improve with PDE-5 inhibitor therapy, and prescribing such therapy is very reasonable. Although hydrochlorothiazide is a potential cause of ED, this patient had sudden-onset ED, and the initiation of hydrochlorothiazide long antedated his symptoms.

CLINICAL PEARL

Inorganic (psychogenic) ED is typically associated with poor libido, sudden onset of symptoms, and the persistence of spontaneous nocturnal erections. Educating patients that this condition is often transient can be reassuring.

CASE 4

A 49-year-old man presents with gradually increasing weak urinary stream, urgency, and frequency. His American Urological Association (AUA) symptom score is 6. His only medical problem is asthma, which is well managed on an albuterol inhaler. The patient's family history is remarkable for his paternal grandfather being diagnosed as having prostate cancer at age 70 years. On physical examination, the patient has mild alopecia in the male-pattern distribution. His genitalia appear normal. His prostate is firm, without nodules, and symmetrically

enlarged at about 30 cm³. Laboratory evaluation is remarkable for a normal urinalysis with microscopy, and the PSA level is 1.6 ng/mL (<2.5 ng/mL [to convert to µg/L, multiply by 1.0]).

You inform the patient that your diagnostic impression is BPH. The patient specifically requests medical therapy with finasteride because he has read that this medication may help him regrow hair.

QUESTION

Which *one* of the following is the *best* treatment option for this patient?

- Finasteride
- Dutasteride
- Tamsulosin
- Watchful waiting
- Transurethral prostatectomy

DISCUSSION

According to the AUA symptom score, this patient has mild symptoms of BPH (mild, 0-7; moderate, 8-19; and severe, 20-35).¹⁰ The AUA symptom index is a reliable and valid method to assist with both diagnosing BPH and monitoring patients' symptoms over time (see Table).¹¹ This patient's PSA level is normal, and his prostate gland is only modestly enlarged. Finasteride and other 5- α reductase inhibitors have been shown to be most effective in men with large prostates (>40 cm³)^{12,13} and moderate to severe symptoms.¹⁰ In such patients, combining finasteride with α_1 receptor-blocking medication has been shown to be particularly effective.¹⁴ However, finasteride and dutasteride would not be the first line of therapy for this patient's BPH.

Finasteride is indicated for treating both BPH and androgenic alopecia because it inhibits the conversion of testosterone to dihydrotestosterone through its action on dihydrotestosterone receptors in both the prostate and hair follicles. However, the finasteride dose for treating androgenic alopecia is 1 mg/d by mouth, whereas the dose for BPH is 5 mg/d by mouth.

The use of finasteride to treat BPH has been debated because the Prostate Cancer Prevention Trial (PCPT) showed that men taking finasteride had a 24.8% reduced risk of prostate cancer, along with a 1.27 relative risk of Gleason grade 7 through 10 tumors.¹⁵ However, the idea that finasteride can prevent prostate cancer is controversial. Experts have suggested that the observation of risk for high-grade cancer in the PCPT may be misleading because modeling studies suggest that the risk of high-grade cancer is unchanged or reduced in patients taking finasteride.¹⁶ An editorial accompanying the PCPT noted that, although finasteride may not be the best option for preventing pros-

tate cancer, it remains a favored treatment for BPH because of its many proven benefits.¹⁷ Consequently, results of the PCPT have not affected our prescribing of finasteride.¹⁸ Nevertheless, patients taking finasteride should be monitored with yearly PSA assessments; because finasteride reduces prostate volumes,¹³ it has been suggested that the PSA values in men taking finasteride be doubled for accurate interpretation.^{19,20} It has also been recommended that *any* increase in PSA level be taken seriously while a patient is taking this medication and that PSA, which should be doubled during the first 1 or 2 years of therapy, be multiplied by higher numbers during subsequent years of therapy.²¹

In a more recent study, authors investigated whether dutasteride reduces the incidence of prostate cancer among men who are at increased risk for the disease. A total of 6729 men were randomized to dutasteride or placebo and underwent prostate biopsy at 2 and 4 years. During the 4-year period, men treated with dutasteride had a 22.8% relative risk reduction for prostate cancer.²²

This patient has very mild symptoms, so medical treatment would not be the best initial choice because of the cost and the potential for adverse effects. Therefore, watchful waiting would be favored over therapy with tamsulosin or any other medication. Invasive therapy would be overly aggressive.

CLINICAL PEARL

Medical therapy for BPH with 5- α reductase inhibitors such as finasteride is generally reserved for patients with large prostates and moderate to severe symptoms. In such patients, combining 5- α reductase inhibitor and α receptor–blocking medications is particularly effective. For men with mild symptoms, watchful waiting is a reasonable strategy.

CASE 5

A 60-year-old man reports the gradual onset of ED during the past year, to the point that he occasionally has “partial” erections that are barely adequate for vaginal penetration. Notably, the patient underwent lower back surgery 1 year previously to treat lumbar radiculopathy. Although the surgery successfully eliminated his radiculopathic symptoms, he never resumed his previous exercise routine and subsequently gained approximately 18 kg (40 lbs). Currently, he feels deconditioned and becomes short of breath when climbing a single flight of stairs. Additional medical history includes borderline hypertension and hyperlipidemia, both adequately managed with diet alone. On physical examination, the patient appears obese. His blood pressure is 128/88 mm Hg. Findings on examination of his heart, lungs, abdo-

men, genitalia, and prostate are normal. Laboratory studies are remarkable for a low-density lipoprotein level of 135 mg/dL (goal for this patient, <160 mg/dL [to convert to mmol/L, multiply by 0.0259]). Chest radiography shows a calcified granuloma in the left lung. Electrocardiography shows subtle T-wave inversion in the inferior leads; no previous electrocardiograms are available for comparison.

QUESTION

Which *one* of the following would be the *best* initial treatment for this patient's ED?

- Sildenafil, 50 mg by mouth, as needed for sexual activity
- Tadalafil, 2.5 mg/d by mouth
- Exercise stress testing followed by gradual weight loss through exercise and calorie restriction
- Alprostadil penile injections
- Penile implant

DISCUSSION

Erectile dysfunction is defined as either the inability to obtain erections adequate for vaginal penetration²³ or the inability to obtain erections 75% of the time. This patient is usually able to obtain erections suitable for vaginal penetration, so he does not fit the strictest definition of ED. Although it may be reasonable to treat this patient with a PDE-5 inhibitor such as sildenafil or tadalafil, he has cardiovascular risk factors and reports new exertional dyspnea, which could represent a symptom of ischemic heart disease. If patients have symptoms potentially representing coronary ischemia, then it is important to perform cardiac stress testing to exclude coronary heart disease before prescribing PDE-5 inhibitors.^{1,24}

This patient has gained about 18 kg (40 lbs) as a result of inactivity. The Health Professionals Follow-up Study showed that physically active men had 30% less ED than physically inactive men.⁸ Furthermore, a randomized trial involving obese men found that erectile function scores improved significantly in men who lost weight through therapeutic lifestyle changes, compared with men who did not achieve weight loss.²⁵ Physicians may overlook that a treatment option for ED in obese men is weight loss through diet and exercise. Intraurethral alprostadil is usually reserved for men who would prefer not to take PDE-5 inhibitors or men in whom PDE-5 inhibitors are contraindicated or fail to achieve results. In general, medical therapy, including penile injections, must fail before penile implants would be offered.¹

CLINICAL PEARL

Weight loss through regular exercise and calorie restriction can cause significant improvement in erectile function, even in the absence of medical therapy for ED.

CASE 6

A 76-year-old man presents for an annual medical examination. His medical history is remarkable for chronic kidney disease that is managed with hemodialysis scheduled 3 times weekly. Since initiating hemodialysis, he has continued to produce small amounts of urine. He has no symptoms and is living independently at home with his wife. However, the patient's wife reports that, during the past year, he has become increasingly forgetful and occasionally exhibits aggressive behavior, which is unusual for him. Notably, he had an elevated PSA level 5 years previously, but findings on a subsequent prostate biopsy were negative for malignancy. Since that time, yearly PSA values, including that for last year, have been within normal limits. On physical examination, the patient appears quiet, reserved, and distracted. His prostate is smooth, nontender, and symmetrically enlarged to about 50 cm³.

QUESTION

Which *one* of the following is the *best* choice in this patient?

- The patient should no longer undergo prostate cancer screening with serum PSA testing
- The patient's history of elevated PSA values increases his risk of prostate cancer, despite negative findings on prostate biopsy and subsequent normal PSA values
- The patient should undergo computed tomography of the head to evaluate for metastatic prostate cancer
- The patient should begin taking tamsulosin for BPH
- The patient should begin taking dutasteride for BPH

DISCUSSION

Unfortunately, no strong evidence supports screening for prostate cancer with annual PSA testing. Preliminary results from the Prostate, Lung, Colorectal, and Ovarian (PLCO) trial showed no mortality benefit from combined screening with digital rectal examination and annual PSA testing.^{26,27} Conversely, early results from the European Randomized Study of Screening for Prostate Cancer (ERSPC), which involved 162,243 men, demonstrated that PSA screening without digital rectal examination had 20% relative risk reduction in prostate cancer death.^{27,28} Although all these findings are conflicting, the PLCO and ERSPC trials, along with other large trials, are ongoing.²⁷ On the basis of current evidence, the US Preventive Services Task Force cites insufficient evidence for or against the use of a screening PSA test in men younger than 75 years and recommends against its use in men aged 75 years or older.²⁹

The current patient is older than 75 years. Furthermore, his life expectancy with end-stage renal disease and suspected dementia is less than 10 years. Therefore,

prostate cancer screening would not be recommended in this patient. Serum PSA values can be elevated for various reasons, including BPH and prostatitis.³⁰ Therefore, this patient's history of elevated PSA values with negative findings on prostate biopsy and subsequently normal PSA values would suggest that he is not at increased risk of prostate cancer. Although the initial differential diagnosis for this patient's cognitive decline should include more than dementia, he has no known history of prostate cancer, and prostate cancer does not commonly metastasize to the brain, so imaging would not be performed solely for that purpose. Finally, this patient is producing only small amounts of urine because of his chronic kidney disease and would not benefit from medical therapy for BPH.

CLINICAL PEARL

Current studies provide no clear direction regarding whether screening for prostate cancer with yearly PSA measurements reduces mortality. On the basis of existing evidence, screening for prostate cancer is not recommended for men older than 75 years.

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Correct answers: Case 1: a, Case 2: e, Case 3: d, Case 4: d, Case 5: c, Case 6: a