

Diagnostic evaluation of sexual dysfunction in the male partner in the setting of infertility: a committee opinion

Practice Committee of the American Society for Reproductive Medicine in Collaboration With the Society for Male Reproduction and Urology

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It is the responsibility of the clinician to assess for the presence of erectile dysfunction, ejaculatory dysfunction, or diminished libido related to hypoandrogenism among men presenting with a primary complaint of infertility. Referral to a reproductive urologist or other appropriate specialist with requisite expertise in the evaluation and treatment of such conditions is often warranted. (Fertil Steril® 2018;110:833–7. ©2018 by American Society for Reproductive Medicine.)

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INTRODUCTION

Sexual dysfunction is a common condition among men of reproductive age. It can be significantly worsened by the stress of infertility. It is important to elicit this information and provide the appropriate referral. This document will present diagnosis, evaluation, and treatment of the most common sexual dysfunction issues seen by fertility providers. These issues drive patients to seek care and offer an opportunity to improve male somatic health.

ERECTILE DYSFUNCTION

Detection

Male sexual dysfunction in the setting of infertility often presents with erectile dysfunction (ED). ED is defined as the consistent inability to attain or maintain a penile erection of sufficient quality to permit satisfactory sexual intercourse (1). ED is prevalent and increases with

age. Severe and moderate-severity ED occur in 5% and 17%, respectively, of men aged 40–49 years. More than 152 million men in 1995 were reported to have ED, and this number is projected to increase to 322 million in 2025 (2). It is present in 18%–89% of men with male infertility (3–6). The prevalence of ED in infertile men is significantly higher than in fertile controls (6). Having an erection is a necessary piece of natural conception and, often, for intrauterine insemination (IUI) or in vitro fertilization (IVF).

ED may be indicative of serious health comorbidities. Men with ED without a history of cardiovascular disease have a 45% increased risk of having a subsequent cardiovascular event within 5 years compared with those without ED (7, 8). ED is associated with a number of other conditions including smoking, diabetes, depression, hypertension, and heart

disease (9). Thus, it is important to inquire about cardiovascular disease in men of all ages who present with ED, regardless of fertility status.

In the setting of infertility, ED can present in two main forms—psychogenic and organic. Psychogenic ED occurs when a man has normal penile blood flow and nerve function and may achieve erection under some circumstances but, typically, not with his partner when trying to conceive. Typically, any form of situational ED, particularly that which presents or worsens after a couple begins trying to conceive, is psychogenic. Organic ED is commonly a result of diminished penile blood flow or nerve dysfunction and results in the inability to achieve or maintain an erection regardless of the situation (10). It is likely to be associated with cardiovascular disease and, more commonly, presents in older men. Regardless of the origin, ED can have deleterious effects on psychosocial and relationship issues (11). The severity of ED may be initially determined through a careful history or validated questionnaire, such as the International Index of Erectile Function (IIEF) or Sexual Health Inventory for Men (SHIM) (SHI form link) (12, 13).

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A comprehensive history and physical examination with focus on risk factors for cardiovascular disease are critical parts of the ED evaluation. Specifically, the man should be queried about whether he has had regular primary care; any comorbid conditions such as diabetes, hypertension, coronary artery disease, or other cardiac conditions; history of penile, prostate, or spine surgery; social history with an emphasis on smoking or other recreational drugs; or family history of cardiovascular disease. Medication use such as beta blockers, hydrochlorothiazide, other antihypertensives, exogenous testosterone use, use of phosphodiesterase type-5 inhibitors (PDE5i) (such as sildenafil, tadalafil, avanafil, or vardenafil), or use of penile injection therapy should also be documented (14). Evaluation of psychogenic ED involves a very thorough sexual history eliciting the onset and exact nature of the problem with emphasis on whether the man has morning erections, ED with self-stimulation, history of ED with prior partners, and onset of the disease (10).

Treatment

The cornerstone of ED treatment for either psychogenic or organic ED is reassurance that, in the vast majority of cases, the problem can ultimately be resolved. Further, it should be made clear to both the patient and his partner that a man's ED is not a function of his attraction or devotion to his partner. Another helpful alternative is a trial of a PDE5i on demand to help restore a man's confidence and improve chances of maintaining an erection (15). In cases of organic ED, identification of comorbid conditions, such as diabetes, can be lifesaving. In all cases, these men should have adequate follow-up with a primary care physician. The shared decision-making model can be used to begin a care pathway starting with lifestyle modifications, substituting alternative medications in place of those that can exacerbate ED, and moving on to PDE5i in patients who have organic causes of ED such as spinal cord injuries, radical pelvic surgery, severe atherosclerosis, or those who fail lifestyle therapy or desire rapid improvement in their ED.

Typically, these men may be started on a PDE5i trial, with appropriate counseling about risk of priapism (defined as an erection lasting longer than 4 hours). Contraindications for PDE5i use include use of nitrates and inadequate cardiac reserve for sexual activity requiring clearance by a cardiologist. Further, these medications should be used with caution in men on an alpha blocker as they can cause an unsafe drop in blood pressure. Side effects of PDE5i agents include headache, facial flushing, muscle aches, nasal congestion, a blue tinge in vision, dizziness, dyspepsia, and priapism. Typical doses of PDE5i are sildenafil 50–100 mg, tadalafil 5–20 mg, vardenafil 10–20 mg, and avanafil 50–200 mg. All of these drugs are expensive, \$10–\$20 per pill; however, generic forms will be available soon. If PDE5i therapy is not effective, patients can be transitioned to penile injection therapy under the care of a urologist (10). Should this fail, surgery to place a penile prosthesis may be indicated.

Patients with spinal cord injury represent a unique population of men with ED. With normal physiologic function, the S2–4 nerve roots cause vasodilation of vessels in the corpora

cavernosum, enabling erections. In general, a complete upper-motor neuron injury above T11 can result in reflex erections in the absence of psychogenic erections, while men with an injury impacting the sacral pathways have psychogenic erections but no reflex erections. PDE5i therapy is first-line treatment for men with SCI. Another option for SCI ED treatment is intracavernosal injections, which should be started at a lower dose than for men with vasculogenic impotence, and these men should be monitored for autonomic dysreflexia.

The evaluation and treatment of psychogenic ED, as it is more likely to present in the infertile man, is of the utmost importance. Objective endpoints to discriminate between psychogenic and organic ED include nocturnal penile tumescence testing and penile duplex Doppler ultrasonography (16, 17). Certainly, a reported history of diabetes mellitus and a prior history of prostate or penile surgery may obviate the need for any further testing as these conditions are reliably associated with organic erectile dysfunction (16). Questionnaires, including the frequently employed IIEF, may not always successfully differentiate between the two presentations (17, 18). Indeed, in two studies each with 36 and 44 patients, 20%–37% of patients with severe-range ED based on IIEF were found to have normal penile ultrasound dynamics underscoring the necessity of further testing to differentiate between organic and psychogenic ED (17, 19). In patients with psychogenic ED, empirical psychotherapy with or without PDE5i therapy under the supervision of an appropriate specialist with requisite expertise should be offered. The importance of accurate diagnosis is underscored by the finding that up to 32% of 285 men with psychogenic ED in one study experienced resolution of symptoms immediately following definitive diagnosis (20). This problem is particularly relevant among men who are unable to provide an ejaculated specimen on the day of oocyte retrieval. Therefore, early identification and treatment of this condition is of paramount importance.

PSYCHOLOGICAL STRESS

The effects of infertility-related stress are not as well studied in the male partner as they are in the female (21). A longitudinal study of infertility-related stress found that women did experience greater anxiety symptoms than men. Importantly, high levels of sexual infertility stress, defined as loss of enjoyment of sexual relations, feelings of pressure to schedule sexual relations, and loss of sexual self-esteem, were noted among 21% of the 295 men studied (22). Increased sexual dissatisfaction among both partners after IVF failure highlights the need to approach the complaint of ED holistically and consider referral to a specialized mental health professional for appropriate counseling (23). Interestingly, long-term follow-up of patients treated with assisted reproductive therapy found similar sexual satisfaction regardless of whether they were able to conceive a child (24).

EJACULATORY DYSFUNCTION

Ejaculatory dysfunction may also have a substantial impact on fertility potential. Aspermia is the absence of an ejaculation with an orgasm. This may be due to the lack of seminal

emission or retrograde ejaculation, which is the backward flow of the ejaculate into the bladder instead of antegrade expulsion out of the urethral meatus. In both circumstances, the men will have a “dry orgasm” (25). Patients who undergo a retroperitoneal lymph-node dissection for testicular cancer may have a loss of emission due to damage to the hypogastric plexus. For this reason, it is important to counsel these men about sperm banking if they desire future fertility. There is no available treatment for restoring seminal emission in these patients. Men with ejaculatory duct obstruction may also have absent or significantly reduced seminal emission; these patients may benefit from a transurethral resection of the ejaculatory ducts to relieve the obstruction. Additional etiologies for lack of seminal emission can include spinal cord injury, radical prostatectomy, pelvic trauma, diabetes mellitus, multiple sclerosis, and Parkinson’s disease. Additionally, patients with ED or ejaculatory dysfunction may want information about sperm banking prior to treatment in the event they cannot produce a semen sample on the day of oocyte retrieval.

Retrograde ejaculation can be secondary to medications inhibiting bladder neck closure (i.e., alpha blockers) or due to surgical procedures on the prostate and/or bladder neck. Other etiologies include various neuropathies affecting bladder neck closure, which can be secondary to diabetes mellitus, spinal cord injury, neurologic disorders, or retroperitoneal lymph-node dissection (26). If retrograde ejaculation is due to an alpha blocker, stopping the medication will restore antegrade ejaculation. Otherwise, medical therapies include alpha agonists and tricyclic antidepressants such as imipramine; these have been utilized with variable results (27, 28). More commonly, sperm can be harvested in men with retrograde ejaculation and used for either IUI or IVF. Conventional protocols include alkalinizing urine for a period of 24 hours, followed by a post-orgasm urinalysis. This is essential for ensuring sperm viability so that it can effectively be used for IUI or IVF, depending on the amount and quality of sperm harvested.

Men with spinal cord injuries may present with aspermia secondary to either the absence of seminal emission or retrograde ejaculation. Many of these men also have anorgasmia, which is the inability to achieve an orgasm. There has been encouraging success with the use of penile vibratory stimulation to enable these patients to reach climax and produce an ejaculate. This is a minimally invasive method to potentially harvest sperm for either IUI or IVF. If there is no ejaculate, then their post-ejaculate urine can be analyzed to diagnose retrograde ejaculation (29). If this is ineffective and an ejaculate is desired for fertility purposes, there have also been promising results with the use of electroejaculation in these patients (30).

Premature ejaculation (PE) refers to the triad of short ejaculatory latency, a lack of control over the ability to delay ejaculation, and personal distress as a result of this condition. Though the definition of PE is still evolving, “lifelong PE” is characterized by ejaculation that occurs within 1 minute of vaginal penetration (31). In patients with “acquired PE,” this latency time may be up to 3 minutes or less (31). Certainly, there are imperfections with this strict definition in that it does not take into account homosexual relationships or early

ejaculations prior to vaginal penetration. However, using this definition, the prevalence of PE has been estimated between 5% and 20% (32). Organic causes of PE have been identified as penile hypersensitivity and 5-hydroxytryptamine (5-HT) receptor hypersensitivity; however, psychogenic influences such as anxiety, depression, and stress may further exacerbate PE. There are several over-the-counter lidocaine-based topical agents aimed to treat penile hypersensitivity (33). These are readily available to all men and are used commonly to delay ejaculation, even without a formal diagnosis of PE. Additionally, selective serotonin reuptake inhibitors (SSRIs) have been successful in treating PE by activating the 5-HT_{2C} receptor and, therefore, readjusting the ejaculatory threshold set point (34). It is also important to emphasize the role of sexual therapy, employing cognitive and behavioral techniques, as part of the treatment algorithm for PE. Involving the partner in the treatment process and encouraging open communication about sexuality may have greater relationship benefits as well.

DECREASED LIBIDO

Hormonal dysfunction is frequently associated with sexual complaints among infertile men, most commonly related to diminished libido. Evaluation of these symptoms may include straightforward query during the medical interview or by employing a validated questionnaire, such as the Androgen Deficiency in Aging Males (ADAM) test (35). Indeed, 43% of 94 men presenting to an infertility clinic with normozoospermia provided a positive response to a validated questionnaire of hypoandrogenic symptoms (34). Men presenting with oligozoospermia have concomitant hypoandrogenism in 42%–50% of cases (34). Correction of hypoandrogenism in the setting of ED should be approached with modest expectations (36, 37). However, men with complaints related specifically to diminished libido in the setting of hypoandrogenism may benefit greatly from hormonal therapy (38).

Exogenous testosterone replacement therapy should be avoided at all costs due to the devastating effects on spermatogenesis. Exogenous testosterone replacement therapy leads to iatrogenic suppression of pituitary gonadotropin secretion, decrease in intratesticular testosterone, and decreased spermatogenesis, often to the point of azoospermia. Alternatively, clomiphene citrate may correct sexual dysfunction among 75% of 175 hypoandrogenic patients studied; more so in men with underlying anxiety disorders (39). Hormonal therapy in the setting of infertility and hypoandrogenism requires further study.

SUMMARY

- Evaluation of sexual dysfunction by a comprehensive history, including validated questionnaires, is a critical part of the evaluation of an infertile couple; when present, referral to the appropriate specialist is recommended.
- ED is a common and very treatable problem that can contribute to infertility; furthermore, significant medical comorbidities may be identified during the evaluation.

- Psychological distress from infertility contributes to male sexual dysfunction.
- Ejaculatory dysfunction occurs in 5%–20% of the general population and consists primarily of premature ejaculation.

CONCLUSIONS

- Normal male sexual function is a necessary component for fertility.
- Treatment and resolution of male sexual dysfunction can serve as a window into improving a man's somatic health.
- Evaluation of male sexual dysfunction is a highly cost-effective and potentially lifesaving component of reproductive health.
- Avoidance of exogenous testosterone and related products is extremely important.

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