Premature Ejaculation

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Premature ejaculation (PE) is one of the most common complaints of men or couples presenting with ejaculatory disorders. Other common names for this entity include early or rapid ejaculation. Similar to erectile dysfunction, PE is not life threatening but may have a significant impact on a patient’s and his partner’s quality of life and sexual satisfaction. Additionally, PE can affect men across all age ranges making this entity the most common male sexual disorder.

Definition

Despite its prevalence, there is no consensus on the definition of PE. Some authors have suggested that PE exists when the man reaches orgasm within 1 minute of vaginal penetration (Waldinger, Hengeveld, Zwinderman, & Olivier, 1998). Others have advocated not defining the disorder with a specific time duration and instead suggest that a diagnosis is made when the man ejaculates too early for female partner satisfaction in greater than one-half of encounters (Masters & Johnson, 1970). The American Urological Association (AUA) proposed a definition of “ejaculation that occurs sooner than desired, either before or shortly after penetration, causing distress to either one or both partners” (AUA Consensus Panel, 2004).

Anatomy

To better understand ejaculatory disorders, a review of the relevant anatomy and physiology is important. The fluid in the ejaculate arises from the seminal vesicles, prostate, and urethral glands. The prostate is formed from epithelial outgrowths of the pelvic urethra during the 8th week of development. Approximately 4 weeks later, the mesonephric (Wolffian) ducts fuse with the ipsilateral rete tubules to form the epididymis and vas deferens (Park, 2002). Distally, outpouching of the mesonephric ducts form the seminal vesicles. A septum divides this outgrowth into ejaculatory ducts at the ampulla of the vas in the prostatic urethra.

The bladder neck lies proximal to the paired ejaculatory ducts and acts as a physiologic sphincter during the ejaculatory process. The smooth muscle surrounding the urethra in this area is under autonomic control and, under normal circumstances, contracts during ejaculation which prevents retrograde flow of semen from occurring. Distal to the ejaculatory ducts and verumontanum lies the external urethral sphincter. This sphincter consists of a central muscle layer under autonomic control surrounded by a muscular layer under somatic control. It also contracts prior to seminal emission to create an enclosed pressure chamber in the prostatic urethra. Normally this sphincter relaxes at the appropriate time to allow for antegrade ejaculation.

Neurologically, the ejaculatory process is under both central and peripheral nervous system control. The cutaneous nerves of the penis are involved in the local stimulus of the ejaculatory process. Stimulatory impulses are transmitted through the pudendal nerve to the spinal cord. Although the specific location of the centrally located ejaculatory center has not been fully elucidated, the hypothalamus seems to play an integral part (Coolen, Allard, Truitt, & McKenna, 2004; Herberg, 1963; Thomas, 1983). Within the central nervous system, serotonin appears to be inhibitory while dopamine acts as an excitatory agent (Kimura, Kisaki, Sakurada, & Tadano, 1976; 1977).

Nerves responsible for the ejaculatory process travel from the cerebral cortex to the thoracolumbar and sympathetic chains at T10-L3 (Thomas, 1983). Post-synaptic adrenergic fibers then course through the superior hypogastric plexus located at the aortic bifurcation prior to dispersing laterally near the bladder and rectum to their end organs.
which include the epididymis, vas deferens, seminal vesicles, prostate, and bladder neck. Expulsion of seminal fluid from the posterior urethra is stimulated through activation of nerve fibers within the pudendal nerve originating from S2-S4.

Physiological Events Of Ejaculation

The ejaculatory process consists of the coordinated activity of deposition of seminal fluid into the posterior urethra with subsequent antegrade expulsion. Three distinct physiological phases of the ejaculatory process have been described as bladder neck contraction, emission, and ejaculation. Detailed evaluation of the ejaculatory process has been evaluated using transrectal ultrasound (Gil-Vernet, Alvarez-Vijande, Gil-Vernet, & Gil-Vernet, 1994), fluoroscopy (Mitsuya, Asai, Suyama, Ushida, & Hosoe, 1960; Sonksen, Ohl, & Wedemeyer, 2001), electromyography studies (Gerstenberg, Levin, & Wagner, 1990), and transurethral pressure catheters (Bohlen, Hugonnet, Mills, Weise, & Schmid, 2000). From these studies it is clear that ejaculatory events occur in a systematic fashion.

During emission, the smooth muscles in the prostate, seminal vesicles, and vas deferens undergo rhythmic contractions that result in seminal fluid being deposited into the posterior urethra. Simultaneously, the bladder neck contracts to prevent retrograde flow of seminal fluid into the bladder (Bohlen et al., 2000). Once the seminal fluid is deposited into the posterior urethra, the external urethral sphincter relaxes while the perirethral skeletal muscles rhythmically contract resulting in pulsatile expulsion of the semen from the urethra. This portion of the ejaculatory process is stimulated by branches of the pudendal nerve that originate from S2-S4. Although the muscles responsible for the projectile phase of ejaculation are skeletal muscles normally under voluntary control, all events of the ejaculatory process are involuntary once the reflex is initiated.

The ejaculatory process normally occurs during sexual activity during which genital sensory input is coordinated with erotic imagery from the cerebral cortex. While it is known that input from the cortex augments sensory stimulation, the ejaculatory reflex can be activated from cerebral input alone as evidenced by nocturnal emission.

Premature Ejaculation

Despite its widespread prevalence, the etiology of PE is not agreed upon. For many years PE was considered a neurosis as a result of unconscious conflict (Waldinger, 2002). Subsequent to this, many researchers attributed the symptoms to a learned behavior as a result of performance anxiety (Masters & Johnson, 1970). More recent literature emphasized neurobiology as the cause with pharmacotherapy for treatment.

Some research showed a decreased vibratory threshold on the penile shaft and glans in patients with PE when compared to normal controls (Xin et al., 1996). Still other researchers have demonstrated significant differences in sacral and cortical somatosensory evoked potentials in patients with PE compared to controls, suggesting an underlying neurological difference (Colpi, Fanciullacci, Beretta, Negrì, & Zanollo, 1986; Fanciullacci, Colpi, Beretta, & Zanollo, 1988). A more recent study suggested that a delay in processing sensory stimuli in the central nervous system may be responsible for PE (Ozcan et al., 2001).

Premature ejaculation has been classified into subtypes: primary or secondary (Godpodinoff, 1989). Patients with primary PE have had the disorder present since puberty. Those with secondary or acquired PE have an onset later in life.

Evaluation

When men present with PE, a thorough sexual history is paramount to the evaluation. It is important to distinguish the presence of PE from erectile dysfunction as some men will confuse the two entities. Patients should be questioned regarding the duration of symptoms (life-long vs. acquired) as well as the frequency. If the PE is acquired, it is important to explore the timing or events surrounding when the PE began and if it is situational and/or with specific partners. In all men, one should also inquire about the nature of the sexual encounters in regards to durations of foreplay, sexual intercourse, and masturbation. The time to ejaculation should be ascertained with sexual stimulation (before or after intromission), as well as the degree of voluntary control over ejaculation that the patient experiences. One should also try to obtain a general sense of the patient’s knowledge about ejaculation. Some men do not understand that the normal physiologic response is loss of erection after ejaculation. Additionally, the degree of bother that the patient and his partner have from the PE should be obtained. In general, no further testing is needed prior to initiating treatment.

Treatment

Because the etiology of PE is disputed, treatment options include behavioral, psychological, and attempts to alter the sensory input or retard the ejaculatory reflex through pharmacologic means. It is important to review all available treatment options and side effects with the patient and preferably with his spouse as well so that an informed decision can be made.
Sex therapy. Because of the belief by some researchers that PE is due to a learned behavior because of performance anxiety, sex therapy became the mainstay of treatment for many years and is still one option for treating PE today. Acquired or situational PE is believed by many to have a psychological basis and most clinicians recommend counseling as at least part of the treatment recommendations.

The most common form of sex therapy is the “squeeze technique” during which the patient and/or his partner squeeze the erect penile shaft before the ejaculatory reflex is stimulated. Using this technique, the patient will learn to voluntarily delay ejaculation while maintaining sexual excitement (Masters & Johnson, 1970). While this technique can have significant improvements for men, therapy is time consuming and requires a partner willing to participate.

The start-stop method, first introduced by Semans (1956), is an alternative treatment option for treating PE. As suggested by the name, this technique involves masturbatory stimulation of the penis until the sensation of heightened arousal is met but prior to the onset of the ejaculatory reflex. The stimulation is then withheld until the sensation resolves. This is repeated until the man reaches the point that extraginal stimulation occurs without ever reaching the sensation of inevitability.

Decreasing penile sensitivity. An alternative option for patients includes the application of 2.5 gms of prilocaine-lidocaine cream to the glans 30 minutes prior to intercourse. After application, a condom is used to hold the cream in place. In a preliminary unblinded study, 81% of men reported improvements in their PE (Berkovitch, Keresteci, & Koren, 1995). Men can titrate the degree of penile numbness by adjusting the exposure time to the cream. It is important to inform patients that the cream should be wiped off completely prior to intercourse to prevent vaginal numbness (Sahin & Bircan, 1996).

An alternative topical agent, SS cream, is available currently in Korea. It is a natural agent derived from nine products. In a double-blind, randomized, placebo-controlled Phase III trial, men with primary PE had a significant improvement in ejaculatory latency when using SS cream when compared to controls (Choi et al., 2000).

Pharmacologic therapy. Treatment of PE may be effective with the use of several different classes of medications. Currently no medication is Food and Drug Administration (FDA) approved for treating PE. Despite this, several medications are routinely prescribed to successfully treat PE.

Initial medical treatments for PE involved use of medications to inhibit alpha receptors. In a small, nonrandomized study, 20 mg to 30 mg of the alpha-antagonist phenoxybenzamine was used successfully to treat PE in nine patients (Shilon, Paz, & Homonnai, 1984). It should be noted that a significant side effect of the medication is aspermatogenesis; therefore, this therapy should not be considered in men wishing to procreate.

The tricyclic antidepressant clomipramine was effective in treating PE in several double-blind placebo-controlled trials with doses ranging from 10 mg to 50 mg per day (Girgis, El-Haggar, & El-Hermouzy, 1982; Haensel, Rowland, & Kallan, 1996; Kim & Seo, 1998; Rowland, De Gouveia Brazao, & Koos Slob, 2001; Strassberg, De Gouveia Brazao, Rowland, Tan, & Slob, 1999). Possible mechanisms for action of the medication include inhibition of the autonomic processes involved in the ejaculatory reflex, diminished psychological arousal, or a direct anxiolytic effect. The most common side effects of clomipramine include dry mouth and fatigue which are due to the anticholinergic properties of the medication and appear to be dose related.

Given the inhibitory effects of serotonin on the central ejaculatory reflex, the efficacy of selective serotonin reuptake inhibitors (SSRIs) in the treatment of PE is not surprising. These inhibitors delay ejaculation in multiple placebo-controlled randomized studies (Biri et al., 1998; Haensel, Klem, Hop, & Slob, 1998; Kara et al., 1996; Kim & Seo, 1998; Waldinger, Hengevald, & Zwinderman, 1994; Waldinger et al., 1998) and is the most common class of medications used to treat PE currently. Dosing of the various SSRIs for the treatment of PE include fluoxetine (20 to 40 mg/day), sertraline (50 to 100 mg/day), paroxetine (20 to 40 mg/day), and fluvoxamine (100 mg/day). Common reported side effects of SSRIs are usually tolerable and include gastrointestinal complaints and anxiety. One study comparing all four SSRIs with placebo reported paroxetine to exert the strongest delay in ejaculation (Waldinger, Hengevald, & Zwinderman, 1998).

A double-blind, placebo-controlled study compared fluoxetine (40 mg QD), sertraline (100 mg QD), and clomipramine (50 mg QD) for the treatment of PE (Kim & Seo, 1998). Although both patient and partner sexual satisfaction were statistically significantly higher with clomipramine when compared to the SSRIs and placebo, the reported side effects of the medication were also significantly higher. Of the remaining medications, sertraline was more effective than fluoxetine and placebo with fewer side effects than clomipramine.

Other studies evaluated if clomipramine (Haensel et al., 1996), sertraline (Kim & Paick, 1999), or paroxetine (McMahon & Touma, 1999) taken as needed
rather than continuously could be effective to increase ejaculat-
yry latency. All of the studies sug-
gested effectiveness in treatment
using this regimen when the
medication is administered 12 to
24 hours (clomipramine); 4 to 8
hours (sertraline); or 3 to 4 hours
(paroxetine) prior to intercourse.

More recently, the use of silde-
nafil citrate as an adjuvant therapy
to paroxetine to treat PE was eval-
uated (Salonia et al., 2002).

Combination therapy with silde-
nafil and paroxetine improved
time to ejaculation and sexual sat-
isfaction compared to paroxetine
alone; however, a slight increase
was noted in drug-related side
effects. This was not a placebo-
controlled trial however, and it is
unclear if phosphodiesterase
inhibitors have a significant phar-
macologic role in treating men
with PE.

Dapoxetine is a new fast-acting
selective serotonin reuptake
inhibitor specifically for PE. Pryor,
Althof, Steidle, Miloslavsky, and
Kell (2005) recently reported on
two multicenter, randomized,
double-blind, placebo-controlled
trials. A total of 2,614 men with
PE were enrolled in the trials
which consisted of a 2-week
baseline period followed by a 12-
week treatment period. Intra-
vaginal latency time (IELT) was
measured by a stopwatch held by
the sexual partner. After the 2-
week baseline period, men with
IELT of less than 2 minutes were
randomized into three groups:
placebo or dapoxetine at either
30 mg or 60 mg used on an as-
needed basis over the next 12
weeks. In addition to IELT, feel-
ings of having control over ejacu-
lation and overall sexual inter-
course satisfaction were mea-
sured. A significant difference
was found between the placebo
each treatment group in all
three outcomes measured. The
IELT improved from 0.9 to 1.75
minutes in the placebo group,
0.92 to 2.78 minutes in the 30 mg
dapoxetine group, and 0.91 to
3.32 minutes in the 60 mg dapox-
etine group. Additionally, both
30 mg and 60 mg of dapoxetine
were significantly better than
placebo in increasing IELT at first
dose. Although the study medici-
appeared to be well toler-
ated, common side effects
included reports of nausea in
8.7% of men taking the 30 mg
dose and 20.1% of men taking
the 60 mg dose. Headache was
also reported in 5.9% and 6.8%
respectively. Additionally, 6.8%
of men reported diarrhea and
6.2% reported dizziness with the
60 mg dose.

In October 2005, this medica-
tion was not approved by the FDA
due to the outcome of the trials
did not show that dapoxetine was
sufficiently superior to placebo.

Other drugs are being investigated.

Conclusion

Premature ejaculation is a
common male sexual disorder
that can have a significant impact
on the quality of life of couples.
Both behavioral and pharmaco-
logical options are available and
effective for men presenting with
this problem. [2]

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significantly alter the teaching that is involved with the diagnosis of prostate cancer (see page 298).

Assessing opinions about health issues cannot occur without successful communication with our patients, regardless of gender. The translation of the Prostate Health Questionnaire into the native dialects of Jamaican and Haitian men offers the opportunity for health care providers at all levels to accurately assess the knowledge level and needs of this distinctive group of patients (see page 304). It similarly raises the question of whether or not this questionnaire and others will better serve our patients when translated specifically to target individual groups.

Not all quality of life interventions must be spectacular or large scale. At times the smallest intervention, such as simply being willing to listen, or validating a concern, can be the most profound contribution of all.

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