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CONTINUOUS EDUCATION FOR BETTER PATIENT OUTCOMES

Erectile Dysfunction – Module 1, Disease Background

Definition

Erectile dysfunction (ED) is a complex sexual arousal disorder in men. It is defined as persistent or recurrent inability to achieve or maintain penile erection that is sufficient for satisfactory sexual performance. A diagnosis of ED is established if the duration of symptoms continues for a period of 3 months except in the case of trauma or surgically-induced ED.

Even though ED is not considered a life-threatening condition it has a significant effect on quality of life of patients and their partners. It is also closely associated with several other conditions.

A critical understanding of the anatomy of the penis and the physiological mechanisms underlying erection is essential to provide a clear perspective of erectile dysfunction.

Anatomy

Anatomy of the penis

The penis consists of the root, which is attached to the perineum, and the body. The tip of the penis is called the glans penis. The body of the penis is comprised of 3 masses of erectile tissue, the right corpus cavernosum, the left corpus cavernosum and the corpus spongiosum. The corpora cavernosa form most of the body of the penis and are enveloped by the tunica albuginea. The corpus spongiosum is also cylindrical erectile tissue which surrounds the urethra and is expanded at the end to form the glans. These structures get engorged with blood during sexual excitement.Each of the corpora cavernosa consist of several sinusoids which are larger in the centre and smaller in the periphery. The sinusoids are interconnected and are partially separated by trabeculae.

Arterial blood supply

Arterial supply to the penis is by the branches of the internal pudendal artery. The corpora cavernosa are supplied by the dorsal arteries and the deep cavernosal arteries which are located in the centre of each of the corpus cavernosum. The corpus spongiosum is supplied by the dorsal artery and by the artery of the bulb of the penis. Many blood vessels from the deep arteries of the penis traverse the spaces in the erectile tissues. In the relaxed state these arteries are coiled and during excitation related nerve impulses result in the uncoiling of these arteries and rapid flow of blood in to the cavernous spaces and cause the penis to become turgid.

Venous drainage

The venous drainage of the penis comprises of the superficial, intermediate and deep venous systems. The superficial system consists of veins draining in to the superficial dorsal vein. Small veins from the corpora cavernosa drain into small vessels in the tunica albuginea called the sub-tunical vessels which in turn drain into veins that run around the circumference of the penis and receive tributaries from the corpus spongiosum. The circumferential veins drain into the deep dorsal vein. This forms the intermediate venous system. The deep venous drainage system consists of the crural veins and the cavernosal veins. The veins of the penis play a significant role in the physiology of erection. Hemodynamic events such as increased blood flow into the sinusoids and restricted drainage of venous blood in the erectile tissues which is caused by smooth muscle relaxation in the corpora cavernosa, arterial dilatation result in erection of the penis with sexual stimulation. The muscles at the root of the penis constrict and compress the veins thereby preventing drainage of blood and maintaining the erection.

Physiology

Vascular dynamics of penile erection

As discussed earlier penile erection is a vascular event and has 2 components which include arterial dilatation and venous occlusion. There is little blood flow to the penis in the detumescent state and the smooth muscle within is in a state of contraction. Arterial and cavernosal smooth muscle relaxation results in a 20 – 40 fold increase in the blood flow to the penis. As a result the sinusoids in the corpora cavernosa get engorged with blood during erection.

As penile erection develops there is an increase in pressure on the surface of the corpora near the tunica albuginea and compresses the veins that drain blood away from the corpora. This trapping of blood increases the pressure in the cavernous tissues. This component of erection is further enhanced by the contraction of the muscles at the root of the penis which further forces blood into the erectile tissues and increases rigidity.

Mechanisms of penile erection

Distinct mechanisms are involved in penile erection. These include the central psychogenic mechanism and the reflexogenic mechanism.

The psychogenic mechanism results in erection and starts as central psychogenic stimuli generated or received in the brain in response to auditory, visual, olfactory, imaginative stimuli in the absence of physical touch. They are believed to be mediated primarily via the sympathetic thoracolumbar path, although the sacral parasympathetic system also may participate.

Reflexogenic erections are elicited in response to direct stimulation of the penis. They are mediated by a spinal reflex pathway through sensory receptors in the penile skin and the glans and the dorsal nerve that joins the pudendal nerve to reach the sacral spinal cord.

Another mode of penile erection is sleep erection which occurs in 95% of rapid eye movement sleep, on an average of 3 to 5 times per night and may last from 30 minutes to 60 minutes.

Molecular mechanisms of penile erection

Smooth muscle contraction, which is an important component of the physiological processes involved in penile erection, is modulated by calcium binding. Intracellular calcium ion concentration is a crucial factor and is regulated by several mechanisms. The nitric oxide-cyclic GMP (NO/cGMP) pathway and the phosphodiesterase mechanisms are 2 mechanisms that have been unravelled and understood in detail.

The NO/cGMP pathway is a major regulator of smooth muscle relaxation in the penis. Nitric oxide, which may be derived from the cavernous nerves or from the endothelium lining the sinuses, initiates and maintains erection. NO activates the membrane bound enzyme guanylyl cyclase which converts GTP to cyclic GMP (cGMP) which in turn causes a cascade of events that eventually reduce the intracellular concentration of Ca2+ by increasing sequestration and extracellular transport while reducing intracellular transportation. Phosphodiesterases (PDEs) are a class of enzymes that degrade cyclic nucleotides such as cGMP and cAMP and the predominant type of PDE in the penile tissues is PDE5 which acts on cGMP. PDE5 breaks down cGMP to 5 prime GMP and reduces the concentration of calcium and eventually promotes flaccidity consequent to smooth muscle contraction.

During sexual arousal inhibition of PDE5 mediated degradation of cGMP promotes increased intracellular concentrations of cyclic GMP and erection

Classification of ED

Types of ED

ED is classified as psychogenic and organic based on the underlying cause. Psychogenic ED was earlier considered to the most common, however it is now recognized that vasculogenic ED is in fact the most common.

Organic causes of ED may further be classified as vasculogenic, neurogenic, anatomic and endocrinological. Psychogenic ED may be generalized or situational. Organic causes of ED such as vascular, neurologic and hormonal abnormalities with an occasional psychogenic component may be common in older men. However, men under the age of 40 years may have psychogenic factors as the most important contributing factor for ED.

Vasculogenic ED

Vasculogenic ED may be arterial, venous (cavernous) or mixed.

The two most common vascular disorders causing ED include focal occlusion of the penile artery and Peyronie's disease. Studies have revealed that subclinical perineal trauma, commonly seen in younger men associated with bicycling, may also cause ED. Bicycling decreases the peak systolic velocity of cavernosal artery to 0 as a result of perineal pressure from bicycle seats. This further occludes the penile blood vessels temporarily leading to focal occlusive arterial disease. Peyronie's disease is thought to arise as a result of repeated trauma to the tunica albuginea leading to formation of plaque causing penile curvature. Plaque formation is time consuming and hence the prevalence of ED increases with age. Mechanism of arteriogenic ED involves structural changes. Arterial insufficiency leads to reduction in oxygen tension in the blood of corpus cavernosum. Formation of PGE1 and PGE2 is oxygen-dependent, hence, an increase in oxygen tension is associated with high levels of PGE2 and suppression of TGF-β1-induced collagen synthesis in the corpus cavernosum. However, a reduction in oxygen tension diminishes the cavernous trabecular smooth muscle content leading to diffuse venous leakage.

Neurogenic and Hormonal causes

Some of the common neurogenic causes that contribute to ED include stroke, Parkinson's disease and multiple sclerosis. Nerve damage leading to ED can be caused by some types of physical trauma and injuries to pelvic region or spinal cord. ED is often under-recognized and under-treated among patients with dementia due to paucity of data. Hormonal causes of ED are uncommon in young individuals. However, low testosterone levels causing ED is seen in elder individuals. Few common hormonal disorders that are associated with ED include diabetes mellitus, hyper-/hypothyroidism, Klinefelter's syndrome, etc.

Psychogenic causes

Psychogenic causes of ED include performance anxiety, fear of negative consequences, interpersonal factors and relationship factors/conflicts. The International Society of Impotence Research has proposed a new classification for psychogenic ED. According to this classification psychogenic ED is classified into generalized type and situational type.

Generalized type of ED can be of either unresponsive type or inhibitory type. Generalized unresponsive type can be due to primary lack of sexual arousability or age-related decline in sexual arousability whereas generalized inhibitory type is due to chronic disorder of sexual intimacy. Situational type of ED can be partner-related, performance-related or psychogenic distress. Partner-related factors include lack of arousability and high central inhibition due to partner conflict. Performance-related factors include rapid ejaculation or fear of failure. Psychogenic distress can be due to depression or stress.

Medication induced

Many medications can cause ED in men by affecting sexual arousal and sexual performance. The common medications include antihypertensives, antidepressants, antihistamines, chemotherapy, etc. Atenolol, Chlorthalidone, Enalapril, Hydrochlorothiazide, Metoprolol, Verapamil, etc are some of the antihypertensive medications that can cause ED.

Amitriptyline, Chlorpromazine, Diazepam, Fluoxetine, Sertraline, etc are some of the antidepressants that can result in ED. Antihistamines that can cause ED include Cimetidine, Meclizine, Promethazine and Ranitidine. Chemotherapy agents such as Flutamide, Busulfan, Ketoconazole and Cyclophosphamide can cause ED in men.

Risk of developing ED

Risk factors

Risk factors for ED are numerous. Individuals more than 40 years of age demonstrate an association between ED and hypertension, dyslipdemia, diabetes mellitus, coronary artery disease and metabolic syndrome. Obesity and sedentary lifestyle also contribute to ED. Recent studies have demonstrated that hypogonadism is also associated with ED.

Modifiable risk factors for ED include smoking, lack of physical activity, obesity, excessive alcohol consumption and recreational drug use.

Chronic diseases & increased risk

Analysis of chronic diseases and its association with ED using a self-assessment questionnaire revealed increased probability of some degree of ED. Age-adjusted odds ratio of developing ED was 4.08 for patients having diabetes mellitus, 2.93 for individuals having prostatic disease, 2.6 for patients with circulatory disease, 1.82 for depressive patients, 1.79 for cardiac disease patients, 1.63 for individuals with cholesterol problems and 1.58 in the presence of hypertension.

Epidemiology

The Massachusetts Male Aging Study (MMAS) is a community-based survey of men in the age group of 40-70 years. 52% of responders in the study reported some degree of ED. Complete ED was noticed in 10% of respondents whereas moderate ED was noticed in 25% of respondents and minimal ED in 17% of respondents. The incidence of moderate or severe ED doubled in the age group of 40-70 years. It is estimated that the global prevalence of ED by the year 2025 would be about 322 million and is possibly related to the ageing population and increase in risk factors.

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Significance of ED

Why diagnose ED?

Not only are couples who are experiencing erectile dysfunction (ED) frequently burdened with significant psychological conditions, ED may also signal the presence of a more serious underlying disease.

It is important to diagnose and treat ED as it is often associated with comorbid conditions that may not have been detected previously, such as cardiovascular disease, diabetes, and depression.

ED-associated distress can have a serious negative impact on the patients' overall quality of life as well as on interpersonal relationships.