

Managing Dubiety/Skepticism in Andrology

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Abstract

Impotence can strike any man, at any time, at any age. Erectile dysfunction decreases with age. An overconsumption of alcohol, stress, fatigue, and anxiety causes impotency. One of the most common age-related causes of impotence is atherosclerosis. Other physical causes are diabetes, obesity, thyroid problems, kidney issues, sleep disorders, blood vessel damage, nerve damage, high blood pressure, high cholesterol, low testosterone, pelvic or spinal cord trauma or surgery, tobacco use and alcoholism [1]. Erectile dysfunction (ED) and benign prostatic hyperplasia are the common urological disorders in males. ED is an inability to maintain penile erection for the successful performance of sexual activity. ED has many physical and psychological causes including vascular disease, medications depression and sequelae to prostatic surgery. It is estimated that 30 million people in USA are suffering from ED. Organic ED may be an early sign of cardiovascular disease and requires evaluation Peyronie disease is a common fibrotic disorder of the penile erectile bodies that causes penile deformity and sexual dysfunction [2].

Keywords: Impotence; Penile Deformity; Erectile Dysfunction; Prostatic Hyperplasia; Peyronie Disease

Abbreviations

ED: Erectile Dysfunction; PDE5-Is: A Phosphodiesterase Type 5 Inhibitor; CVD: Cardiovascular Disease; SD: Sexual Dysfunction; NO•: Nitric Oxide Radical; OH•: Hydroxyl Radical

Introduction

Obesity has profound medical, psychological, and emotional consequences and is associated with sexual difficulties [3]. Sexual functioning is an integral component of health; therefore, one could theorize a correlation between sexual functioning and obesity [4]. Sexual dysfunction in multiple sclerosis (MS) is a significant, but often underestimated and overlooked suffering. Interventions to treat sexual dysfunction (SD) in MS are rare [5]. In addition, the impact of psychological as well as cognitive factors as depression, anxiety, stress etc. on SD should also be considered during the treatment of SD [6]. For the treatment of SD, psychotherapeutic interventions as e.g. cognitive behavioral therapy have been proposed as gold standard [7].

Prevalence of erectile dysfunction in diabetes searching major databases from inception to November 2016 for studies reporting erectile dysfunction in men with Type 1 and Type 2 diabetes mellitus [8].

Increasing attention is focusing on erectile dysfunction in men with diabetes due to its multifactorial pathophysiology and the concurrence of the same components as vasculopathy, neuropathy and depression [9]. The prevalence of diabetes is rising in high [10].

Erectile dysfunction is an increasing issue, especially in young man. Whereas the current treatment strategies are mostly focused on older men, young patients are seeking more for a longer lasting or definitive solution, rather than a life-long medical treatment. Possibly, this is a reason why currently 70% of men with erectile dysfunction are not under treatment [11].

Treatment schemes are currently mainly focused on dealing with the relevant chronic disorders in elderly patients. The current first choice treatment option is applying a phosphodiesterase type 5 inhibitor (PDE5-Is) [12].

In ED etiology, among the major causes are chronic diseases, such as hypertension, diabetes mellitus, and coronary artery diseases (CAD), as well as the negative effects of the drugs used for these conditions [13]. Neurogenic nitric oxide (NO•) is considered as the most important factor for the relaxation of corpora cavernosa (CC) and the penile vessels necessary for erectile response [14]. Melatonin is a hormone secreted from the pineal gland and has anti-oxidative and anti-inflammatory effects [15]. Studies have shown that melatonin detoxifies highly reactive hydroxyl radical (OH•) *in vitro* and sweeps free radicals [16]. The Massachusetts Male Aging Study (MMAS) found that 52% of men between 40 and 70 years old reported having some form of erectile dysfunction (ED) [17].

Among the phenomena in the ageing man are a decrease in erectile function and testosterone levels. Add to these, increased risk for cardiovascular disease (CVD), muscle wasting, decrease in bone density and libido, with all of these factors having an interplay with testosterone metabolism [18].

Erectile dysfunction or male impotence is defined as the inability to have or sustain an erection long enough to have a meaningful sexual intercourse. ED tends to occur gradually until the night time or early morning erections cease altogether or are so flaccid that successful intercourse does not occur. Sexual health is an important determinant of quality of life [19]. Diabetes is considered the main risk

factor for the development of erectile dysfunction and since the 1970s the association between diabetes and the development of erectile dysfunction has been documented both in animal models and humans [20].

History

During the late 16th and 17th centuries in France, male impotence was considered a crime, as well as legal grounds for a divorce. The practice, which involved inspection of the complainants by court experts, was declared obscene in 1677 [21].

John R. Brinkley initiated a boom in male impotence cures in the U.S. in the 1920s and 1930s. His radio programs recommended expensive goat gland implants and “mercurochrome” injections as the path to restored male virility, including operations by surgeon Serge Voronoff. In modern times, the genuine clinical study of sexual problems is usually dated back no further than 1970 when Masters and Johnson’s *Human Sexual Inadequacy* was published. It was the result of over a decade of work at the Reproductive Biology Research Foundation in St. Louis, involving 790 cases. The work grew from Masters and Johnson’s earlier *Human Sexual Response* (1966).

Prior to Masters and Johnson the clinical approach to sexual problems was largely derived from the thinking of Freud. It was held with psychopathology and approached with a certain pessimism regarding the chance of help or improvement. Sexual problems were merely symptoms of a deeper malaise and the diagnostic approach was from the psychopathological.

Modern drug therapy for ED made a significant advance in 1983, when British physiologist Giles Brindley dropped his trousers and demonstrated to a shocked Urodynamics Society audience his papaverine-induced erection [22]. The drug Brindley injected into his penis was a non-specific vasodilator, an alpha-blocking agent, and the mechanism of action was clearly corporal smooth muscle relaxation. The effect that Brindley discovered established the fundamentals for the later development of specific, safe, and orally effective drug therapies [23]. Peyronie condition is named for François Gigot de La Peyronie, who described it in 1743; the condition may have been described around 100 years before that [24].

In 2013, the US FDA approved the first drug specifically for Peyronie’s; the drug was collagenase clostridium histolyticum (Auxilium) [25,26].

Significant gap in research

Data show that gout is associated with an increased risk of developing erectile dysfunction [27]. Erectile function among men with vasculogenic erectile dysfunction improved significantly after 6 weeks of treatment with an aspirin dosage of 100 mg/day [28]. Meta-analysis of studies conducted around the world found that men with diabetes have more than 3.5 times increased risk for erectile dysfunction [29]. A new study found a 52% higher risk for the future development of Parkinson’s disease among men with erectile dysfunction [30].

A vacuum erection device helps draw blood into the penis by applying negative pressure. This type of device is sometimes referred to as penis pump and may be used just prior to sexual intercourse. Several types of FDA approved vacuum therapy devices are available with a doctor’s prescription. When pharmacological methods fail, a purpose-designed external vacuum pump can be used to attain erection, with a separate compression ring fitted to the penis to maintain it.

Major advances and discoveries

Despite major advances in the understanding of the physiology of penile erection and the pathophysiology of ED, together with an increase in the available pharmacotherapies, ED remains a significant global male health problem. Oral tablets, in particular, PDE5 inhibitors, have revolutionized the treatment of ED by decreasing reliance on more invasive options [31]. Topical therapies are a promising alternative to the current second-line therapies, as they can be safe and easy to use and do not require intraurethral or intracavernosal instrumentation. One of the leading candidates for this type of administration is a medication termed Topiglan. It consists of prostaglandin E1 (alprostadil) combined with SEPA (soft enhancer of percutaneous absorption). Topical alprostadil has been studied in cats and humans and has been shown to induce erectile responses with minimal side effects [32]. The benefit of this topical therapy is maximized when used as part of a combination regimen such as those including PDE5-Is. This medication has been approved in Canada. Another topical therapy being investigated is topical sildenafil, currently in phase IIa and actively recruiting study participants [33]. Gene therapy is a potential therapeutic option that is another area of investigation for the treatment of ED. Genetic material can be easily injected into the penis, which is advantageous as this direct injection avoids potential systemic complications. Furthermore, the effects of gene therapy are more prolonged in the penis because of a slow turnover rate of the tunica albuginea [34]. In the first human trial, Melman, et al. administered a single-dose cavernosal injection of hMaxi-K, a ‘naked’ DNA plasmid carrying the human cDNA encoding the gene for the alpha subunit of the human smooth muscle Maxi-K channel [35]. Stem cell therapy is a new treatment option that offers the potential to reverse the underlying causes of ED and reduce patient reliance on the transitory effects of PDE5-Is medications. It has been studied in several

animal models in subjects who poorly respond to PDE5-Is (cavernous nerve injury and DM). Stem cell regenerative therapy is based on the rationale that stem cells can differentiate into a wide variety of cells including endothelial cells, Schwann cells, smooth muscle cells, and neurons [36]. It is clear that both hypotheses of functional antagonism and a structural basis of ED play a role in an integrated molecular pathology of ED. The challenge awaiting researchers and clinicians is to understand the physiology and pathophysiology of ED so as to develop pharmacotherapeutics to treat a wide etiology of patients while addressing preservation of potency [37].

Where the research go next?

Often, as a last resort, if other treatments have failed, the most common procedure is prosthetic implants which involve the insertion of artificial rods into the penis [38,39].

There are no approved pharmaceuticals for addressing female sexual disorders, although several are under investigation for their effectiveness. A vacuum device is the only approved medical device for arousal and orgasm disorders. It is designed to increase blood flow to the clitoris and external genitalia. Women experiencing pain with intercourse are often prescribed pain relievers or desensitizing agents. Others can be prescribed lubricants or hormone therapy [40]. Estrogens are responsible for the maintenance of collagen, elastic fibers, and vasculature of the urogenital tract, all of which are important in maintaining vaginal structure and functional integrity; they are also important for maintaining vaginal pH and moisture levels, both of which aid in keeping the tissues lubricated and protected. Prolonged estrogen deficiency leads to atrophy, fibrosis, and reduced blood flow to the urogenital tract, which is what causes menopausal symptoms such as vaginal dryness and pain related to sexual activity and/or intercourse [41]. Erectile dysfunction is one of the most common conditions affecting middle-aged and older men. Nearly every primary care physician, internist and geriatrician will be called upon to manage this condition or to make referrals to urologists, endocrinologists and cardiologists who will assist in the treatment of ED. This article will briefly discuss the diagnosis and management of ED. In addition, emerging concepts in ED management will be discussed, such as the use of testosterone to treat ED, the role of the endothelium in men with ED and treating the partner of the man with ED. The first stem cell study for the treatment of ED was published in 2004. This study used embryonic stem cells to treat ED. At this time, there is a total of 36 published basic studies assessing stem cell therapy for ED, with two clinical trials. The mechanism of action of stem cells is to generate angiogenesis with subsequent increase in cavernosal smooth muscle cells within the corporal bodies [42].

Current Debate and Conclusion

Men with total cholesterol higher than 240 mg/dl were twice as likely to have trouble achieving or maintaining an erection than men whose cholesterol levels were below 180 mg/dl. Men who had low levels of cholesterol levels of HDL “good” cholesterol were also twice as likely to suffer from impotence. The same high-fat diet that narrows arteries and blocks blood flow to your heart also narrows the arteries that carry blood to your penis. Blood has to be able to get to your penis in order for you to have an erection. A recent study of 4,462 male Vietnam veterans showed that smokers have a 50% higher risk of impotence than nonsmokers were impotent, and almost 4% of current smokers were impotent. Smoking contributes to blockages in the arteries that lead to the penis. Without adequate blood flow, your penis can't maintain an erection. The solution to this problem is simple: Don't smoke. Impotence can strike any man, at any time, at any age. But instead of going under the surgical knife, you may be able to exercise your way back to full sexual capacity. When blood doesn't flow to the penis properly or it drains from the area prematurely, doctors often prescribe medication or surgery. But the cure can be as bad as the problem.

Recently, a team of Belgium urologists treated 150 men who suffered from impotence. Some men had operations and others did special pelvic muscle exercises, called Kegels. Kegels are contractions of the pelvic floor muscles-an exercise pregnant women have been doing for years to help with childbirth. One year after treatment, 58% of the men who performed the Kegels were completely cured or were so satisfied with their improvement that they did not opt for surgery. The men who had surgery had better short-term results than the men who exercised, but more of the men who had surgery had trouble with impotence returning over the long run. Some skeptical doctors say that the pelvic muscles don't have any influence on the blood flow to the penis. They say the men in the study improved because of the beneficial psychological effects of the therapy [43]. Therapy for erectile dysfunction includes penile implants, intrapenile injections of alprostadil, intraurethral suppositories of alprostadil and oral phosphodiesterase-5 (PDE-5) inhibitors. Because of the efficacy, ease of the use, and safety of PDE-5 inhibitors, these drugs are now considered first-line therapy for ED. Four PDE-5 inhibitors (sildenafil, vardenafil, tadalafil, and avanafil) are approved for the treatment of ED [44].

Conflict of Interest

No conflict of interest.

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