Chapter 38

Lifestyle Modifications for Erectile Dysfunction

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38.1 Introduction

Sexual health plays an important role in the lives of many men and, for some, erectile function, specifically, helps define one's sense of masculinity. Erectile dysfunction (ED), referring to the inability to attain and/or maintain an erection sufficient for sexual activity, is one component of sexual health. ED is common in the United States, affecting over 18% of men over the age of 20 with the risk of experiencing ED increasing as men age [1]. Moreover, the disease is often debilitating for men and can lead to significant psychosocial consequences [2]. ED results in decreased physical and emotional satisfaction from sexual activity as well as an overall decrease in quality of life. Fortunately, a variety of medical and surgical options exist to restore erectile function, including oral medications, vacuum erection devices, penile constriction rings, medicated urethral suppositories, intracavernosal injections, and penile implants.

Lifestyle modification, considered first-line therapy for many disease processes, is often overlooked and underdiscussed in the management of men presenting with ED. Early initiation of lifestyle changes can help improve function in these men, as well as reduce the risk of developing dysfunction [3]. Furthermore, some men prefer a less medicalized approach to the treatment of ED, as one study involving Mexican men demonstrated [4]. Modifications to lifestyle or initiation of alternative medicines were the preferred source of change in this subset of men who described their view of medications, such as phosphodiesterase 5 (PDE5) inhibitors, for the treatment of ED as physically dangerous due to the significant side effects mentioned on television commercials. Though pharmacologic and surgical interventions to restore erectile function are important tools in the armamentarium of the healthcare provider, the authors believe that discussions regarding pertinent lifestyle modification should play a role at time of patient presentation and throughout the treatment process.

The aim of this chapter is to review the literature assessing lifestyle modification for the treatment of ED. Medications for the treatment of ED are directly marketed to consumers via television with commercials for Viagra® and Cialis®, alone, exceeding $300 million a year [5]. The authors believe that behavioral modification should be marketed as a prevention strategy, standalone treatment strategy, and as an adjunct to current pharmacotherapy by healthcare providers who treat those with ED. We hope to clarify what is currently known about efficacy of lifestyle modification so as to improve the clinician's ability to educate patients on the importance of making healthier choices and to spawn ideas for future work to address gaps in knowledge.

38.2 Pathophysiology of Erection

Understanding the pathophysiology of obtaining and maintaining an erection is critical in order to comprehend the effects of lifestyle modification on both processes.

38.2.1 Nitric Oxide

Nitric oxide (NO) is a metabolite of L-arginine (catalyzed via nitric oxide synthases [NOS]) and is considered the principal neurotransmitter and vasoactive metabolite for erection [6]. Upon sexual arousal, NO is released by nerve terminals and endothelial cells where it activates guanylyl cyclase that increases intracellular concentrations of cyclic guanosine monophosphate (cGMP). This ultimately leads to smooth muscle relaxation, engorgement of corporal bodies, and, through tension on the tunic albuginea, creates an erection. Individual NO molecules are only transiently present before being metabolized to nitrate or nitrite in the blood as are intracellular cyclic GMP before being hydrolyzed to GMP by PDE5. Loss of erection occurs when NO-induced vasodilation terminates and blood is drained from the corporal bodies leaving less tension on the tunica and thus cessation of penile engorgement.

Sildenafil, vardenafil, tadalafil, and avanafil are all FDA-approved drugs to treat ED by blocking this PDE enzyme activity. By working on the cGMP pathway, these medications work indirectly on the NO pathway to promote erectile function, the same pathway impacted by nonpharmacologic interventions. As a result, these medications may have improved efficacy when combined with lifestyle modifications [7].

38.2.2 Reactive Oxygen Species

Reactive oxygen species (ROS) also play an important role in erectile function as they expedite NO destruction, thereby contributing to decreased effectiveness of both initiation and maintenance of erections [7]. ROS, including superoxide, peroxide, and peroxynitrite, are byproducts of normal bodily functions and

can be heavily influenced by daily activities. Human bodies are protected from this biochemical process by antioxidants such as glutathione, which block the harmful effects of ROS. A study that demonstrates this association of vascular health and ROS assessed angiotensin receptor blockade and demonstrated the ability to reduce oxidative stress as a result of this blockade [8]. Those taking losartan had lower levels of 8-isoprostanes (a marker of oxidative stress) compared to those taking atenolol. While oxidative stress markers and the end point of flow-mediated dilation (FMD; a measurable variable suggestive of endothelial responsiveness to molecular triggers) of the brachial artery were affected, other contributing factors including hemoglobin A1c, c-reactive protein (CRP), and systolic blood pressure, remained unaffected suggesting that losartan's effect on ROS was significant enough to affect FMD and endothelial health. This mechanism and effect on dilation of systemic vasculature helps explain the improvement in erectile function noted in those taking losartan not seen with other antihypertensives. This study illustrates the important role of ROS in erectile function and suggests an underlying mechanism by which lifestyle changes can impact erections.

38.2.3 Cytokines

Cytokines such as tumor necrosis factor (TNF), interleukin 6 (IL-6), interleukin 8 (IL-8), and interleukin 18 (IL-18) are proinflammatory markers that affect serum NO throughout the body, including erectile tissue. Rats undergoing induction of periodontitis showed a decrease in NO expression in cavernosal tissue with concomitant increases in expression of TNF and CRP throughout the body [9]. Those with chronic systemic diseases, such as diabetes and/or obesity, have higher levels of these proinflammatory cytokines circulating throughout the body, which may help explain the higher rates of ED in these populations [10]. Presence of circulating proinflammatory markers also suggests a mechanism by which lifestyle changes addressing chronic diseases are effective in treating ED as suggested by endothelial dysfunction as a result of chronic low-level inflammatory states [11]. These chronic low-level inflammatory states refer to constant levels of mildly elevated inflammatory markers during which time the body has continued exposure. Proinflammatory markers are mildly increased in obesity and there is a direct relationship between acute phase (proinflammatory) markers and insulin resistance. As a result, acute phase markers may contribute to endothelial dysfunction in humans as described in the periodontitis study.

38.3 Lifestyle Changes

Proposed lifestyle modifications for those with ED closely resemble recommendations one might have to promote overall health and wellness.

38.3.1 Exercise

Coital and systemic exercise can improve erectile function. Exercise, in general, is considered to be the most significant single factor to improve erectile function as part of initial conservative management [12,13]. Coital exercise (i.e., getting and maintaining an erection) causes increased amount of blood to shunt to the penis and, when done repetitively, correlates with decreases in rates of ED by up to 50% in those 55–75 years old [12]. Increased blood flow to the penis, resulting in increased penile artery shear stress, has been shown to increase vascular NO levels with a suspected increase in FMD. Greater than one sexual episode per week was associated with reduced risk of developing ED. Systemic exercise (i.e., working multiple muscle groups throughout the body) also results in improved erectile function, thought secondary to increased systemic NO turnover that may lead to improvements in glucose disposal and insulin sensitivity [13]. Sedentary lifestyles have, conversely, been found to impair erectile function, though with moderate to high levels of exercise, improvement in erectile function may result. Forty minutes of moderate to high levels of aerobic exercise or 160 minutes of weekly exercise at the same moderate to high levels were effective in partially restoring erectile function for some patients. This association was demonstrated in 10 separate studies, all of which showed a statistically significant difference pre and post exercise initiation measuring erectile function using the International Index of Erectile Function (IIEF) questionnaire, a validated tool for evaluating erectile function [14]. Of note, extreme exercise, such as that performed by endurance athletes, increases muscular damage due to ROS, especially in those not accustomed to this level of exertion [15]. This is thought to be secondary to high oxidative damage from overwhelming typical physiologic barriers, namely glutathione, which is involved in many reduction-oxidation reactions throughout the body. This study, although not directly discussing erectile health, can act as a surrogate for suspected effects to erectile function with the superimposed variable of high ROS damage from extreme exercise.

38.3.2 Pelvic Floor Physical Therapy

Pelvic floor physical therapy (PFPT) may also improve erectile function mechanically, rather than chemically, by activating the ischiocavernosus and bulbocavernosus muscles that, when strengthened, can reduce venous outflow from the penis [16]. A randomized controlled study assessing pelvic floor exercises, in conjunction with lifestyle changes (subjects received counseling on weight loss, smoking cessation, reducing alcohol consumption, and avoiding bike saddle pressure) resulted in 40% of men returning to normal erectile function and another 35.5% of participants with improved erectile function as measured via the IIEF questionnaire. This study attempted to compare these lifestyle changes with PFPT plus lifestyle changes, but due to the overwhelming success of PFPT, all subjects were placed on PFPT. This study excluded men with known physical etiologies for ED such as those post prostatectomy or those with neurological conditions. Pelvic floor exercises included retraction of the penis and lifting the scrotum, gaining maximum contractions twice daily lying, sitting, or standing,

submaximal work while walking, and tightening the bulbocavernosus muscle after urination to help eliminate urine.

Association between ED and postmicturition dribble caused by pelvic floor weakness has also been reported [17]. A similarly designed randomized controlled trial with a crossover arm of the same group of men showed that 65.5% of the men had postmicturition dribble (PMD) and pelvic floor exercises significantly improved this PMD. Men with PMD, in addition to ED, appear to experience improvements in both with PFPT. Presence of concomitant PMD may also help identify those presenting with ED who may benefit from PFPT although definitive data are lacking.

38.3.3 Weight Management

Weight management can also improve erectile function. Those who are overweight experience more systemic inflammation, increased ROS from increased caloric consumption, and decreased insulin sensitivity [18]. Similar to the effects of inflammation and ROS previously discussed, insulin sensitivity also impacts levels of endothelial NO. Decreased insulin sensitivity, demonstrated by increased circulating insulin, leads to less circulating NO [19]. Fortunately, erectile function can improve with weight loss. One study showed that a third of obese men reversed their ED after two years of behavior modifications aimed at losing weight [20]. Behavior modifications included personalized dietary, exercise, and counseling sessions aimed at a 10% reduction in weight over two years. Erectile function was measured using the IIEF and other parameters measured included inflammatory markers and endothelial responsiveness to the vasoactive molecule L-arginine. Even those who only lost a minimal amount of weight but participated in these weight-conscious behavior modifications had improved erectile function, suggesting that the modifications alone were enough to produce results regardless of achieving objective weight loss. Decreases in CRP and IL-6 levels, markers of reduced systemic inflammation elevated in obesity, are thought be the source of the improvement in endothelial function leading to improved erections.

38.3.4 Nutrition

Fat and sugar intake can affect erectile function. A high fat meal transiently decreases FMD of the brachial artery likely due to ROS and inflammatory molecules [21]. Active adults did not experience decreases in FMD with the bolus of a high fat meal, while inactive adults experienced significant decreases in responses to these boluses, suggesting that activity level may be protective from these inflammatory- and ROS-rich states. Furthermore, isolated increases in blood sugar result in increases of inflammatory factors such as TNF alpha and IL-6. Diabetes is a significant risk factor for ED both due to the pathophysiology of increased blood sugar but also the comorbidities (obesity, insulin resistance, sedentary lifestyle) typically associated with diabetes, which are independent risk factors for ED. Diabetics experience increases in ROS in response to even transient hyperglycemia, which can affect erectile function by shortening the half-life of NO within the penile vasculature [22].

38.3.5 Drug Use

Tobacco and alcohol can worsen erectile function. Cigarette smoke leads to increased systemic oxidative stress. Endothelial NO synthase is also uncoupled by cigarette smoke and leads to the production of superoxide (a free radical form of O_2) that may lead to additional systemic oxidative damage [23]. Fortunately, smoking cessation in both the short and long term can decrease the impact ROS have on NOS function and thus erectile function [24]. Mild to moderate alcohol intake (1–2 drinks per night) increases NO, though excess alcohol leads to decreased vascular NO [25]. The vasodilatory effects of minimal to moderate alcohol use can improve erections transiently, though heavy alcohol intake is associated with exacerbation of ED, for which the mechanism is not clearly understood. Levels of toxic alcohol metabolites, as well as cognitive impairment associated with heavy alcohol consumption, would be suspected sources of ED in this population.

38.3.6 Antioxidants

Inflammation and free radical formation are the most important molecular factors in erectile function and, therefore, it is not surprising that antioxidants can help prevent damage from free ROS and improve erectile function [26]. Important antioxidants, such as Vitamins C and E, are present in many foods such as broccoli, cauliflower, red bell peppers, pomegranate, nuts, and strawberries, and are present in high quantities (1,000 mg/day of Vitamin C and 800 IU of Vitamin E) in many supplements used to mitigate the effects of ROS on the body. FMD is one endpoint in the objective measurement of the effect of lifestyle modifications on ED and has been used as a dependent variable in studies assessing vascular health. FMD was measured in smokers and nonsmokers before and after steady-state levels of antioxidant supplementation with Vitamins C and E [27]. High levels of antioxidant supplementation (measured by steady-state levels above 100 microM of ascorbate or microM/total lipid of alpha-tocopherol) in smokers mitigated the effects on NO and led to improved FMD in the brachial artery (nearly 300% increase in FMD before and after supplementation, respectively [$p<0.05$]) whereas in nonsmokers, vitamin supplementation had no significant effect. This improvement in FMD highlights the importance of mitigating the consequences of ROS, especially in smokers, who have an elevated amount of ROS damage.

38.3.7 Treatment of Sleep Apnea

Obstructive sleep apnea (OSA) is another chronic medical condition commonly seen in men presenting with ED and has been demonstrated to worsen erectile function. Frequent pauses in breathing have been shown to impair endothelial function, resulting in decreased circulating NO, increased oxidative stress, and increased inflammation [28]. Men with OSA

are more likely to have ED than the general population and this association holds true even when adjusting for other comorbidities. In two separate studies, ED was found in 51% and 48% of newly diagnosed OSA patients [29–31]. Continuous positive airway pressure (CPAP) therapy has been shown to improve erectile function (determined by IIEF questionnaire) along with gonadal function, orgasmic function, intercourse satisfaction, overall satisfaction, and overall sexual function when comparing outcomes before and after initiation of CPAP therapy in one study though a second study showed no significant difference. Therefore, limited research suggests possible improvement of ED with CPAP therapy for OSA.

38.3.8 Impact of Psychological Factors

One's emotional state also has implications on sexual function. One study using quality of life surveys found that emotional components led to a more profound impairment on erectile function compared to physical components [32]. The physical and emotional domains were assessed through a health-related quality of life (HRQOL) questionnaire with each domain scored separately from 0 to 100, with higher scores representing better HRQOL. A significant decrease in overall emotional well-being correlated with ED suggesting an association between the two, though causality cannot be determined. Early viewpoints portrayed erectile problems to be principally physiologic in nature and thus there has been a substantial predilection toward medicalization of ED. The introduction of oral PDE5 inhibitors such as sildenafil also reinforced the notion of ED being a medical condition [33]. Even when presumptive medical factors are present, psychological distress may also be a contributing factor [34]. The prevalence of significant psychiatric pathology (major depression, substance abuse, anxiety disorders, and schizophrenia), excluding interview stress, was present in 33% of men with ED although only 16 of 40 cases were recognized and highlighted in the initial assessments by treating urologists. This psychogenic component of ED is important for healthcare providers to recognize so that these factors may be addressed alone or in combination with other therapies for ED.

38.3.9 Limitations

Few studies objectively assess changes in erectile function with various lifestyle modifications. Much of what we know about lifestyle interventions on the vascular system comes from its effect on the cardiovascular system with little objective data showing effects on cavernosal blood flow. Future research is warranted to better assess the effect of lifestyle modification behaviors on objective measurements of erectile function.

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