Conclusion

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In this supplement, an eminent group of authors have described the epidemiologic relationships among erectile dysfunction (ED), cardiovascular disease (CVD), diabetes mellitus, and depression. The authors have provided practicing clinicians with a clear understanding of the pharmacology of the three phosphodiesterase type 5 (PDE-5) inhibitors in clinical use today: sildenafil, tadalafil, and vardenail. Going beyond pharmacokinetics, they also discussed the clinical efficacy and safety of PDE-5 inhibitors and suggested ways to optimize therapeutic response and patient adherence.

Erectile dysfunction and CVD are known to share etiologic and pathophysiologic features, and ED is recognized as an important sentinel symptom of occult CVD.[1-5] Clinicians who recognize ED as a CVD harbinger and take appropriate action have the potential to protect patients from the development or progression of CVD,[1] which accounts for nearly 40% of all deaths in the United States.[6] Erectile dysfunction may be an early sign of endothelial dysfunction, which precedes the development of overt CVD and manifests itself as blunted vasodilation and suboptimal penile rigidity.[2-5] It may result either from impaired production or release of the endothelial-derived vasorelaxant nitric oxide or from a cellular abnormality in the vascular endothelium.[7] The relationship between ED and CVD is so close that the Second Princeton Consensus Conference on Sexual Dysfunction and Cardiac Risk recommended that men with ED of uncertain etiology receive screening for vascular disease, including: glucose levels, lipid levels, and hypertension. In addition, it proposed that men with ED and no cardiac symptoms should be considered at risk for CVD until proven otherwise. [8]

Erectile dysfunction affects as many as 75% of all men who have diabetes.[9] In addition, recent research has shown that men who have ED are more than twice as likely to have diabetes as men without ED. The younger the man with ED, the stronger the relationship between the two conditions.[10] The implications of this two-way relationship between ED and diabetes have immediate clinical importance. First, physicians treating patients for diabetes have an opportunity to inquire about the possibility of ED and may spare the patient the difficulty of introducing a sensitive subject.[9] Further, physicians whose patients present with ED may have an opportunity to diagnose diabetes in its early stages and encourage patients to seek appropriate care, possibly preventing or slowing diabetes complications.[9,10]

The identification of close relationships among ED, CVD, and diabetes naturally raises the question of how lifestyle changes might affect the course of ED. Recent research indicates that familiar CVD risk factors, including smoking, hypertension, hyperlipidemia, and diabetes are also potent risk factors for ED. Endothelial dysfunction is the apparent common denominator shared by these risk factors. Studies conducted to date have demonstrated that weight loss and increases in physical activity levels may improve erectile function. The possibility of improved erectile function may be a powerful incentive for patients to make lifestyle changes that not only improve sexual health but also reduce cardiac risk. Patients also need to understand that smoking is a risk factor for ED and that cessation may also help restore erectile function. Control of other risk factors, including blood pressure, may also help, and future studies may shed more light on how the control of other CVD risk factors affects ED.

Compared to men who are not depressed, men with major depression are approximately twice as likely to have ED. Diminished libido and reduced sexual activity overall have been associated with depression, as well.[11] ED is associated with high incidence of depressive symptoms independent of age, marital status, or comorbid conditions. Depressed patients with ED have a

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lower libido than patients who do not exhibit depression and are less likely than others to continue a treatment for ED.[12] Further complicating the association between depression and ED is the documented relationship between ED and antidepressant medication. Tricyclic antidepressants and selective serotonin reuptake inhibitors (SSRI) are independently associated with ED.[13] The primary sexual side effect of SSRIs is impairment of ejaculation and orgasm. Sexual desire and erections are affected to a lesser extent. The mechanisms by which SSRI antidepressants might impair sexual function are unknown. An evolving area of ED research encompasses the possibility that successful treatment of ED may lead to improvements in depressive symptoms. Treatment with a PDE-5 inhibitor may help restore sexual function in a patient taking antidepressants, and restoration of sexual function may help alleviate depressed mood. Depression and low testosterone levels may cause similar symptoms, making it difficult to determine the correct diagnosis. The two conditions may also coexist in the same patient, and preliminary evidence suggests that testosterone treatment may help alleviate symptoms of depression in patients with low testosterone levels.

NO TREATMENT HAS BEEN MORE SUCCESSFUL THAN PDE-5 INHIBITORS.

Clinicians have a variety of drugs, delivery methods, and combination therapies to help patients achieve and maintain satisfying erections, regardless of comorbid health conditions that may be present. No treatment has been more successful than the PDE-5 inhibitors.[14] These agents have been evaluated in numerous placebo-controlled, double-blind trials and open-label studies using a variety of outcome measures, patient subgroups, and regional populations. Although differences in trial designs and outcome measures make it impossible to compare the three drugs in a parallel manner, most studies suggest that the PDE-5 inhibitors have similar efficacy and toxicity profiles.[14] Phosphodiesterase type 5 inhibitors are now considered first-line treatment for most men with ED. Sildenafil, tadalafil, and vardenafil are efficacious, safe, and easy to use in various patient populations and ED etiologies. When initial PDE-5 treatment does not achieve the desired result, patient re-education, lifestyle modification, dose adjustment, switching PDE-5 inhibitors, improvement in cardiovascular risk factors, sexual or relationship counseling, and/or androgen replacement for hypogonadism can help boost response rates to the PDE-5 inhibitor. Treatment is generally well tolerated and patient drop out due to adverse events is low. Understanding the shared pathophysiology between ED and CVD, understanding the pharmacology of PDE-5 inhibitors and knowing how to counsel the male patient are the keys to successful treatment of ED.

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