Do phosphodiesterase-5 inhibitors have a cardioprotective effect?

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Erectile dysfunction (ED) affects 18 million men in the United States alone[1]. Its prevalence is 52% among men aged from 40 to 70 years and 70% among those older than 70[2]. This condition may be related to changes in penile blood flow since the etiology is vascular in 60% of patients[1].

Cardiovascular disease (CVD) and ED share the same risk factors, such as age, smoking, hypertension, obesity, diabetes mellitus, sedentary lifestyle, depression, and metabolic syndrome[1,3]. Such factors lead to endothelial dysfunction, the formation of atherosclerotic plaque, and the inflammation of small blood vessels and are, therefore, related to both cardiovascular events and ED. The evaluation of the temporal relation between ED and subclinical CVD may encourage a change in risk behaviors and prevent the occurrence of CVD[4]. Studies have demonstrated that patients with ED have an increased risk for cardiovascular events and mortality and that ED may be a symptom or even an independent predictor of coronary artery disease (CAD)[1,2].

Arterial hypertension is related to the development of atherosclerosis and is one of the risk factors for the development of CAD and ED but is also a protective factor against ED in patients with CAD, as it improves penile function[1]. In ED, the increase in vascular pressure initially improves penile flow and perfusion but is harmful in the long term since it implies an increase in atherosclerosis and arterial occlusion[1]. In urology, the pharmacological treatment of ED is based on the use of vasodilators, especially the class of phosphodiesterase-5 (PDE-5) inhibitors, which improve blood flow and sexual performance (sildenafil, vardenafil, tadalafil, and avanafil)[5].

PDE-5 inhibitors diminish the catabolism of cyclic guanosine monophosphate (cGMP) through the inhibition of the enzyme PDE-5, which results in the relaxation of smooth muscles and consequent vasodilation, besides offering a cardioprotective effect related to the action of nitric oxide[5]. The discovery that PDE-5 is also expressed in the myocardium led to a change in views regarding the direct effect of these inhibitors

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on this tissue[6]. The expression of PDE-5 suggests that inhibitors of this enzyme exert beneficial effects on the heart through changes in regional and systemic hemodynamics related to anti-apoptotic and anti-inflammatory properties as well as reductions in hypertrophy, ventricular arrhythmia, myocardial fibrosis, and oxidative stress[5].

There is evidence of the effectiveness of PDE-5 inhibitors in heart failure with reduced ejection fraction. Such evidence is sustained by the effects on pulmonary vasodilation, cardiac remodeling, improved diastolic function, reductions in fibrosis and interstitial inflammation, and an improvement in coronary microcirculation[6]. Regarding myocardial infarction, the use of PDE-5 inhibitors seems to increase the tolerance threshold for ischemia/angina and is related to a lower mortality rate after the event[6]. For pulmonary hypertension, treatment with PDE-5 inhibitors is effective due to vasodilation, a reduction in cell proliferation, and the stimulation of apoptosis, which have the potential to reduce pulmonary pressure[7].

In a retrospective study conducted in Denmark, patients in treatment with PDE-5 inhibitors for ED with no history of cardiovascular disease had a lower risk of acute myocardial infarction in comparison to the general male population[3]. Moreover, the risk of heart failure and all cardiovascular diseases diminished in the first three years after the start of treatment for ED[3]. This effect may be explained by the pharmacological action of PDE-5 inhibitors through the reduction of systolic blood pressure after the beginning of treatment, the long-term cardioprotective effect, or factors associated with behavioral changes in patients[3].

Since the recognition of this vasodilating effect, the interest in employing PDE-5 inhibitors for the treatment of CVD has increased and these drugs are currently used in patients with ischemic heart disease, congestive heart failure, pulmonary hypertension, Raynaud's phenomenon, peripheral vascular disease, and cerebral hypoperfusion[7]. Further prospective, randomized, clinical investigations are needed to explore the therapeutic potential of PDE-5 inhibitors as well as determine the effectiveness and safety of these drugs with regards to the cardioprotective effect.

Conflicts of Interest

The authors have no conflicts of interest to declare.

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