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Efficacy of Continuous Dosing of Tadalafil Once Daily vs Tadalafil On Demand in Clinical Subgroups of Men With Erectile Dysfunction: A Descriptive Comparison Using the Integrated Tadalafil Databases

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ABSTRACT

Introduction: Various factors play a role in the development of erectile dysfunction (ED).

Aim: To provide a descriptive comparison of erectile function response for tadalafil on-demand (PRN) and once-daily (OAD) dosing regimens in patients with common comorbid conditions, treatments, or risk factors that can be considered when treating ED.

Methods: In total, 17 PRN and 4 OAD placebo-controlled studies were included in the integrated database in these pooled analyses. Data were analyzed from patients treated with placebo, tadalafil 10 mg (low dose), and 20 mg (high dose) for the PRN studies and placebo, tadalafil 2.5 mg (low dose), and 5 mg (high dose) for the OAD studies.

Main Outcome Measures: The effects of tadalafil were measured using the International Index of Erectile Function administered from baseline to week 12. A descriptive comparison of the efficacy of tadalafil PRN vs OAD was examined in the clinical populations.

Results: Baseline characteristics of 4,354 men were comparable between the PRN and OAD groups, with differences seen only in the variables of race, body mass index (BMI) of at least 30 kg/m^2, and alcohol use. Tadalafil was efficacious at improving erectile function for all clinical populations, except for the low-dose OAD group, which demonstrated a weaker effect vs placebo than the high-dose OAD group, and the low- and high-dose PRN groups vs placebo for patients with BMI of at least 30 kg/m^2 for patients without a cardiovascular disorder, smokers, patients with ED duration shorter than 1 year, and patients without previous phosphodiesterase type 5 inhibitor use. Tadalafil was efficacious for patients with or without diabetes mellitus, arterial hypertension, hyperlipidemia, and alcohol use at baseline.

Conclusion: Tadalafil OAD and PRN regimens showed efficacy in patients with ED. No clinical populations of patients with ED seemed to benefit overwhelmingly from one dose regimen over the other.

Key Words: Erectile Dysfunction; Phosphodiesterase Type 5 Inhibitors; Tadalafil; Data Pooling; Treatment Efficacy

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INTRODUCTION

Numerous factors such as age, weight, diabetes mellitus, cardiovascular disorders, smoking, arterial hypertension, and alcohol use can play a role in the development of erectile dysfunction (ED).[1–6] Owing to the various physical and psychosocial aspects of ED,[7] treatment of ED extends beyond improving erectile function (EF) response and satisfaction.[8–11]

Phosphodiesterase type 5 (PDE5) inhibitors represent the first-line drug treatment for ED.[12,13] The PDE5 inhibitor tadalafil, with on-demand (PRN)[14–17] and once-daily (OAD)[18–22] dosing regimens, has demonstrated efficacy and safety in the treatment of ED. Psychosocial outcomes, spontaneity, and time concerns have shown significant improvement

after treatment with long-acting compared with short-acting PDE5 inhibitors.[23,24] Treatment with tadalafil OAD has improved EF in patients with mild and mild to moderate impairments in EF after PRN PDE5 inhibitor therapy.[21,25] Other studies have shown that the OAD dosing regimen leads to high treatment satisfaction for the patient and his partner[19,25–27] and allows patients to have spontaneous sexual activity, thereby changing the requirement for dosing and sexual activity to be linked. An OAD dosing regimen also improves the patient's ability to achieve and maintain erections and improves treatment satisfaction and psychosocial outcomes.[28] In addition, early initiation of the tadalafil OAD regimen protects against penile length loss after nerve-sparing radical prostatectomy.[29]

Few clinical trials have compared the OAD and PRN regimens in the same study directly. Some researchers have reported the tadalafil OAD regimen is more efficacious in treating ED compared with the PRN dosing regimen,[30,31] whereas others have reported no significant differences between tadalafil OAD and PRN dosing regimens in improving erection and sexual satisfaction of patients with ED.[32] In 2014, Porst et al[33] reported on an integrated analysis of data from six placebo-controlled studies (OAD 2.5 or 5 mg) in patients with different ED characteristics and comorbidities and determined that treatment with the tadalafil OAD regimen resulted in clinically important improvements in patients with mild, moderate, or severe ED. In that study, there was an improvement in International Index of Erectile Function erectile function domain (IIEF-EF) scores in patients with arterial hypertension, cardiac disorder, or hyperlipidemia after treatment with tadalafil 2.5 or 5 mg; however, patients who were obese, smokers, and those with psychogenic ED reached a minimal clinically important difference (MCID; defined as mean improvement in IIEF-EF scores of at least four points[34]) only after treatment with tadalafil 5 mg. Lewis et al[35] evaluated the efficacy of tadalafil in men with ED by demographic and ED characteristics and determined that the tadalafil PRN dosing regimen improved EF across a broad range of patients with ED, including patients with different comorbid conditions.

To our knowledge, there are no published integrated analyses that have looked at the efficacy of tadalafil PRN and OAD dosing regimens in the same context. Clinicians often seek prescribing information and guidance on the two regimens to provide the patient with information to assist in making appropriate treatment decisions.

AIM

In this article, we provide a descriptive comparison of EF and orgasmic function (OF) response to tadalafil PRN and OAD dosing regimens using the integrated tadalafil clinical trial databases. The purpose of this report is to offer this descriptive comparison of pooled data from tadalafil ED studies in patients with common comorbid conditions, treatments, or risk factors that might be considered when treating ED.

METHODS

Studies

In total, 17 PRN[14–17,36] and 4 OAD[19–21,37] placebo-controlled studies in men with ED were included in the integrated (March 2013) database that was used in these pooled analyses. Tadalafil studies in men with lower urinary tract symptoms associated with benign prostatic hyperplasia were excluded from these analyses owing to differences in the study population. Details about the general study design for these studies have been published.[14–17,19–21,36,37] For the 17 PRN studies that had identical study designs, data were analyzed from patients treated with placebo, tadalafil 10 mg (low dose), and tadalafil 20 mg (high dose). For the OAD studies, data were analyzed from patients treated with placebo, tadalafil 2.5 mg (low dose), and tadalafil 5 mg (high dose). The 5-mg PRN dose was not included in the analyses for this report because it is not a globally approved dose by regulatory authorities for the treatment of ED; therefore, for this report, the 10-mg PRN dose is considered low-dose PRN. Two studies were OAD registration studies that included men with ED,[19,20] and one study determined the impact of OAD treatment for men with ED on the sexual quality of life of their female partners.[21] One study evaluated OAD treatment in PDE5 inhibitor-naive men with ED.[37]

Patient Population

Patients were men (≥18 years old) with at least a 3-month history of ED who remained sexually active with the same heterosexual partner. Some exclusion criteria included a history of certain cardiovascular diseases (eg, unstable angina, recent myocardial infarction, recent myocardial revascularization, and poorly controlled blood pressure), a history of radical prostatectomy with subsequent failure to achieve erections, and patients who had penile implants or deformities, clinically significant renal or hepatic insufficiency, and current treatment with nitrates, cancer chemotherapy, or antiandrogens. The details about the inclusion and exclusion criteria for some of these studies have been published.[14–17,19–21,36,37]

Clinical Populations

Using the IIEF-EF and IIEF-OF outcomes, we completed analyses according to the following subgroups (referred to as clinical populations): age (<50, 50–64, or ≥65 years), baseline BMI (<30 vs ≥30 kg/m^2), diabetes mellitus at baseline (yes vs no), baseline cardiovascular disorder (yes vs no), baseline hypertension (yes vs no), baseline hyperlipidemia (yes vs no), smoking or current use of tobacco (yes vs no), current use of alcohol (yes vs no), previous PDE5 inhibitor use (yes vs no), number of antihypertensive medications (none, one, or more than one), and ED duration (<1 vs ≥1 year). Some cardiovascular disorders included cardiomyopathy, myocardial infarction, angina, arrhythmia, tachycardia, atrioventricular block, cardiac failure, congenital cardiac conditions, pulmonary hypertension,