Brief Report

Erectile Response to Vardenafil in Men with a History of Nonresponse to Sildenafil: A Time-From-Dosing Descriptive Analysis

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ABSTRACT

Background: The efficacy and tolerability of vardenafil hydrochloride in men with erectile dysfunction (ED) and a history of nonresponse to sildenafil citrate have previously been reported.

Objective: The aim of this descriptive analysis was to assess the efficacy and tolerability of vardenafil at various times after dosing in men with ED and a history of nonresponse to sildenafil and who chose to attempt sexual intercourse between 0.25 and 6 hours after dosing with vardenafil.

Methods: This analysis used data from a previously published 12-week, prospective, randomized, double-blind, flexible-dose, placebo-controlled study conducted at 41 hospitals and outpatient clinics across Australia, Europe, Asia, and North America. In that study, men with ED and sildenafil nonresponse, defined using 6 rigorous criteria (including nonresponse to the highest recommended dose, 100 mg/d) were assigned to receive vardenafil 10 mg or placebo QD. At study weeks 4 and 8, patients in both groups were given the option to maintain the 10-mg/d dose, or have the dose titrated to 5 or 20 mg/d. The present analysis used data from patient diaries completed daily, which included information concerning attempts at sexual intercourse, time from dosing to attempt, penetration, and maintenance of erection sufficient for successful intercourse. At week 12, diary data were categorized into time intervals (in hours) after dosing. For each interval, the per-patient success rate was based on the total number of attempts made in that interval. Comparative statistics were not performed on the time-interval analysis. Tolerability was monitored throughout the study. Data concerning the primary end point were reported previously.

Results: A total of 463 men were enrolled, of whom 457 were included in the safety analysis (vardenafil, n = 231; placebo, n = 226) and 454 in the intent-to-treat analysis (vardenafil, n = 229; placebo, n = 225; mean age, 60.1 vs 59.0 years; mean body mass index, 28.7 vs 28.0 kg/m^2). Six patients were excluded

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from the safety analysis (2 patients did not use study medication [placebo group], postbaseline safety data unavailable in 4 patients [2 in each study group]). Men receiving vardenafil had numerically greater penetration and completion success rates compared with those receiving placebo at all time intervals. Penetration success rates were numerically higher with vardenafil compared with placebo as early as within 0.25 hour after dosing (62% vs 30%); efficacy continued beyond 6 hours after dosing in 77% and 50% of patients, respectively. Similarly, vardenafil-treated patients had numerically greater completion success rates compared with those receiving placebo at 0.25 hour (53% vs 12%) and beyond 6 hours after dosing (70% vs 24%). The most common drug-related adverse events in the vardenafil and placebo groups were flushing (7% vs 1%), headache (6% vs 2%), and nasal congestion (5% vs <1%).

Conclusions: This descriptive analysis suggests that erection sufficient for penetration and intercourse completion was achieved within 0.25 hour and lasted for >6 hours after dosing with vardenafil 10 mg in these men with mostly moderate to severe ED and a history of nonresponse to sildenafil and who chose to make attempts during those intervals. The drug was generally well tolerated. (*Clin Ther.* 2005;27:1452–1461)

Key words: erectile dysfunction, impotence, oral therapy, phosphodiesterase type 5 inhibitor, vardenafil, clinical trial.

INTRODUCTION

Erectile dysfunction (ED) can increase marital tension, reduce self-esteem, and diminish quality of life for men and their partners.[1–5] An important aspect of sexual satisfaction is spontaneity in initiating sexual activity. Oral ED therapy with phosphodiesterase type 5 (PDE-5) inhibitors, therefore, offers a great advantage over earlier treatments for ED (eg, vacuum constriction devices, intracavernosal injection therapy) by providing couples with more flexibility in the timing of treatment and initiation of sexual activity. Two such PDE-5 inhibitors, sildenafil citrate and vardenafil hydrochloride, have been shown to be effective in clinical trials in a broad population of men, including those with ED that is traditionally considered challenging to treat (eg, in men with diabetes mellitus).[6–12] Although the efficacies of these 2 PDE-5 inhibitors have not been directly compared to date (MEDLINE search; key terms: *vardenafil, sildenafil, erectile dysfunction,* and *clinical trial*; years: 1998–2005), vardenafil has been shown to be effective and generally well tolerated in men with a history of nonresponse to sildenafil.[13]

The prescribing information for vardenafil[14] recommends that 1 tablet (all doses) be used ~1 hour before sexual intercourse, based on the timing used in clinical trials. However, couples might desire more convenience regarding their sexual activity. Thus, it is important to understand the time course of the efficacy of any ED treatment.

The purpose of this prospective, descriptive analysis of data from a previously reported study[13] was to determine whether the efficacy and tolerability of vardenafil could be demonstrated across various time intervals in men with a history of nonresponse to sildenafil and who attempted sexual intercourse 0.25 to 6 hours after dosing with vardenafil.

MATERIALS AND METHODS

This analysis used data from a previously published 12-week, prospective, randomized, double-blind, flexible-dose, placebo-controlled study by Carson et al,[13] conducted at 41 hospitals and outpatient clinics across Australia, Europe, Asia, and North America. The study protocol was approved by the institutional review board or independent ethics committee at each participating center, and all patients provided written informed consent to participate. The study was conducted in accordance with regulatory standards of Good Clinical Practice[15] and the Declaration of Helsinki and its amendments.[16]

Men aged ≥18 years with ED, as defined by the National Institutes of Health Consensus Statement,[17] and who had been in a heterosexual relationship for >6 months were eligible for recruitment. In addition, all patients must have had a history of nonresponse to sildenafil by fulfilling each of 6 criteria (**Table I**).[13]

Patients were excluded for any of the following reasons: anatomic penile abnormality; primary hypoactive sexual desire; ED after spinal cord injury; history of radical prostatectomy; total serum testosterone level >10% less than the lower limit of normal; unstable angina pectoris, history of myocardial infarction or stroke; electrocardiographic ischemia (except stable angina) or life-threatening arrhythmia within 6 months before enrollment; any medical, psychiatric, or substance-abuse