Prospective, Randomized, Open-Label, Fixed-Dose, Crossover Study to Establish Preference of Patients with Erectile Dysfunction after Taking the Three PDE-5 Inhibitors

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DOI: 10.1111/j.1743-6109.2006.00297.x

ABSTRACT

Introduction. We conducted a prospective, randomized, open-label, fixed-dose preference study, with a crossover design, using sildenafil, vardenafil, and tadalafil.

Aim. To assess patient preference for sildenafil (100 mg), vardenafil (20 mg), and tadalafil (20 mg) for the treatment of erectile dysfunction. Secondary objectives included finding out whether patients would follow treatment with a second or third option, in the event that the preferred drug was not available, and to assess side effects.

Main Outcome Measures. Patient preference for any treatment, and evaluation of the elements that patients would assess when choosing one of these drugs.

Material and Methods. Sildenafil (100 mg), vardenafil (20 mg), and tadalafil (20 mg) were taken at least six times over a period of 45–60 days with a washout period of 7 days. A total of 132 patients were enrolled to achieve a valid sample of 90 cases (15 per randomized group, total of six groups). Enrolled patients had mild to moderate erectile function.

Results. The International Index of Erectile Function (IIEF) score improved from baseline and was statistically significant in all cases ($P < 0.0001$). When we compared the IIEF scores, we found a statistically significant difference between tadalafil and vardenafil ($P = 0.0002$) favoring the former; similar results were obtained with the Erectile Dysfunction Inventory for Treatment Satisfaction (EDITS) Questionnaire ($P = 0.000075$). We also found a significant difference ($P = 0.012$) between tadalafil and sildenafil, again in favor of the former. In assessing drug preference, 25 patients (27.77%) chose sildenafil, 18 (20%) vardenafil, and 47 (52.22%) tadalafil. A total of 94% of patients would be willing to take another drug if the preferred choice was not available. All drugs were well tolerated.

Conclusions. Although this is a preference study based on subjective elements, statistically significant differences comparing the IIEF score and the EDITS Questionnaire lead us to believe that beyond patients' subjective preference *per se*, said preference is probably also based on a genuinely superior response to one drug over another.

Tolrà JR, Campaña JMC, Ciutat LF, and Miranda EF. Prospective, randomized, open-label, fixed-dose, crossover study to establish preference of patients with erectile dysfunction after taking the three PDE-5 inhibitors. J Sex Med 2006;3:901–909.

Key Words. Erectile Dysfunction; Sildenafil; Vardenafil; Tadalafil; Phosphodiesterase-5 Inhibitors; Patient Preference; Randomized Study

Introduction

Erectile dysfunction affects some 152 million men worldwide [1]. It is a disorder that impairs their self-esteem, marital relations, and compromises the quality of life of both patients and their partners [2–6].

Joint decision making between patients and physicians is becoming more and more common; hence, the assessment of patient preference is of growing relevance [7].

Studies addressing preference between oral drugs (sildenafil) and other treatment modalities have been carried out [8,9], and studies that deal

with preference between two phosphodiesterase (PDE)-5 inhibitors (sildenafil and tadalafil) have begun to appear [10–12]. But there are few reports comparing these three PDE-5 inhibitors.

Numerous studies back up the efficacy and tolerance of the three PDE-5 inhibitors in the treatment of erectile dysfunction [13–20]; but, these are only two of the factors that are involved in a person's decision to continue using a given treatment. There are other issues, such as the couple's relationship, privacy, and quality of life [21–24], that can tip the balance to one side or the other when deciding.

Moreover, in the treatment of disorders for which there may be more than one drug of the same treatment group (as is the case with PDE-5 inhibitors), patient preference can be a very important criterion that physicians should take into account, particularly in the case of erectile dysfunction, in which response depends heavily on subjective factors.

Consequently, the main objective of the present independent and unsponsorized study was to evaluate efficacy and patient preference throughout treatment periods of 6–8 weeks with sildenafil 100 mg, vardenafil 20 mg, and tadalafil 20 mg, taken as per their respective instructions for administration. Secondary objectives consisted of determining patient tolerance to the drugs and finding out whether the patients would continue treatment with another drug other than the one they had chosen, in the event that it was unavailable.

Materials and Methods

Study Design

We used a prospective, open-label, randomized, fixed-dose trial with a crossover design in order to establish the degree of preference in patients with erectile dysfunction after taking the three PDE-5 inhibitors, administered sequentially, and using the patients as their own controls.

The doses at start-up were the following: 100 mg of sildenafil and vardenafil, and 20 mg of tadalafil. Patients had to try each drug a minimum of six times, and medication was not provided by investigators, reflecting usual standard of care.

The instructions given to patients were the specific instructions of use for each treatment each time the medication was prescribed.

Each drug had to be taken a minimum of six times over a period of 45–60 days; furthermore, a drug washout time was established, during which participants would remain without treatment for 1 week in order to avoid the residual effect when switching medication. This study was conducted June 2003 through September 2005.

Patients

Patients were enrolled in the study if they met all inclusion and none of the exclusion criteria, based on the following: men aged 18 years or older, with heterosexual relations, erectile dysfunction of more than 6-month evolution, and presenting figures indicative of moderate to mild dysfunction according to the International Index of Erectile Function (IIEF) administered at the evaluation visit.

All patients were naïve to treatments and had not previously taken any PDE-5 inhibitor. Patients undergoing treatment with nitrites, who had a recent history of myocardial infarction (less than 6 months previous) or unstable angina were not candidates for enrollment in the study. Patients with resting hypertension of systolic pressure (SP) > 170 or diastolic pressure (DP) > 110, or resting hypotension of SP < 90 were also excluded from participation in the study, as were men with retinitis pigmentosa or a history of hepatitis B or C. Finally, patients taking androgens, cytochrome P-450-3 A4 inhibitors, or alpha blockers also were excluded.

Patients gave verbal informed consent before participating in the study. Because this is an open-label study with three commercialized drugs, written informed consent was considered unnecessary. Patients received usual standard of care drug instructions and were asked whether they would like to participate in this trial to evaluate the three drugs.

Randomization and Sample Size

The same number of patients was randomized to each treatment arm until the entire sample was completed.

Six treatment groups were set up with the following sequences:

Group 1: sildenafil 100, vardenafil 20, and tadalafil 20 mg;
Group 2: sildenafil 100, tadalafil 20, and vardenafil 20 mg;
Group 3: vardenafil 20, sildenafil 100, and tadalafil 20 mg;
Group 4: vardenafil 20, tadalafil 20, and sildenafil 100 mg;