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Effectiveness and treatment satisfaction of patients with erectile dysfunction in Spain: EDOS study

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ABSTRACT

Introduction: Erectile dysfunction (ED) is a worldwide health problem with an ever increasing prevalence, affecting the quality of life of many patients.
Objective: The aim of this study was to describe treatment effectiveness and patient satisfaction with ED treatment in the Spanish cohort of the EDOS study.
Material and methods: This observational, pan-European study assessed treatment effectiveness and patient satisfaction with ED treatment under routine clinical settings, using standard questionnaires. Men ≥18 years about to initiate or change ED treatment were enrolled. Patients were assessed at baseline, 3 and 6 months.
Results: A total of 1,029 patients were analyzed (12.8% of the total European sample). In general, the Spanish population characteristics are consistent with the overall population. At baseline 56.6% of patients received tadalafil, 16.6% sildenafil, 19.6% vardenafil, and 7.2% received other treatments. At 3 months, a higher proportion of patients on tadalafil reported improved erections (GAQ 1: 96.5% tadalafil, 85.7% sildenafil and 87.2% vardenafil), satisfaction with treatment (EDITS: 84.2% tadalafil, 75.0% sildenafil and 76.0% vardenafil), and sexual self confidence (SF-PAIRS: 2.73 tadalafil, 2.39 sildenafil and 2.55 vardenafil), in comparison with sildenafil and vardenafil. At 6 months, differences between treatments were not significant. The mean±SD time elapsed from drug intake to sexual intercourse was higher for patients on tadalafil (18.6±26.4 h) compared to sildenafil (3.6±7.5) and vardenafil (8.6±19.4).
Conclusions: The longer duration of action for tadalafil, and thus, the longer period of time between dosing and sexual intercourse may contribute to enhance sexual spontaneity, patient satisfaction with the treatment and greater self-confidence.

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Efectividad y satisfacción con el tratamiento en pacientes con disfunción eréctil en España: Estudio EDOS

Palabras clave:
Disfunción eréctil
Efectividad
Satisfacción
Sildenafilo
Tadalafilo
Vardenafilo

RESUMEN

Introducción: La disfunción eréctil (DE) es un problema de salud mundial con una prevalencia creciente que afecta la calidad de vida de muchos pacientes.
Objetivo: Analizar la efectividad y satisfacción con el tratamiento en la cohorte española de pacientes con DE incluidos en el estudio observacional de disfunción eréctil.
Material y método: Estudio observacional, paneuropeo, que analizó la efectividad y satisfacción de los tratamientos para la DE en la práctica clínica habitual, utilizando cuestionarios estándares. Participaron varones ≥18 años que iniciaron o cambiaron su tratamiento para la DE. Los pacientes fueron evaluados en la visita basal, a los 3 y 6 meses.
Resultados: Se analizaron 1.029 pacientes (12,8% de la muestra europea total). En general, las características de la población española son consistentes con las de la población global. En la visita basal 56,6% recibió tadalafilo, 16,6% sildenafilo, 19,6% vardenafilo y 7,2% otros tratamientos. A los 3 meses, una mayor proporción de pacientes con tadalafilo experimentó mejorías en la erección (cuestionario de evaluación global 1: 96,5% tadalafilo, 85,7% sildenafilo, 87,2% vardenafilo), se observó una mayor satisfacción con el tratamiento (inventario de satisfacción con el tratamiento para la DE: 84,2% tadalafilo, 75,0% sildenafilo y 76,0% vardenafilo) y mayor autoconfianza (escalas psicológicas y de relaciones interpersonales: 2,73 tadalafilo, 2,39 sildenafilo y 2,55 vardenafilo). A los 6 meses, las diferencias entre tratamientos no resultaron significativas. El tiempo medio±desviación estándar entre la toma del fármaco y la relación sexual fue mayor en los pacientes con tadalafilo (18,6±26,4 h) vs. sildenafilo (3,6±7,5) y vardenafilo (8,6±19,4).
Conclusiones: La mayor duración del efecto de tadalafilo y en consecuencia el mayor tiempo medio entre la toma y la relación sexual podría contribuir a aumentar la espontaneidad en las relaciones sexuales, la satisfacción con el tratamiento y mayor autoconfianza.

Introduction

Erectile dysfunction (ED) is defined as the inability to achieve or maintain an erection sufficient for satisfactory sexual intercourse[1]. ED affects the quality of life of many men and their partners.

In Spain, the prevalence of ED has been estimated to range between 12.1 and 18.9% in men of 25–70 year of age, depending on the definition of ED[2]. Risk factors for ED include age, diabetes mellitus, hyperlipidemia, cardiovascular disease, and hypertension, and lifestyle factors: smoking, a sedentary life, and stress[3-7].

Phosphodiesterase type 5 (PDE5) inhibitors sildenafil, vardenafil, and tadalafil are considered the first-choice treatment for most patients with ED. However, only about 10% of men who experience erection problems actively seek treatment[8]. It is important to assess the efficacy of the available treatments for ED and the degree of satisfaction with them in order to understand the reasons for treatment discontinuation[9-13].

The Erectile Dysfunction Observational Study (EDOS) is a pan-European study designed to describe treatment efficacy and patient satisfaction with the ED treatments used in standard clinical practice, and to describe ED treatment changes and the variables associated with these changes. The overall European results have been published already[14-16].

In this article we present the data from the Spanish population participating in EDOS. Our specific objectives: 1) describe the sociodemographic and clinical characteristics of the study subjects; 2) assess the efficacy of tadalafil, sildenafil, and vardenafil for the treatment of ED; 3) analyze the patients' treatment satisfaction during the 6 months of the study, and 4) assess psychological and behavioral issues associated with sexual functioning in ED patients.

Material and methods

Study design and patients

EDOS is a 6-month prospective, non-interventional, observational, longitudinal study conducted in nine European countries. Recruitment took place between April 2003 and April 2004[15]. In Spain, 64 centers from 11

Autonomous Communities (Andalucía, Navarra, Galicia, Castilla-León, Asturias, Valencia, Cantabria, Canarias, La Rioja, Murcia, and País Vasco) participated. The study included men aged 18 years and older initiating or changing ED treatment. The study was conducted in accordance with the recommendations of Declaration of Helsinki. Patients gave their written consent to participate in the study.

Data were collected following standard clinical procedures at the time of enrollment (when the ED treatment was assigned), and at 3 and 6 months. At the baseline visit, sociodemographic and clinical data were collected, and the severity of the ED was assessed with the erectile function (EF) domain of the International Index of Erectile Function (IIEF) (severe [1–10], moderate [11–16], mild [17–25], and no ED [≥26])[17].

Treatment efficacy

ED treatment efficacy was assessed with the Global Assessment Questions (GAQ) and quantifying the number of patients who answered "Yes" to the question: "Has the treatment you have been receiving over the past 4 weeks improved your erections?" (GAQ1). If the answer was yes, the patient was asked: "Has the treatment improved your ability to engage in sexual activity?" (GAQ2).

Additionally, therapeutic efficacy was assessed by quantifying the amount of time between drug intake and sexual intercourse. This interval should not be considered a measure of the duration of efficacy, since it only represents the maximum time from drug intake to sexual activity. Patients answered the following question: "¿Over the past month, for approximately how long was the ED drug effective, from the time you took it to sexual intercourse?"

Treatment satisfaction

Patient satisfaction was assessed with Question 1 of the Erectile Dysfunction Inventory of Treatment Satisfaction (EDITS)[18]: "In general, during the past 4 weeks ¿how satisfied are you with your ED treatment?" The percentages were noted of patients who answered "Very satisfied" or "Somewhat satisfied" (in a scale with categories Very satisfied, Somewhat satisfied, Neither satisfied nor unsatisfied, Somewhat unsatisfied, Very unsatisfied).

Psychological and behavioral aspects of sexual functioning

The Short Form of the Psychological and Interpersonal Relationship Scales (SF-PAIRS)[19] that assesses the psychological component and the behavior of ED patients was used. SF-PAIRS consists of 15 items within the following conceptual domains: concern about the time between drug intake and the sexual encounter, spontaneity, and self-confidence. Each question is scored on a scale from 1–4, where 1: completely disagree, and 4: completely agree. A low score in the time concern domain indicates less concern about the interval between the drug intake and the sexual encounter. A high score in the spontaneity and self-confidence domain indicates more spontaneity and sexual confidence.

Statistical analysis

This article analyzes only data from patients who stayed on the same treatment until the end of the study. Continuous distribution variables are summarized as mean and standard deviation, median, and confidence interval; discrete variables are shown as tables of frequencies.

Multivariate models were used for efficacy and satisfaction analyses, after adjusting for baseline differences between cohorts. An ANCOVA test for continuous variables, and a logistic regression model for binary variables were used. Initial analyses using linear regression for each dependent variable were done with the purpose of identifying significant predictive variables. These models include all the variables collected at the baseline visit, except for treatment in the case of binary dependent variable. Variables were selected using the stepwise method.

Table 1 – Sociodemographic characteristics of the Spanish population in EDOS at the baseline visit (n=1029)

Characteristics	% patients
Age (years, mean [range], n=1023)	55.9 (21–83)
Marital status (n=1029)	
Single	7.1
Married/cohabitating	83.3
Divorced	6.3
Widower	3.3
Currently in a relationship (% yes, n=1014)	94.3
Employment status (n=1026)	
Disabled	2.5
Unemployed	2.0
Retired	34.7
Employed part-time	6.3
Employed full-time	52.3
Other	2.0
Educational level (n=1025)	
No formal education	6.3
Completed elementary school	30.2
Completed high school	29.4
Professional training	9.3
University/post-graduate	23.9
Unknown	0.9
Smoking (n=1025)	
Non-smoker	23.3
Current smoker	33.1
Ex-smoker	43.6
Alcohol consumption (units/week, n=1026)	
0	23.1
1–7	50.8
8–14	19.1
15–21	5.6
≥22	1.5

Results

The EDOS study in Spain included a total of 1040 patients, of whom 1029 met the selection criteria and were analyzed. The Spanish population represented 12.8% of the total European sample[15].

Of the total Spanish population, 69.6% of patients initiated a new treatment, and 30.4% changed it. At the baseline visit, 56.6% of patients received tadalafil, 16.6% sildenafil, 19.6% vardenafil, and 7.2% other treatments.

In the IIEF-EF scale, patients had a mean ±SD score of 11.5±7.2 (slightly lower than the 13.3±7.2 of the European sample).

Of the 53 physicians participating in the study, 83% were urologists.

Table 2 – Clinical characteristics of the Spanish population in EDOS at the baseline visit (n=1029)

Characteristics	% patients
BMI (kg/m^2, mean±SD, n=1021)	27.3±3.3
Duration of ED (n=1026)	
≤3 months	4.7
>3–≤12 months	30.8
>1–≤5 years	51.1
>5–≤10 years	9.7
>10 years	3.7
Severity of ED per IIEF-EF score (n=1024)	
Normal	4.1
Mild	20.6
Moderate	25.9
Severe	49.4
Severity of ED per researcher (n=1029)	
Mild	16.7
Moderate	49.7
Severe	33.6
Etiology of ED (n=1025)	
Psychogenic	20.3
Organic	40.1
Mixed	39.6
Comorbidities	
Diabetes	20.8
Pelvic surgery or prostatectomy	13.6
Spinal cord injury	1.9
In the past 6 months	
Angina	3.6
Other cardiovascular diseases	17.8
Endocrine disorders	8.3
Neurologic disorders	3.7
In the past 4 weeks	
Depression or anxiety	18.1
Premature ejaculation	13.5
Loss or decrease of libido	22.6

ED: erectile dysfunction; IIEF-EF: erectile function domain of the international index of erectile function.

Sociodemographic and clinical characteristics

In general, the characteristics of the Spanish population in EDOS are comparable to those of the overall population, and are shown in table 1. The mean age of patients was 55.9 years (range: 21–83), which is very similar to the 56.5 years of the overall population (range: 18–90).

Table 2 shows the clinical characteristics of the population at the baseline visit. The following are some of the most important characteristics. The mean BMI was 27.3 kg/m^2 (27.2 kg/m^2 in the overall population), which means that this is an overweight population (BMI≥25 kg/m^2)[20]. ED symptoms had been present for 1–5 years in 51.1% of patients (52.9% in the European sample); 49.4% had severe ED, according to the IIEF-EF scale. This percentage was slightly higher than that observed in the overall population (42.5%)[16].

The etiology was organic (40.1%) or mixed (39.6%) in most patients. The most common comorbidities in the 6 months prior to the study were diabetes (20.8%) and cardiovascular diseases (except angina) (17.8%).

The ED, according to the EF domain of IIEF (IIEF-EF), was more severe in patients who had experienced the symptoms for a longer time (fig. 1).

Treatment efficacy

All treatments were highly effective (fig. 2). However, at 3 months, a significantly larger proportion of patients experienced improved erection (GAQ1) in the group treated with tadalafil (96.5%) vs. sildenafil (85.7%; p<0.0001) and vardenafil (87.2%; p=0.0001). Of the patients who experienced improved erection, 96.1% of those treated with tadalafil, 91.7% of those treated with sildenafil, and 88.1% of those

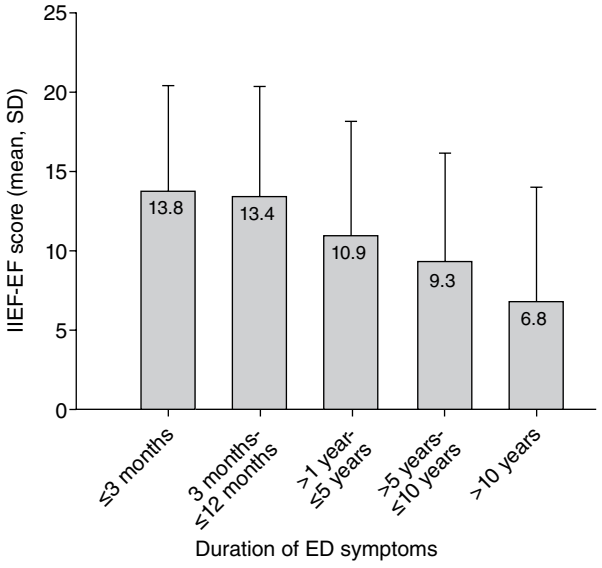
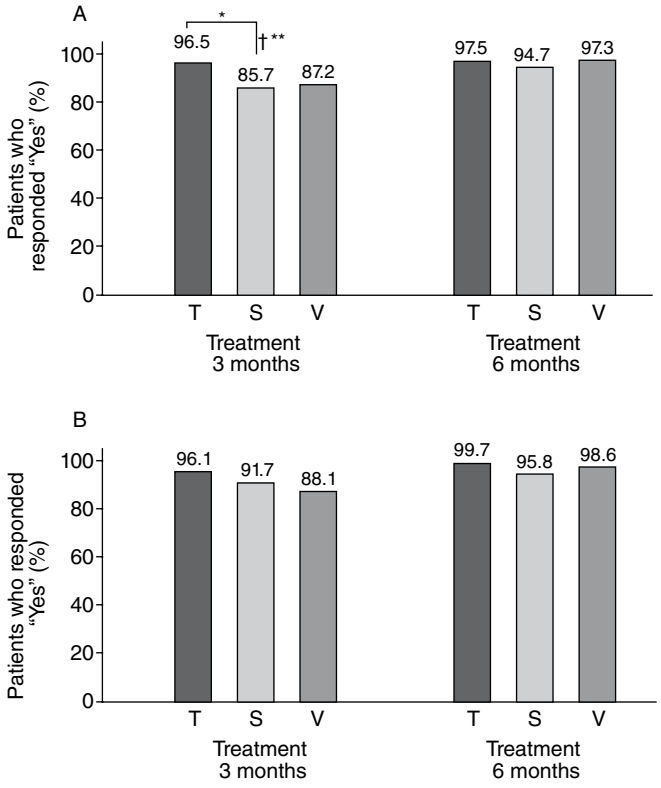


Figure 1 – Relationship between the erectile function domain score of the international index of erectile function (IIEF-EF) and the duration of ED symptom in the total population. A lower score indicates a more severe ED.



S: sildenafil; T: tadalafil; V: vardenafil.
*p<0.0001.
**p=0.0001 (logistic regression).

Figure 2 – Treatment efficacy: responses to the global assessment questions (GAQ) at 3 and 6 months. Percentage of patients experiencing improved erection (GAQ1) and percentage of patients reporting an increased ability to engage in sexual intercourse (GAQ2).

treated with vardenafil, reported an improved ability to engage in sexual intercourse (GAQ2) (the differences between treatments are not significant). At month 6, the differences between treatments were not significant for either question (GAQ1: tadalafil 97.5%, sildenafil 94.7%, and vardenafil 97.3%; GAQ2: tadalafil 99.7%, sildenafil 95.8%, and vardenafil 98.6%).

The mean±SD time between drug intake and the sexual encounter was significantly longer for patients on tadalafil (18.6±26.4 hours) vs. sildenafil (3.6±7.5; p<0.0001) and vardenafil (8.6±19.4; p=0.0017).

Figure 3 shows the cumulative maximum time interval between drug intake and the sexual encounter at 6 months of treatment. More than 50% of patients treated with tadalafil had sexual intercourse beyond 4 hours after taking the medication. For more than two thirds of the population on sildenafil and vardenafil, the maximum time between the dose and the sexual encounter was less than 4 hours.

Treatment satisfaction

According to the EDITS questionnaire (fig. 4), at 3 months a higher treatment satisfaction was found in patients treated with tadalafil (84.2%) than in those treated with sildenafil (75.0%; p=0.0042) or vardenafil (76.0%; p=0.0030). However, these differences were not significant at 6 months (tadalafil [90.8%] vs. sildenafil [89.6%], p=0.3260; tadalafil vs. vardenafil (93.7%), p=0.4291).

Psychological and behavioral aspects of sexual functioning

Figure 5 shows the results of various domains of the SF-PAIRS questionnaire to assess the psychological component of ED. At both 3 and at 6 months, patients treated with tadalafil were less concerned about the time between taking the medication and the sexual encounter (2.29 and 2.19 are the means for months 3 and 6, respectively), compared to patients on sildenafil (2.53 and 2,51, p<0.0001 in both moments) and vardenafil (2.55 and 2.43, p<0.0001 in both moments) (fig. 5A). At 3 months, patients on tadalafil were significantly more spontaneous in the sexual encounter (3.14), compared to patients on vardenafil (3.05, p=0.0346) and sildenafil (2.93; p=0.0002). However, these differences between treatments were not maintained at 6 months (fig. 5B). Regarding the sexual self-confidence component (fig. 5C), at 3 months of treatment patients in the tadalafil group had a significantly higher self-confidence (2.73) than patients in the vardenafil (2.55; p=0.0093) and sildenafil (2.39; p<0.0001) groups. However, at 6 months a significant difference was observed only for tadalafil (2.93) vs. sildenafil (2.60, p=0.0013).

Discussion

Over the past few years, PDE5 inhibitors have revolutionized the treatment of ED, as they provide high rates of efficacy and safety, which allows a usage adjusted to the patient's needs. Our results suggest that despite high levels of efficacy and satisfaction with all treatments, tadalafil was superior to the other PDE5 inhibitors studied, especially because of the temporal dissociation between the medication intake and the sexual encounter.

One important contribution of this study is the description, based on routine clinical practice, of the profile of the Spanish ED patient who actively seeks treatment, and the description of specific patterns that may have been masked in the European study. Better knowledge of this population allows for the design of ED preventive strategies or focusing efforts on patients at risk of diabetes mellitus or cardiovascular disease.

In general, the characteristics of the Spanish population are comparable to those observed in the European study[15]. However, ED is more severe in Spanish patients with symptoms for more than one year. The Spanish population had an almost 50% decrease in the IIEF-EF score from the 3-month category to the >10 years category (fig. 1). In the overall European population, however, the decrease was much smaller (about 20%). Of interest also is the disparity between the perception of severity of ED by physicians and the IIEF-EF score, which suggests that physicians tend to underestimate the severity of ED.

The European study[16] did not find differences in the efficacy of the various treatments measured with GAQ at months 3 and 6. However, in our population the efficacy of tadalafil at 3 months (GAQ1) was higher than that of the other PDE5 inhibitors. These results, rather than reflect a decrease in efficacy at 6 months, may be due to a different appreciation once the patients the therapeutic benefits of sildenafil and vardenafil.

The duration of the efficacy of tadalafil (36 hours) compared to that of other PDE5 inhibitors has been consistently documented[13,16,21]. In the European population in EDOS[16], 68% of patients on treatment with tadalafil reported having sexual intercourse beyond 4 hours after medication intake, compared to 30% and 39% of patients receiving sildenafil and vardenafil, respectively. Similar ratios were observed in the Spanish population, where 50% of patients on tadalafil had sexual intercourse beyond 4 hours after medication intake (fig. 3). For more than two thirds of the patients on sildenafil and vardenafil, however, the maximum time between the dose and the sexual encounter was less than 4 hours. This long response period of tadalafil, given by its long half-life (17.5 h)[22], may contribute to the patient perceiving the sexual encounter more naturally, compared to other PDE5 inhibitors (half-life of sildenafil and of vardenafil: 4–5 hours)[23,24]. The

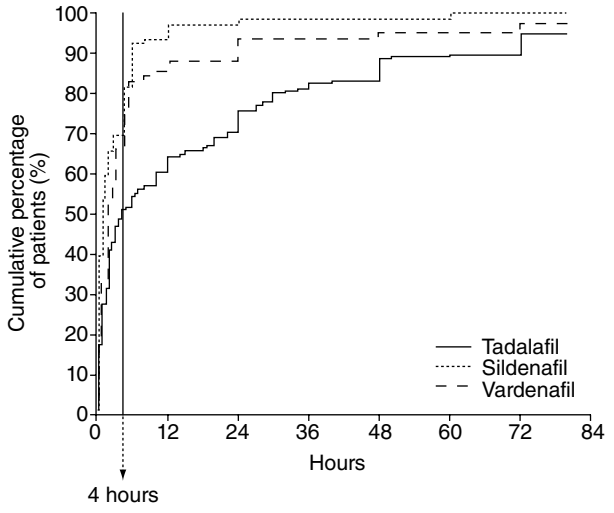
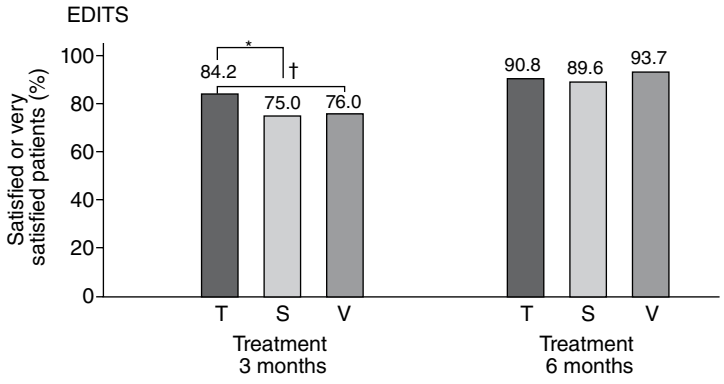
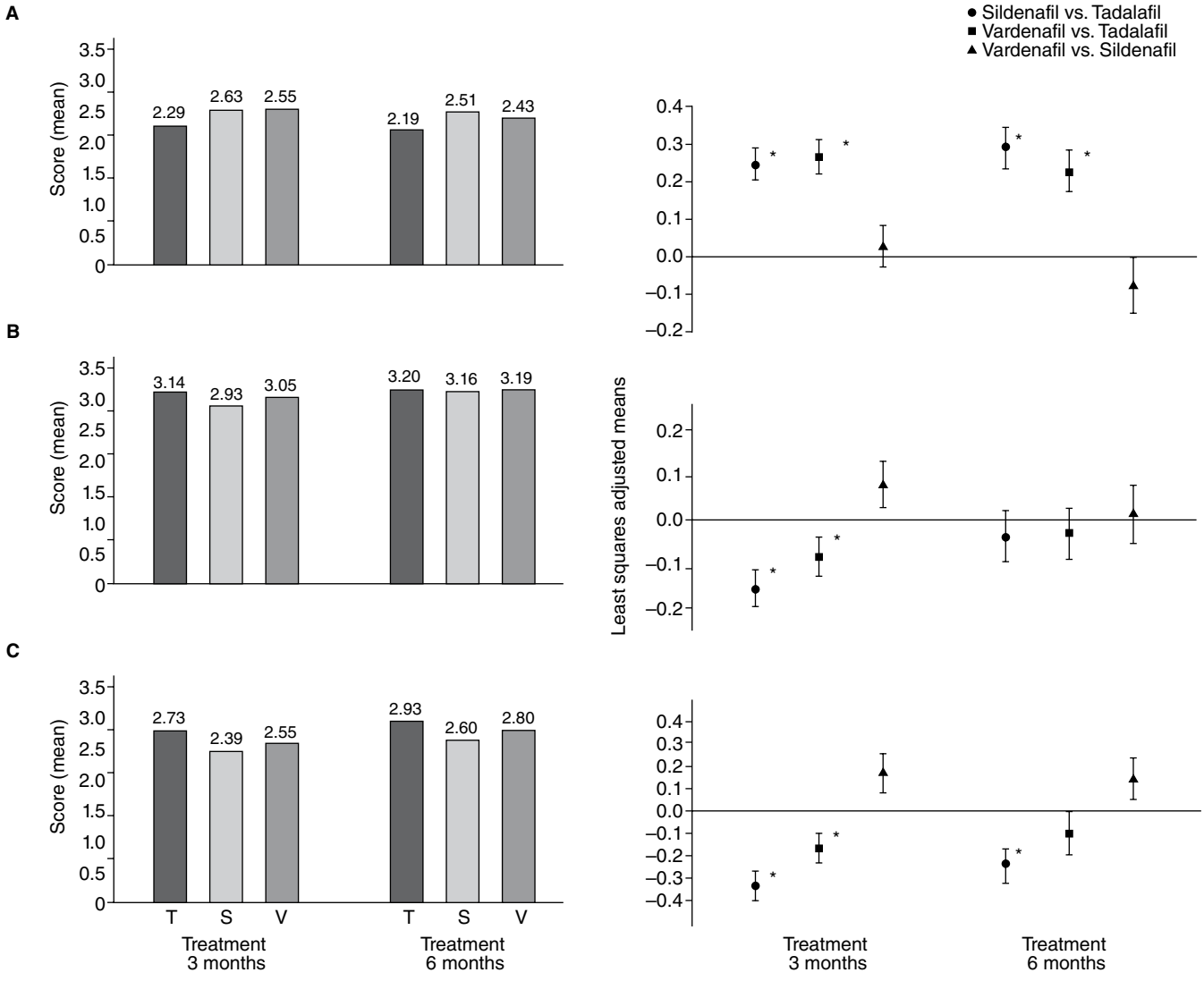


Figure 3 – Cumulative maximum time interval between drug intake and the sexual encounter at 6 months of treatment.



S: sildenafil; T: tadalafil; V: vardenafil.
*p=0.0042.
**p=0.0030 (logistic regression).

Figure 4 – Treatment satisfaction: responses to EDITS questionnaire at 3 and 6 months.



S: sildenafil; T: tadalafil; V: vardenafil.

Figure 5 – SF-PAIRS score (mean) at study 3 and 6 months. A) Concern about the interval between taking the medication and the sexual encounter. B) Sexual spontaneity. C) Sexual self-confidence. A low score in the time concern domain indicates less concern about the interval between the drug intake and the sexual encounter. A high score in the spontaneity and self-confidence domain indicates more spontaneity and sexual confidence. The least squares adjusted means are shown on the right; they permit to see significant differences between treatments (p<0.005) (ANCOVA model).

duration of the effect and the interaction or lack thereof of the drug with food and/or alcohol are important non-medical factors of great value for patients when selecting their ED treatment[25]. The length of action of tadalafil may contribute to the spontaneity in sexual encounters and to reduce psychological pressures that negatively affect sexual functioning and quality of life[26].

With the growing availability of highly effective ED treatments, it is increasingly important to have tools with which to assess holistically the efficacy of the treatments. This must include not only sexual functioning scales, but also psychological and behavioral aspects that determine the long-term maintenance of, and satisfaction with, the treatment[16,27]. Significant differences were found for efficacy and satisfaction at 3 months only. In conclusion, the longer duration of action for tadalafil, and thus, the longer period of time between dosing and sexual intercourse may contribute to enhance sexual spontaneity in sexual encounters, patient satisfaction with the treatment, and greater self-confidence.

Since this is an observational study, no accurate data on the dosing are available, and the optimum dose was not evaluated. However, in most cases urologists recommend to initiate treatment with maximum doses (tadalafil 20 mg,

sildenafil 100 mg, vardenafil 20 mg) in order to avert failure. In daily clinical practice, however, the initial doses may be lower if the drug insert recommendations are followed (20, 50, y 10 mg of tadalafil, sildenafil, and vardenafil, respectively). This fact may have influenced the differences in the 3-month results and help explain why the differences disappear at 6 months. Furthermore, when comparing treatment groups, it is important to bear in mind the limitations of the sample size of each group and other confounding factors and risks inherent to observational studies such as EDOS.

Nonetheless, despite these limitations, an observational study such as ours offers a closer reflection of the healthcare reality than controlled clinical studies do.

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Conflict of interest

Dr. Carmen Turbí Disla belongs to the department of Lilly SA.

The other authors state that they have no conflicts of interest.

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