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Real-Time Management of Erectile Dysfunction with PDE5 Inhibitors in Italy: Results of the Opti.M.E.D. Survey

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Abstract

The real-life use of Phosphodiesterase type 5 Inhibitors (PDE5Is) for the treatment of erectile dysfunction (ED) might differ across Institutions and physicians. We performed the *Optimizing Management of Erectile Dysfunction* (OPTI.M.E.D.) survey to outline the real-life practice of ED management in Italy. The OPTI.M.E.D. Survey tested the hypothesis that the new formulation of sildenafil oral suspension may show higher patient satisfaction and better clinical outcomes compared to other PDE5 inhibitors. The Survey involved 59 Italian urologists/andrologists, with data from a total of 1,150 patients. In the first Step, a Webinar was held for the presentation of the survey, and the Physician Interview Form used in the survey was presented. In Step 2, the forms were completed and collected, and the data obtained were subsequently analyzed. In Step 3, a final Webinar was held, during which the results were presented by the Scientific Board to all participants. In 88.9% of patients already treated with PDE5Is, the previously used molecule/formulation was changed at the first visit, because of treatment ineffectiveness and/or because of poor tolerability or compliance. According to the physicians' reports, sildenafil oral suspension was the most commonly prescribed drug at the first visit (75.9% of Cases), both in naïve patients and in those previously taking other PDE5Is. The prescription of sildenafil oral suspension was also confirmed at the second visit (after 60-90 days) in 97.9% of patients. The OPTI.M.E.D. survey provided a "real-life" snapshot of the management of ED patients seen in daily clinical practice in andrology and urology settings in Italy. According to the results of this survey, sildenafil oral suspension is associated with a high degree of patient satisfaction, also thanks to its peculiar formulation, which facilitates dosage modulation and is characterized by convenience and discretion of use as it does not require water to take it.

Keywords: Erectile Dysfunction; PDE5 Inhibitors; Sildenafil Oral Suspension; Real-life Survey

List of Abbreviations: ED: Erectile Dysfunction; IIEF-EF: International Index of Erectile Function-Erectile Function domain; OPTI.M.E.D.: OPTImizing Management of Erectile Dysfunction; PDE: Phosphodiesterase; PDE5Is: Phosphodiesterase type 5 inhibitors; QoL: Quality of Life

Introduction

Erectile dysfunction (ED) is defined as the persistent or recurrent inability to achieve and maintain an erection sufficient for satisfactory sexual performance [1]. ED is a very common disorder, especially in men over the age of 40 [2]. ED affects the sexual and social life of the patient and his partner, lowering their quality of life (QoL) [3-7].

Phosphodiesterase type 5 inhibitors (PDE5Is) are currently the most commonly used oral drugs for the treatment of ED [8-10]. Four PDE5Is oral formulations (sildenafil, tadalafil, vardenafil, and avanafil) are currently available in Italy:

- Sildenafil: tablet formulations (25, 50 and 100 mg), chewable tablets (25, 50 and 100 mg), orodispersible tablets (50 and 100 mg), orodispersible film (25, 50, 75 and 100 mg), and oral suspension bottle (30 ml, 25 mg/ml);
- Tadalafil: tablet formulations (5, 10 and 20 mg);
- Vardenafil: tablet formulations (5, 10 and 20 mg) and orodispersible tablets (10 mg);
- Avanafil: tablet formulations (50, 100 and 200 mg).

The efficacy of the various PDE5Is, at comparable dosages for the different molecules and formulations, is approximately similar [11]; however, differences may exist in terms of speed of action and tolerability [12]. Important aspects in the choice of a given PDE5I formulation are also dosage flexibility and convenience of use, which favor therapeutic adherence [13]. In clinical practice the use of a specific PDE5I is the result of the therapeutic alliance between the physician and the patient, taking into account the couple's intimate relationship, drug efficacy, tolerability and speed of action, as well as patient's preference over a specific administration route [14].

As a whole, there is a lack of studies investigating the real-life use of PDE5Is for ED and physician/patient satisfaction about the proposed treatment. Therefore, we conducted the OPTImizing Management of Erectile Dysfunction (OPTI.M.E.D.) Survey with the aim to depict the real-life management of ED in Italy, based on the clinical experience of a representative sample of andrology specialists, with particular reference to the use of PDE5Is on the market and the degree of satisfaction and preferences reported by physicians and patients regarding the different formulations used.

The current relevance of this survey is underlined by the recent introduction in Italy of a new PDE5I formulation, the sildenafil oral suspension, whose efficacy and preference for use were evaluated against "traditional" formulations.

Materials and Methods

The survey was conducted in several steps. In the first one, i.e. in September 2023, a Webinar was held for the presentation of the survey by the Scientific Committee (Board), consisting of the three authors of this paper. On this occasion, the Physician Interview Form used in the survey was presented (Figure 1).

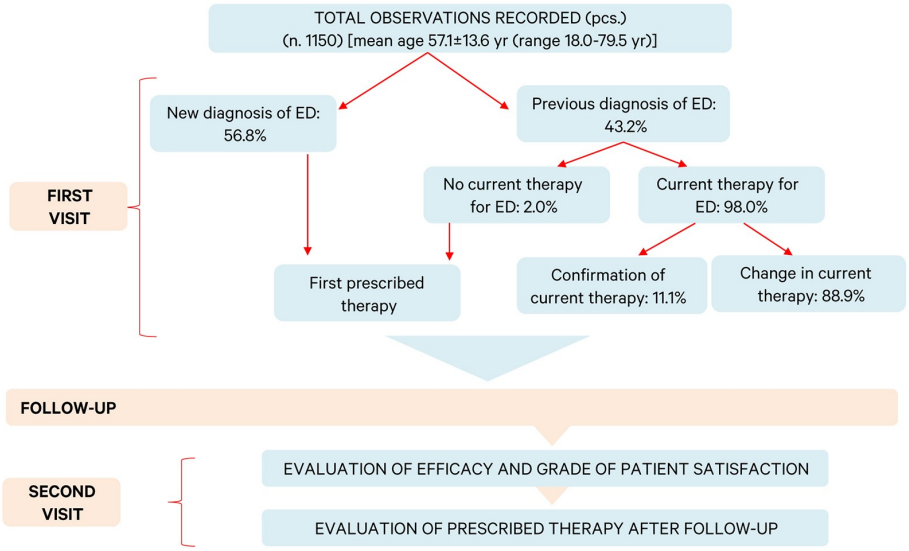

Figure 1: Steps of the OPTI.M.E.D. Survey.

In Step 2, data related to the real-life clinical experiences of participating physicians were completed and collected by October 31, 2023, and the data obtained were subsequently analyzed.

In the third Step (December 2023), a final Webinar was held, during which the results emerging from the analysis of the data were presented by the Board to all participants. In this step, interaction among participants was facilitated by the presence of a "chat box" which provided an opportunity to ask potential questions.

According to the aim of this survey, data of the first visit could be collected retrospectively, while the follow up examination was performed within the study period.

At the first visit, physicians made the diagnosis of ED (new diagnosis or confirmation of previous diagnosis) and the severity of ED was assessed using the Erectile Function domain of the International Index of Erectile Function (IIEF-EF) [15]. Using the IIEF-EF, ED severity categories are no ED (score ≥26 out of 30), mild ED (score 17-25), moderate ED (score 11-16), and severe ED (score ≤10) [15]. In addition, physicians reported which ED medications was prescribed to their patients (first prescription for treatment-naive patients, or confirmation or modification of previous prescription for patients already on PDE5Is treatment).

Between the first and second visits, physicians were given the opportunity to change the PDE5i used and/or the dosage of the previously prescribed medication.

At the follow-up visit, physicians were asked to rate the severity of patients' ED (using the IIEF-EF questionnaire), as well as the patient's satisfaction with the prescribed therapy using a 10-point scale (10=highest satisfaction, <5=dissatisfaction). Physicians were also asked whether they intended to confirm or change the current therapy. In line with what is usually done in clinical practice, the two visits were separated by a period of time normally required in "real-life" to evaluate the efficacy of PDE5I therapy (i.e. 60-90 days) [16].

Figure 1 is a schematic representation of the various steps of the OPTI.M.E.D. Survey. Descriptive statistics were used to describe the whole cohort.

Results

The Survey involved 59 specialists (urologists/andrologists) from all over the country (20 regions, including the two islands), collecting data from a total of 1,150 patients.

The mean ± SD age of patients was 57.1±13.6 years (range 18.0-79.5 years), and 57.6% of them were married.

The time from the first to the second visit was between 20 and 90 days for most patients (25.8% at 30 days and 16.9% at 60 days); mean ± SD, 56.26 ± 8.14 days. Ninety-six percent of patients receiving PDE5Is reported no adverse effects between the first and second visits. In the remaining 4% of patients, most of the adverse events reported were mild and transient; no serious adverse event was reported.

Degree of ED in the First Visit

At the first visit, a new diagnosis of ED was made in 56.8% of patients, while the remaining 43.2% had a confirmed previous diagnosis of ED.

At the first visit, 37.8% of patients had mild ED, 47.0% had moderate ED, and 15.2% had severe ED.

Patients Already Treated with PDE5Is

At the first visit, 98.0% of patients with a previous diagnosis of ED were already receiving PDE5Is. Ongoing treatment with PDE5Is included, in order of frequency: tadalafil (46.1%), sildenafil tablets (17.0%), avanafil (11.9%), sildenafil orodispersible film (11.1%), vardenafil (10.0%), and sildenafil oral suspension (3.9%) (Figure 2 A).

In 88.9% of cases, at the first visit, the previously used PDE5I was changed by the treating physician with a switch to a different PDE5I (both in terms of molecule and pharmaceutical formulation). In this group of patients, the main reason for a change in PDE5I therapy was inefficacy (52.6% of cases), followed by poor compliance (14.8%) and poor tolerability (15.0%).

Figure 2B Shows the new PDE5Is prescribed as a therapeutic switch at the first visit. In most cases (75.9%), the new medication prescribed for the above reasons was sildenafil oral suspension.

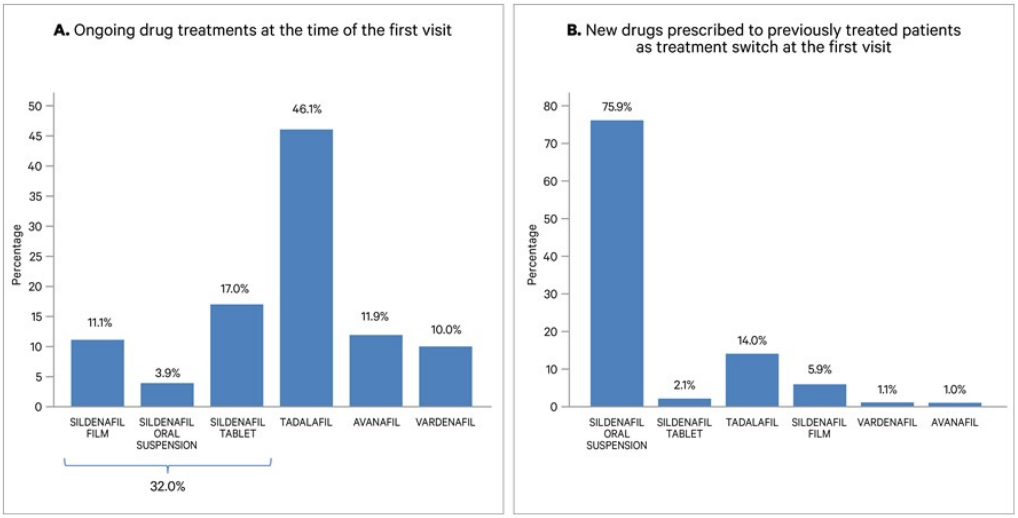

Figure 2: (A) Ongoing drug treatments at the time of the first visit; (B) New drug treatments prescribed as treatment switch at the first visit.

Naïve Patients

In patients newly diagnosed with ED, and in those previously diagnosed with ED who were not treated with oral medications, a PDE5I was prescribed. The newly prescribed medications were, in order of frequency: sildenafil oral suspension (80.5%), tadalafil (11.5%), sildenafil orodispersible film (3.0%), sildenafil tablets (3.0%), avanafil (1.0%), and vardenafil (1.0%).

Degree of ED in the Second Visit

At the second visit, 50.2% of patients had no ED, 35.0% had mild ED, 12.0% had moderate ED, and 2.8% had severe ED. Figure 3 compares the degree of ED at the first and second visits.

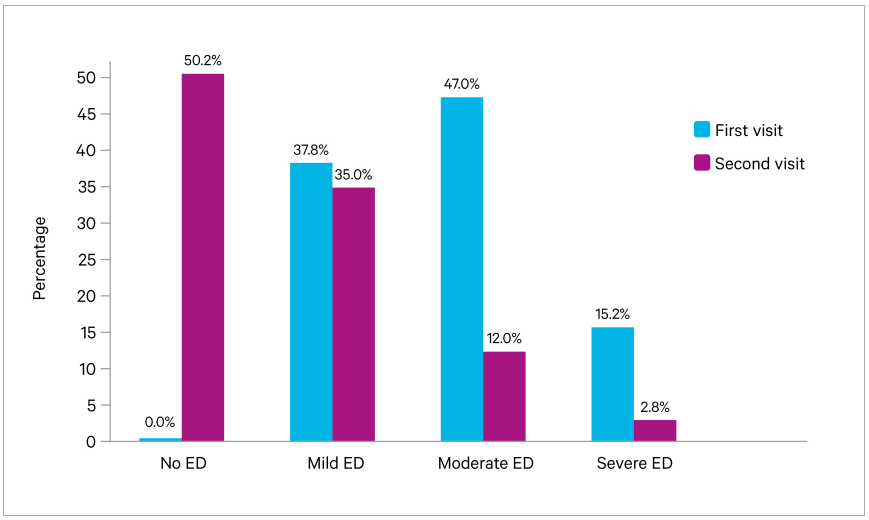

Figure 3: Degree of ED at the first and second visits

Medications Prescribed at the Second Visit

Medications prescribed (confirmed or changed) at the second visit included, in order of frequency: sildenafil oral suspension (79.9%), tadalafil (13.1%), sildenafil orodispersible film (4.0%), sildenafil tablets (2.0%), avanafil (1.0%), and vardenafil (1.0%) (Figure 4).

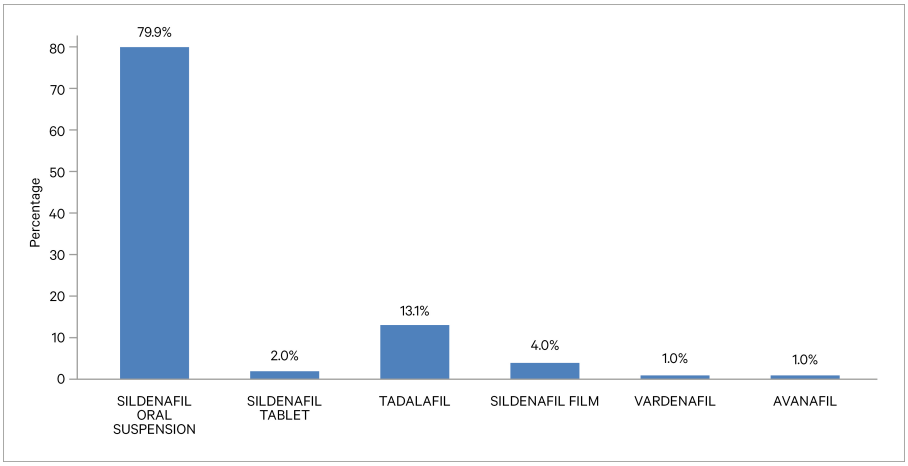

Figure 4: Medications prescribed (confirmed or changed)

Since the patients treated with sildenafil oral suspension was by far the majority at the time of the second visit, some data specific to these patients are presented below.

Patients Treated with Sildenafil Oral Suspension

Among patients who were treated with sildenafil oral suspension in the first visit, the initial dosage was 50 mg, 25 mg and 75 mg in 48.5%, 16.0% and 10.7% of participants, respectively (Figure 5A).

Compared to the first visit, the dosage distribution of sildenafil oral suspension at the second visit was virtually unchanged, although the percentage of patients with a final dose of 25 mg increased (31.1%). Specifically, the dosage of sildenafil oral suspension was not changed between the first and second visits in 72.5% of patients, while it was titrated "down" in 13.5% of subjects and "up" in 13.0% of subjects (Figure 5B).

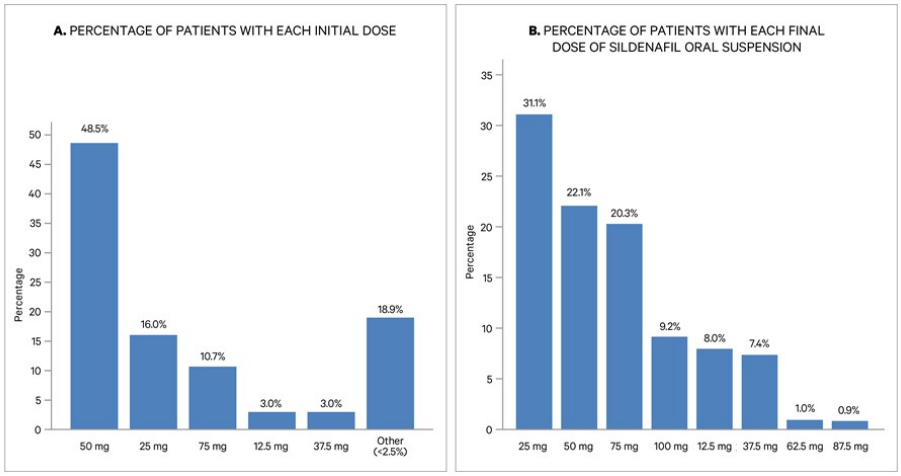

Figure 5: (A) Initial dose (at the first visit) in patients treated with sildenafil oral suspension; (B) Dosage at the second visit in patients treated with sildenafil oral suspension

At the second visit, 64.8% of patients treated with sildenafil oral suspension had no ED, 28.2% had mild ED, 7.0% had moderate ED, and 1.0% had severe ED.

At the second visit, 95.8% of patients treated with sildenafil oral suspension were satisfied with the treatment (Figure 6A). Reasons given by patients for being satisfied with sildenafil oral suspension treatment were: efficacy (33.8%), ease of use (21.0%), efficacy/tolerability ratio (17.2%), dosage modulation (17.1%), and palatability (9.9%) (Figure 6B).

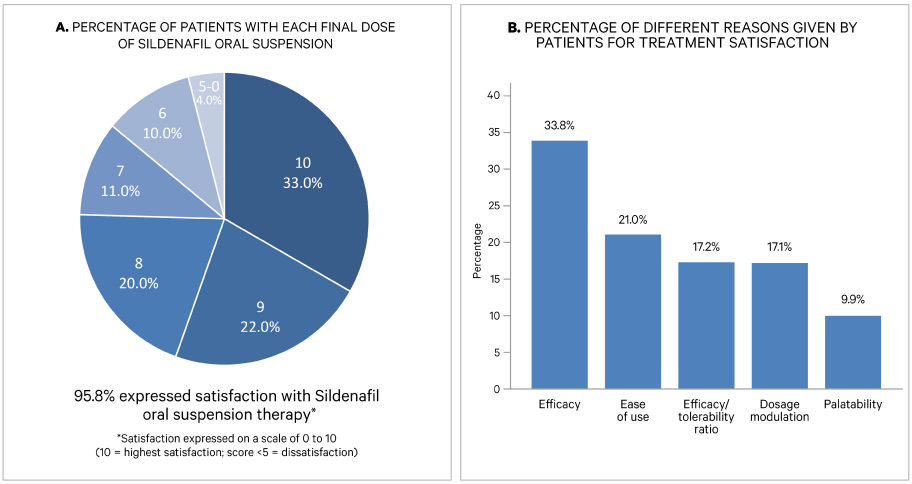

Figure 6: (A) Degree of satisfaction with Sildenafil oral suspension therapy expressed at the second visit; (B) Reasons given by patients satisfied with the treatment

According to physician reports, treatment with sildenafil oral suspension was also confirmed at the second visit in 97.9 % of patients, given the improvement in ED and the high level of satisfaction with the therapy.

Discussion

The results of the OPTI.M.E.D. survey offer interesting contributions to a better understanding of the real-life use of PDE5Is in the andrology and urology setting in Italy, providing a sufficiently reliable "snapshot" of both the efficacy of different molecules and formulations and the preferences of physicians and patients. This is particularly relevant given the introduction, since 2019, of a new PDE5I formulation, the sildenafil oral suspension, which, as highlighted by the survey, may offer advantages over "traditional" formulations in terms of convenience and discretion of use, while maintaining the same efficacy.

A relevant finding reported by physicians is that in 88.9% of patients already treated with oral medications, the previously used PDE5I molecule/formulation was changed at the first visit, primarily because of treatment ineffectiveness and secondarily because of poor tolerability or compliance.

In this regard, it is interesting to note that, among patients already on treatment at the first visit of the survey, tadalafil was the most commonly prescribed PDE5I (46.1%), while sildenafil oral suspension, one of the most recently introduced formulations, was used in only 3.9% of cases.

Sildenafil oral suspension 25 mg/ml was the most commonly prescribed drug for ED at the first visit, both in treatment-naïve patients (80.5 %) and as a therapeutic switch from another PDE5I (75.9%). The use of sildenafil oral suspension resulted in favorable outcomes both in terms of ED improvement and patient satisfaction with therapy.

Indeed, patients treated with sildenafil oral suspension at the second visit, who represented the vast majority of patients at that time, showed significant improvement in ED severity and high level of satisfaction with the treatment. Specifically, at the second visit, 93.0% of patients treated with sildenafil oral suspension had no or mild ED and 95.8% of patients reported good satisfaction; therefore, at the second visit, treatment with sildenafil oral suspension was confirmed in 98% of cases. While many patients previously treated with other PDE5Is, particularly tadalafil, reported ineffectiveness or poor tolerability at the first visit, they experienced significant improvement in both ED and treatment satisfaction after switching to sildenafil oral suspension. Overall, the responses obtained in the survey may suggest that the switch to the prevalent use of sildenafil oral suspension may have contributed to a better overall management of real-life ED patients.

The formulation of sildenafil oral suspension marketed in Italy is an oral suspension free from foreign substances, with a characteristic mint odor. This formulation allows adjustment to the minimum effective dosage and facilitates dose titration/flexibility; it also helps to minimize adverse events. The recommended dose of sildenafil oral suspension is 4 sprays, equivalent to 50 mg of sildenafil, to be taken as needed, approximately one hour before sexual activity. Based on efficacy and tolerability, the dose can be reduced to 2 sprays (25 mg of sildenafil). The maximum daily dose of sildenafil oral suspension is 4 sprays, equivalent to 50 mg of sildenafil.

It is interesting to note that the results of the present survey are similar to those of a recent multicenter observational study conducted in Spain [13]. In this study, including 30 urologists and/or andrologists, a representative sample of ED patients receiving sildenafil oral suspension (40.9% with moderate ED and 24.9% with severe ED) were asked to report by questionnaire their perception of efficacy/tolerability and their level of satisfaction with treatment, as well as their reasons for doing so. The results of the Spanish study showed that treatment with sildenafil oral suspension is associated with good efficacy/tolerability and a high level of satisfaction; according to the opinions of both physicians and patients, these beneficial effects of sildenafil oral suspension can also be attributed to its unique formulation, which facilitates dosage modulation and a convenient and discreet use

[13]. These favorable properties of sildenafil oral suspension seem to be confirmed by the results of the present study and may have a significant impact on improving adherence and, consequently, clinical efficacy of ED treatment.

Conclusions

The OPTI.M.E.D. survey provided a "real-life" snapshot of the management of ED patients seen in daily clinical practice in andrology and urology settings in Italy.

According to the physicians' reports, sildenafil oral suspension was the most commonly prescribed drug at the first visit, both in naïve patients and in those previously taking other PDE5Is, particularly tadalafil. For the most part, the latter patients generally changed the therapy because of efficacy/tolerability issues with the previous therapy.

Responses from physicians indicated that treatment with sildenafil oral suspension was associated with high patient satisfaction and significant improvement in ED severity. This was confirmed in 98% of cases at the second visit (after a period of up to 90 days).

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Author Contribution Statement

All Authors have equally contributed to the manuscript; all Authors have read and approved the final version submitted.

Competing Interests

None

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