The Treatment of Erectile Dysfunction study: focus on treatment satisfaction of patients and partners

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INTRODUCTION

Erectile dysfunction (ED) is defined as the inability to achieve and maintain an erection sufficient for satisfactory sexual intercourse [1]. Inclusion of the term ‘satisfactory’ by the National Institutes of Health consensus panel reflected the importance of patient satisfaction in the definition of ED as a clinical entity. More than 150 million men across the world have ED [2], including 2–3 million Canadians [3] or potentially more, given that 49.4% of Canadian men aged 20–88 years had ED in a recent primary-care survey [4]. The number of men with ED in North America is projected to increase by 77%, from 1995 to 2025 (to ≈21 million) [2].

Many men with ED have sexual dissatisfaction and anxiety, distress, reduced self-esteem, diminished quality of life, reduced physical satisfaction, marital discord, and/or depression or depressive symptoms [5–12]. Depressive symptoms in the patient might be related to ED through sexual dissatisfaction [13]. In addition, many sexual partners feel responsible for, or even guilty about, the problem of ED, misconstrue reduced intercourse frequency as emotional withdrawal on the part of the patient, and/or experience their own sexual dissatisfaction or sexual dysfunction [14–17]. ED can also signal the presence of comorbidities, including hypertension, coronary artery disease, and diabetes mellitus [18–20].

The first-line therapy for most men with ED is treatment with an approved oral phosphodiesterase type 5 (PDE-5) inhibitor, i.e. sildenafil citrate (sildenafil), tadalafil, or vardenafil HCl (vardenafil). These medications potentiate nitric oxide–mediated smooth-

OBJECTIVE

To assess patient and partner preferences for, and satisfaction with, tadalafil or sildenafil (phosphodiesterase type 5 inhibitors) in routine clinical practice for treating erectile dysfunction (ED), as these are important outcomes that might influence treatment adherence.

RESULTS

Of 2425 patients, approximately 98% completed the study and 295 partners participated. When patients changed from sildenafil to tadalafil (1722 men) the mean EDITS index scores increased significantly for both patients (from 61.6 to 78.3) and partners (from 65.0 to 82.6; both P < 0.001). When patients changed from tadalafil to sildenafil (703 men), the mean EDITS index scores increased slightly but significantly for patients (from 68.8 to 70.2; P = 0.007) but not partners (from 76.8 to 86.9; P = 0.066). For the individual EDITS questions, mean scores increased significantly from baseline to endpoint on all questions for patients (all 11 questions; P < 0.001) and partners (all five questions; P < 0.001) in the sildenafil-to-tadalafil group, and in the tadalafil-to-sildenafil group, mean scores for patients decreased on nine of 11 questions (seven of nine significantly; P < 0.041) and mean scores for partners decreased on all five (two significantly; P < 0.049). For treatment preference, regardless of the change in treatment (i.e. sildenafil-tadalafil or tadalafil-sildenafil), a significantly higher percentage of patients and partners preferred tadalafil to sildenafil.

CONCLUSIONS

These data indicate that patients with ED (and their partners) who changed from sildenafil to tadalafil treatment or vice versa in a routine clinical practice setting had higher treatment satisfaction when taking tadalafil than sildenafil, as assessed by most measures of EDITS. The higher treatment satisfaction with tadalafil might help to explain the greater preference for tadalafil compared with sildenafil in both patients and partners in this observational study.

KEYWORDS

erectile dysfunction, phosphodiesterase type 5 inhibitor, treatment satisfaction, sildenafil citrate, tadalafil, treatment outcome
Given the psychosocial component of ED, nonmedical lifestyle factors might shape patients’ and partners’ attitudes toward ED treatments, including their convenience, cost, ease of administration, and ‘naturalness’ in promoting erection [25]. These factors in turn might be influenced by pharmacokinetic or pharmacodynamic differences among agents, including the onset and duration of action. The purpose of the present prospective observational study of men with ED was to further characterize patient and partner satisfaction with two PDE-5 inhibitors in routine clinical practice. As reported previously [26], this observational study also assessed physician-rated patient preference and patient- and partner-rated preferences for tadalafil or sildenafil.

**PATIENTS AND METHODS**

This was a multicentre, non-interventional, observational study conducted at 266 centres across Canada. Most (>95%) investigators were GPs, and the remainder were urologists. Patients with a diagnosis of ED who had used sildenafil or tadalafil within the previous 8 weeks and expressed a desire to change to the other medication in the course of usual clinical practice were invited to participate in the study. Partners were included if they accompanied the patient to either of two clinic visits and consented to participate. The first patient was enrolled on 26 May 2004, and the last patient visit was on 7 May 2005. The study was conducted in accordance with the Declaration of Helsinki and in accordance with the Guidelines for Good Clinical Practice. Each patient gave written informed consent and the study was approved by a central research ethics board and local ethics boards, in conformity with applicable laws and regulations.

Data were collected at study entry (baseline; visit 1) and 4–12 weeks after baseline (endpoint; visit 2). Consistent with the naturalistic, observational, non-interventional study design, there was no mandated washout period between treatments, and patients were not subjected to any physician visit, procedure or investigation beyond routine clinical practice except as specified below. The physician could see the patient, and the patient could follow-up with the physician, at any time outside of the two data-collection visits. The sponsor had no direct role in patient selection and did not provide study medications. Physicians had sole discretion over ED treatment, including doses, dose adjustments, and/or discontinuations, according to their own practices, but were expected to follow product labelling for contraindications. As given in the Canadian Product Monographs, the recommended dose of tadalafil is 20 mg and the recommended dose of sildenafil is 50 mg for men in the general ED population. The medications should be taken before anticipated sexual activity at a maximum dosing frequency of once per day.

Investigators recorded patients who were changing treatment from sildenafil to tadalafil (or vice versa) in the course of clinical practice. Vardenafil was not included in the study because the drug was approved in Canada after the inception, design development, and review board submission of the study. Physicians were instructed to attempt to enrol an equal number of patients wishing to change therapy from sildenafil to tadalafil or vice versa. Partner participation was also documented.

For the assessments, information relevant to ED treatment, including demographics, partner status, alcohol and tobacco use, specified medical conditions, and use of concomitant medications, was collected at baseline. A sexual history questionnaire was also completed at baseline to collect data on the duration, cause (organic, psychogenic, mixed), and severity of ED, as well as previous PDE-5 inhibitor use. Treatment preference, the primary study endpoint, was rated by the physician, patient, and partner, and the results of this assessment were published previously [26].

To determine treatment satisfaction, patients and their partners completed the Erectile Dysfunction Inventory of Treatment Satisfaction (EDITs) at the baseline and endpoint visits. EDITs is a reliable and valid instrument to evaluate satisfaction with ED treatments [27]. The patient version of the EDITs has 11 items, scored from 0 (no satisfaction or dissatisfaction) to 4 (high satisfaction). The 11 items include overall satisfaction, degree to which treatment met expectations, likelihood of treatment continuation, ease of use, satisfaction with onset of action, satisfaction with duration of action, impact of treatment on sexual confidence, partner satisfaction with treatment, how the partner felt about the patient’s continuing with treatment (by patient self-report), naturalness of erections, and naturalness of erection hardness. The partner version of the EDITs has five items scored on the same 5-point Likert scale, including overall satisfaction, degree to which treatment met expectations, how treatment affected the partner’s sense of sexual desirability, partner satisfaction with duration of action, and how the partner felt about the patient continuing to use the treatment.

EDITs scores were presented as the mean of responses to all items and were transformed to EDITs index scores ranging from 0 (least satisfied) to 100 (most satisfied) by multiplying the EDITs score by 25. Mean EDITs scores were computed at each of the two visits for patients and partners with valid responses to every EDITs question. A positive change in the EDITs score from baseline to endpoint indicated increased satisfaction with treatment. An overall assessment question (‘Did treatment improve erections?’) and treatment preference questionnaires were completed by physicians, patients, and partners at endpoint only. (Preference and overall assessment data were reported previously [26]).

Primary outcome measures, including the proportions of patients who preferred to continue with tadalafil or sildenafil, preferred a treatment other than these agents, or preferred to discontinue treatment, were reported earlier [26]. Secondary outcome measures included mean scores on the patient and partner versions of the EDITs; mean changes in scores for each of the items of the patient and partner EDITs questionnaires from baseline to endpoint; the number (%) of patients who were accompanied by their partners to medical appointments; and the number (%) of patients who informed their partners of using PDE-5 inhibitors for ED (by patient self-report).

All statistical analyses were done separately for patients at entry who (i) changed from sildenafil to tadalafil (sildenafil-tadalafil group) and received tadalafil during the study, or (ii) changed from tadalafil to sildenafil (tadalafil-sildenafil group) and received...
sildenafil during the study. All variables were summarized using descriptive statistics, including number (%) for categorical variables and mean (SD) for continuous variables. Mean changes from baseline in EDITS index scores for patients and partners were analysed by Wilcoxon signed-rank test to assess statistically significant differences within treatment groups (i.e. sildenafil-tadalafil, tadalafil-sildenafil). All subjects with a baseline and at least one observation after baseline were included.

We also compared the changes from baseline to endpoint in patient and partner EDITS index scores in the tadalafil-sildenafil group with changes in the sildenafil-tadalafil group. Analysis of covariance on ranked change scores was used to compare patient and partner EDITS index scores between groups. This model included treatment group (i.e. sildenafil-tadalafil, tadalafil-sildenafil), severity of ED, and baseline value of the outcome. Additional covariates were also included to adjust for statistically significant baseline differences or potential confounders.

RESULTS

In all, 2425 (91%) of 2661 men with ED who provided consent used medications allowed by the study description. Of these, 1722 (71%) were taking sildenafil at baseline and changed to tadalafil, while 703 (29%) changed from tadalafil to sildenafil. Approximately 98% of patients with ED in each group completed the study; 41 (2.4%) of 1722 patients in the sildenafil-tadalafil group discontinued and eight (1.1%) of 703 patients in the tadalafil-sildenafil group discontinued.

The characteristics of the patients were described in detail previously [26], and were comparable between the groups, except that 214 (30%) patients in the tadalafil-sildenafil group had received previous treatment with sildenafil, whereas only 71 (4%) patients in the sildenafil-tadalafil group had received previous treatment with tadalafil. Most patients (~80% in each group) had ED of organic or mixed aetiology and/or had ED for ≥1 year, and the ED severity was mild or moderate in ≈82% of patients (in the opinion of the investigator).

In all, 295 sexual partners attended clinic visits and their partners (i.e. patients) used the correct treatment, representing 12.2% of the 2425 patients enrolled in the study. There were 207 partners of men in the sildenafil-tadalafil group and 88 partners of men in the tadalafil-sildenafil group. Although only 12.2% of partners attended clinic visits, 774% of patients reported that their partners were aware that patients were receiving ED treatment. Four sexual partners were male. Patients in the sildenafil-tadalafil group with available data on doses were taking doses of sildenafil before entering the study of 25 mg in 77 (4.5%), 50 mg in 974 (56.8%) and 100 mg in 665 (38.8%), and were taking tadalafil at the end of the study of 10 mg in 79 (4.6%) and 20 mg in 1639 (95.4%). Patients in the tadalafil-sildenafil group with available data on doses were taking doses of tadalafil before entering the study of 10 mg in 45 (6.4%) and 20 mg in 657 (93.6%), and were taking doses of sildenafil at the end of the study of 25 mg in 21 (3.0%), 50 mg in 484 (69.2%) and 100 mg in 194 (27.8%).

FIG. 1. The mean scores on the patient and partner EDITS index in the sildenafil-tadalafil (upper panel) and tadalafil-sildenafil (lower panel) groups. The values at the bottom of the bars are the numbers of patients and partners with a baseline and at least one observation after baseline, and values under the bars are the numbers of patients and partners enrolled. An EDITS value of 0 indicates extremely low treatment satisfaction, while a value of 100 indicates extremely high treatment satisfaction.
FIG. 2. The mean changes from baseline to endpoint on items of the patient EDITS questionnaire. Each item is scored on a scale from 0 (no satisfaction or dissatisfaction) to 4 (high satisfaction); positive values indicate increased satisfaction and negative values decreased satisfaction. *P < 0.001 for change from baseline to endpoint (sildenafil-tadalafil group); †P < 0.041 for change from baseline to endpoint (tadalafil-sildenafil group). Between-group comparisons (sildenafil-tadalafil vs tadalafil-sildenafil) of changes from baseline to endpoint were statistically significant for each EDITS item (P < 0.001). #Question 3 was assumed as ‘very unlikely’ (score 0) at baseline.

FIG. 3. Partner EDITS. Mean changes from baseline to endpoint on items of the partner EDITS questionnaire. Each item is scored on a scale from 0 (no satisfaction or dissatisfaction) to 4 (high satisfaction); positive values indicate increased satisfaction and negative values decreased satisfaction. *P < 0.001 for change from baseline to endpoint (sildenafil-tadalafil group); †P < 0.049 for change from baseline to endpoint (tadalafil-sildenafil group). Between-group comparisons (sildenafil-tadalafil vs tadalafil-sildenafil) of changes from baseline to endpoint were statistically significant for each EDITS item (P < 0.004).
individual item of the partner EDITS was significantly different among sexual partners in the sildenafil-tadalafil group compared with partners in the tadalafl-sildenafil group (P < 0.004), indicating significantly higher partner satisfaction with tadalafl.

**DISCUSSION**

The Treatment of ED study was a prospective observational trial in Canada designed to assess preferences for, and satisfaction with, treatment with two PDE-5 inhibitors among patients with ED and their partners, in routine clinical practice. The mean EDITS index scores increased significantly for both patients and their partners when patients changed from sildenafil to tadalafl, indicating higher treatment satisfaction with tadalafl for both patients and partners in this group. For patients changing from tadalafl to sildenafil, there was a 1.4-point increase in the mean EDITS index score (statistically significant), with no significant change in partner EDITS index scores, indicating higher treatment satisfaction with sildenafil for patients, but not partners in this group. When changes from baseline to endpoint were compared between treatment groups, patients and partners in the sildenafil-tadalafil group had significantly greater improvements in treatment satisfaction than patients and partners in the tadalafl-sildenafil group. Physicians prescribed tadalafl and sildenafil based on the Canadian Product Monographs and most patients were on tadalafl 20 mg or sildenafil 50 mg during this observational study. As reported previously [26], efficacy was similar in patients in the sildenafil-tadalafil group compared with the tadalafl-sildenafil group, with 89% and 86% of patients, respectively, responding yes to an overall assessment question (i.e. Has the treatment improved your erections?).

Increased treatment satisfaction with sildenafil, tadalafl, and vardenafil was reported in clinical trials. The EDITS and other assessment indices (e.g. International Index of Erectile Function, Sexual Encounter Profile diary) were used to show improved treatment satisfaction of patients with ED and/or their partners with sildenafil [16,28–30]; increased intercourse satisfaction and overall satisfaction in men with ED treated with vardenafil [31,32]; and improved sexual satisfaction and overall satisfaction with tadalafl among ED patients with varying degrees of ED severity, and their partners [33–35].

However, to our knowledge, the present trial is the first to compare treatment satisfaction between two PDE-5 inhibitors in both patients and partners in routine clinical practice. Greater treatment satisfaction with tadalafl might help to explain the treatment preference results from this study [26], which showed that 72% of patients in the sildenafil-tadalafil group preferred tadalafl, according to physician ratings, whereas 20% preferred sildenafil. In the tadalafl-sildenafil group, 61% of patients preferred tadalafl and 29% preferred sildenafil, according to physician ratings. (The percentages do not add to 100% because some patients in each group preferred treatments other than sildenafil or tadalafl, or preferred to discontinue treatment.) In a previous study comparing sildenafil with alternative ED therapies, treatment satisfaction as measured by EDITS index scores was highly correlated with patients’ final treatment preference [30].

Patients with ED who chose sildenafil therapy had a mean EDITS index score of 72, compared with a mean of 40 in patients choosing alternative treatments, including intracavernosal injection therapy [30]. Previous open-label studies showed significantly higher EDITS index scores for sildenafil (vs intracavernosal injection therapy) in patients changing to sildenafil [36,37]. The present study shows consistency between improvements in treatment satisfaction with tadalafl (compared with sildenafil) and patient and partner preferences for tadalafl.

In all, 12.2% of sexual partners in the present study accompanied men with ED to their medical appointments and ~75% were aware of their partner’s ED treatment. Although consensus guidelines recommend that sexual partners be actively involved in the assessment and/or treatment of patients with ED [38,39], this might not be achievable in many busy primary-care practices. Educational literature to help partners understand ED and its treatment might foster consistency between treatment expectations of the partners and actual experience with therapy, as well as treatment satisfaction and long-term adherence to the regimen. Perhaps it is more realistic to insist on partner visits in the setting of suboptimal treatment outcomes, including low satisfaction and/or adherence. In these cases, discussions with the couple might reveal sexual dysfunction in both the man and his partner. For example, in a clinical trial, the incidence of sexual dysfunction was significantly higher in women who were dissatisfied with sildenafil treatment than in those who were satisfied [16].

There are some limitations of the present observational study; it was not randomized and there were imbalances in sample sizes in the two groups (sildenafil-tadalafil and tadalafl-sildenafil). However, the statistical model was adjusted to include baseline differences and other potential disparities between the groups as covariates. Although each physician was instructed to attempt to enrol similar numbers of patients expressing a desire to change from one PDE-5 inhibitor to the other, ~71% of study participants were changing from sildenafil to tadalafl, compared with 29% changing from tadalafl to sildenafil. This imbalance might reflect differences in the level of experience with the two PDE-5 inhibitors. In Canada, tadalafl was approved in September 2003, while sildenafil was approved in 1999. Thus, at the start of the study there were more patients who had previous experience with sildenafil than those with tadalafl. In addition, the doses of tadalafl and sildenafil prescribed were at the discretion of the physician. This might have led to imbalances in the proportions of patients who took the highest approved dose of each PDE-5 inhibitor and might reflect instructions in the Canadian Product Monographs; >93% of patients in the sildenafil-tadalafil and tadalafl-sildenafil groups took tadalafl 20 mg, whereas 39% of patients in the sildenafil-tadalafil group and 28% of patients in the tadalafl-sildenafil group took sildenafil 100 mg. Although the overall assessment question showed that the efficacy at endpoint was similar for patients in the sildenafil-tadalafil and the tadalafl-sildenafil group [26], the EDITS results reported here should be interpreted in view of the different medication doses prescribed to patients.

The strengths of the present observational study include its similarity to routine clinical practice, including minimal involvement of the sponsor. For example, medications were not provided and patients/partners received a limited number of questionnaires at the two study visits. This type of observational study might help to reduce subject bias (‘Hawthorne
effect [40–43]) toward the sponsor’s medication.

In conclusion, in this Canadian observational study, patients with ED (and their partners) who changed from sildenafil to tadafalif treatment or vice versa in a routine clinical practice setting had greater treatment satisfaction when taking tadafalif than sildenafil, as assessed by most measures of EDITs. Enhanced treatment satisfaction with tadafalif might help to explain the greater preference for tadafalif over sildenafil in both patients and partners in this observational study.

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CONFLICT OF INTEREST

G. Brock, S. Carrier, L. Salgado, A.H. Klein, C. Lang and R. Horner were all investigators in this sponsor-funded study; G. Brock is a consultant/speaker for Bayer, Lilly and Pfizer; J. Chan is an employee of sponsor; S. Carrier is a paid consultant to sponsor and has a financial relationship to competitors of mentioned product; M. Chan is an employee of sponsor; S. Gutkin is a paid consultant to sponsor; R. Dickson is an employee of sponsor.

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Abbreviations: (ED)ITS, (Erectile Dysfunction) Inventory of Treatment Satisfaction; PDE-5, phosphodiesterase type 5.