Assessment of comparative treatment satisfaction with sildenafil citrate and penile injection therapy in patients responding to both

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Study Type – Therapy (outcomes research)
Level of Evidence 2c

OBJECTIVE

To survey patient satisfaction, using validated questionnaires, in a group of men with erectile dysfunction who had used and responded to both sildenafil citrate and intracavernosal injection (ICI) therapy.

PATIENTS AND METHODS

In all, 300 patients on ICI therapy were mailed questionnaire packets containing a survey enquiring about the patients’ medical history, and two sets of the International Index of Erectile Function (IIEF) and the Erectile Dysfunction Inventory of Treatment Satisfaction (EDITS) sexual function surveys. If patients were using sildenafil alternating with ICI they were asked to complete the IIEF and EDITS questionnaires for each therapy. To identify only patients who had an adequate response to each agent, a score of ≥22 on the EF domain of the IIEF for sildenafil and ICI was required for inclusion in the final analysis.

RESULTS

In all, 178 packets were evaluable; 123 men (69%) responded to ICI but not sildenafil, and 11 (6%) responded only to sildenafil and not ICI, leaving 37 patients who responded to both; these patients comprised the study population. There was no difference in EF domain score of the IIEF between the treatments; EDITS scores were significantly higher for ICI therapy than for sildenafil (P < 0.001).

CONCLUSIONS

In patients who alternate the use of sildenafil and ICI therapy, satisfaction appears to be higher with ICI, although the erectogenic performance is similar. This suggests that patient satisfaction does not depend solely on erection performance, and that patients might benefit from various treatment options.

KEYWORDS

sildenafil, intracavernosal injections, satisfaction, rigidity, erectile dysfunction
INTRODUCTION

Erectile dysfunction (ED) is a common urological problem, affecting >20 million men in the USA [1]. Several treatment options are currently available for ED, with various methods of delivery. Two of the most popular treatments include intracavernosal injection (ICI) therapy and oral pharmacotherapy, the first of which is sildenafil citrate [2]. There have been numerous publications reporting the efficacy and side-effect profiles of these agents. To our knowledge, there been no comparative analysis of these two treatments using validated instruments assessing patient satisfaction among men who were using both strategies successfully.

Several validated questionnaires have been developed to assess various aspects of sexual function and erectile function (EF). The International Index of Erectile Function (IIEF) was developed to evaluate medical therapy for ED [3]; it consists of 15 questions, encompassing five domains, the largest of which is the EF domain. The Erectile Dysfunction Inventory of Treatment Satisfaction (EDITS) was developed to assess patient and partner satisfaction with medical therapy [4,5]. Both are widely accepted as robust tools for clinical research.

The negative effects of ED on quality of life, and the positive effects of successful treatment, have been well documented [6–9]. However, the determinants of patient satisfaction are not well understood. Patient satisfaction with a treatment is multifactorial, and depends on more than the production of an adequate erection. The present study was undertaken to define comparative satisfaction profiles in men who were using and responding to both ICI and sildenafil, using validated instruments.

PATIENTS AND METHODS

The study was conducted in accordance with a protocol approved by our institution’s ethics review board. We identified 300 consecutive patients in our ED clinic who were being treated with ICI therapy; each was mailed a questionnaire packet comprising an introductory letter that asked the patient to complete and return the enclosed questionnaires if they were alternating the use of ICI therapy with sildenafil, and responding to both with an erection of sufficient rigidity for penetration and that permitted sexual intercourse. The packet contained a brief survey of the patient’s medical history, the IIEF and EDITS, marked for the patients’ experience with sildenafil, and another IIEF and EDITS marked for the patients’ experience with ICI. For the purposes of this analysis, only patients with scores ≥22 after treatment on the IIEF EF domain were included in the final analysis. This threshold was based on previous reports indicating that the vast majority of patients with EF domain scores ≥24 are capable of having sexual intercourse whenever they [10].

The results were analysed statistically using Student’s t-test, comparing the overall IIEF, EF and satisfaction domains and the overall EDITS scores. Differences between the scores for the two treatment groups was evaluated using the sign test for nonparametric paired data; in all tests statistical significance was defined as P < 0.05 (Fig. 1).

RESULTS

We received packets from 195/300 (65%) patients; 17 were not useable as the surveys were incomplete and thus evaluable questionnaires were received from 178 patients. Using an EF domain score threshold 22, 123 (69%) responded only to ICI and 11 (6%) only to sildenafil. Thus 37 patients responded to both therapies and were included in the final analysis. The demographic profile of these patients is representative of the general population seen by urologists (Table 1).

The mean (SD) total IIEF score for sildenafil and ICI therapy was 65 (5) and 66 (5), respectively (P = 0.018). There was no statistically significant difference in EF domain score between sildenafil and ICI therapy, at 27 (2) vs 27 (3), respectively (P = 0.22). The difference in IIEF satisfaction domain score between ICI and sildenafil was statistically significant, at 17 (2) vs 18 (1) (P = 0.02), as was the difference in EDITS scores between sildenafil and ICI therapy, at 57 (10) vs 67 (8), respectively (P < 0.001).

DISCUSSION

While the incidence of clinically meaningful ED varies geographically, with an incidence of 19–35%, it is accepted that ED is a common problem [11–13]. The Massachusetts Male Aging Study cited an incidence of any degree of ED of 52% in men aged 40–70 years [14]. In the present analysis, moderate to severe ED was reported by 35% of men; the incidence of complete ED, the inability to have any sexual intercourse, was 5% at 40 years and 25% at 70 years old. These figures extrapolate to >20 million men in the USA and >100 million men worldwide with any degree of ED.

Laumann et al. [15] showed that emotional and physical satisfaction are markedly lower in men with ED than in the general population. In another study, 94% of people believe that sexual satisfaction adds to the quality of life at any age [16]. The health-related quality of life of men with ED is significantly poorer than that of age-matched

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean (SD) or %</th>
</tr>
</thead>
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<tr>
<td>Patient age, years</td>
<td>64 (13)</td>
</tr>
<tr>
<td>Duration of ED years</td>
<td>3 (2)</td>
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<tr>
<td>Hypertension</td>
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<td>Hyperlipidaemia</td>
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<td>Diabetes mellitus</td>
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<tr>
<td>Radical retropubic prostatectomy</td>
<td>16</td>
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<tr>
<td>Pelvic external beam radiation</td>
<td>9</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>16</td>
</tr>
<tr>
<td>Cigarette smoking</td>
<td>9</td>
</tr>
</tbody>
</table>

TABLE 1

The patient demographics

FIG. 1. The questionnaire algorithm.
men with no ED, especially among men aged <65 years who have a comorbid illness [17]. The psychological effects of ED substantially compromise health-related quality of life, specifically low physical satisfaction, low emotional satisfaction and low general happiness [18]. ED leads to a decline in mental and physical health [14].

ICI has been used by urologists since 1983; this strategy permits intercourse in 60–90% of men with ED, depending upon the injection agent used [19]. The most successful agents are combined medications, specifically a triple mixture of papaverine, phentolamine and prostaglandin E. This latter combination is the therapy most frequently used by our centre, and in our hands this allows > 90% of men to obtain a reproducible erection of sufficient rigidity for penetration, with an infrequent and well-tolerated side-effect profile. Oral therapy in the form of sildenafil citrate permits about two-thirds of men with ED to achieve an erection of sufficient rigidity for penetration and have successful sexual intercourse. Sildenafil is effective across many causes of ED, in patients with diverse comorbidities and across varied degrees of ED [2].

Patient satisfaction in response to erectogenic drug therapy is a complicated issue, it thought to be multifactorial and is difficult to measure. An improvement in erectile function can help restore patients to feeling better about themselves. Treatment of ED with injectable and transurethral alprostadil has been shown to improve quality of life among men [7,20]. The successful management of ED with sildenafil also significantly improves both patient and partner measures of quality of life. Satisfaction itself is complex, and is related to such issues as penile rigidity, durability of response, side-effect profile, consistency of response and partner satisfaction. Currently, two inventories permit the assessment of patient satisfaction in response to drug therapy. The EDITS is a validated instrument, which is completed only after treatment and not at baseline [4]. The IIEF has a satisfaction domain, including questions 7, 8, 13 and 14, which can compare scores before and after treatment [3]. The present study used both of these instruments to compare the therapies.

The 37 patients with an EF domain score of ≥22 for both sildenafil and ICI therapy who were included in the analysis were representative in age and comorbidity profile of the general population with ED (Table 1), thus we think that these data are readily extrapolated. We chose this score threshold as previous work showed that most men with EF domain scores above this level believe that they have fully functional erections. Teloken et al. [10] studied 100 patients who had used sildenafil citrate on at least four occasions who completed the IIEF. Patients were asked a series of global assessment questions about their ability to have sexual intercourse, their satisfaction with their erectogenic medication, the ability of the medication to improve erectile rigidity and the ability of the medication to improve their capacity to have sexual intercourse. Patients were subcategorized into four groups based on treatment IIEF scores (≥26, 22–25, 18–21 and 11–17). The IIEF scores were compared to the responses to the global assessment questions. In the group with ED scores of 22–25, 67% agreed that they could have sex whenever they wanted and 66% were satisfied with their erectogenic medication.

Using an EF domain score threshold of ≥22 there were statistically significant differences between sildenafil and ICI therapy for the IIEF satisfaction domain (P = 0.02) and EDITS scores (P < 0.001). Even if a treatment EF domain score of ≥26 were used (defining no ED), while there were only 21 patients meeting this criterion for both sildenafil and ICI therapy, the statistically significant differences in satisfaction were retained with significant differences between the groups in IIEF satisfaction domain score (P = 0.02) and EDITS score (P < 0.001).

As treatment for ED is undertaken by specialists other than urology, it is important that there is good reason to offer patients various treatment options. As shown by the group studied here, some men are more satisfied with ICI despite a highly effective response to sildenafil. A study by Hatzichristou et al. [21] identified a similar group; 155 men on ICI therapy for at least a year were given a trial of sildenafil, and those who responded were asked to continue treatment exclusively with sildenafil for a month. Patients were then asked to use the treatment of their choice for 3 more months; 27% of those responding to sildenafil chose to resume using ICI and 12% chose to alternate both therapies. Efficacy was measured only by patient self-report of rigidity adequate for satisfactory intercourse, and variables of satisfaction were not formally evaluated. There was a trend towards a higher preference for sildenafil in men on lower doses of ICI agents. The authors hypothesized that erectile response is most closely related to patient preference, and that erectile response to sildenafil is less rigid in men on higher doses of ICI therapy as they probably have more severe corporal smooth muscle pathology. Our data do not support this, as neither sildenafil nor ICI dose appeared to have any significant impact on satisfaction, although there were relatively few patients assessed.

In the present patients, although the erectogenic ability of both agents, as measured by the EF domain of the IIEF was similar, there was higher satisfaction with ICI therapy using EDITS to define patient satisfaction. A score of >50 on this scale is deemed to be representative of satisfaction [5,22], and both treatments had scores of >50 but ICI resulted in a EDITS score 10 points higher than with sildenafil. In a study by Giuliano et al. [8], 176 men on stable ICI therapy with ≤20 µg of prostaglandin E₂ were changed to sildenafil. Patients completed the EDITS and questions 3 and 4 of the IIEF questionnaire during treatment on their usual dose of prostaglandin E₂, and again after 12 weeks of exclusive sildenafil use. In 69% of patients the EDITS score after 12 weeks of treatment with sildenafil was equivalent to or higher than that for treatment with ICI. Scores on IIEF questions 3 and 4 were similar between the groups. No mention was made by the authors of what treatment patients eventually chose to continue to use. The present study involved a different population who continued to use ICI therapy even though they had responded to sildenafil. Furthermore, cultural issues might be at play, thus the discrepancy in findings between the present study and that of Giuliano et al. [8]. Obviously the present patients perceived an advantage with ICI therapy, to warrant its continued use in the light of its more invasive administration.

The strength of the present analysis is its use of two validated satisfaction instruments. However, the study has several limitations; there were relatively few patients; there was no clinically meaningful difference in the EDITS score; while there was a statistically significant difference in IIEF satisfaction domain score, the difference was only one point, thus the clinical meaningfulness of
such a change is probably low; this was not a randomized study, thus there might have been a sequence effect; as the vast majority of patients started ICI before sildenafil use; no event log was used and thus it is not known what the frequency of use of either ICI or sildenafil was, and thus defining the impact of satisfaction with use is impossible.

While further study will be required to determine which features of a treatment contribute to patient satisfaction, in the present study using validated instruments, despite similar erectogenic ability, satisfaction with ICI therapy was higher for ICI therapy.

**CONFLICT OF INTEREST**

John Mulhall and Jennifer Simmons are Research Consultants for Pfizer Inc.

**REFERENCES**


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Abbreviations: ED, erectile dysfunction; ICI, intracavernosal injection; III(EF), International Index of (Erectile Function); EDITS, Erectile Dysfunction Inventory of Treatment Satisfaction.