Study of quality of life in patients with benign prostatic hyperplasia under treatment with silodosin

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Received 18 July 2013; accepted 11 October 2013
Available online 12 March 2014

Abstract
Objectives: To assess the impact of urinary symptoms associated with benign prostatic hyperplasia and its treatment with silodosin on quality of life (QoL) and sexual function, depending on age, severity of symptoms, time on treatment and prostate size.

Material and methods: A cross-sectional, observational study was conducted in 305 urology practices throughout Spain. Socio-demographic and clinical data were collected and patients filled the following questionnaires: EQ-5D, Sexual Function Index (SFI) and International Prostate Symptom Score (IPSS). Multiple regression models were used to determine factors independently associated with patients’ QoL.

Results: A total of 1019 patients were enrolled; mean (SD) for: age 62.7 (5.7), EQ-5D 89.9 (13.9), sexual drive-SFI 3.71 (1.67), erection-SFI 6.11 (3.08), ejaculation-SFI 4.50 (2.06), problems-SFI 6.85 (3.37) and overall satisfaction-SFI 2.00 (0.99). The EQ-5D and SFI score were statistically lower with older age, severe LUTS and greater prostate size (P < .01), but no differences were found related to time on treatment with silodosin. The EQ-5D score was positively associated with sexual satisfaction and desire size of SFI and the EQ-5D VAS score, and negatively with disability, semi-urban residence and comorbidities in the multiple regression analyses.

Conclusions: Severe LUTS and older age are associated to a greater deterioration in sexual function and quality of life. However time on treatment with silodosin does not produce deterioration in the quality of life.

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Estudio de calidad de vida en pacientes con hiperplasia benigna de próstata en tratamiento con silodosina

Resumen
Objetivos: Evaluar el impacto de los síntomas urinarios asociados a hiperplasia benigna de próstata y su tratamiento con silodosina sobre la calidad de vida (CV) y la función sexual, en función de la edad, la gravedad de los síntomas, el tiempo en tratamiento y el tamaño prostático.

Material y métodos: Estudio transversal, observacional, realizado en 305 consultas de urología de España. Se recogieron datos sociodemográficos y clínicos y los pacientes cumplimentaron los cuestionarios EQ-5D, Sexual Function Index (SFI) e International Prostate Symptom Score (IPSS). Se determinaron los factores asociados independientemente a la CV de los pacientes mediante análisis de regresión múltiple.

Resultados: Se seleccionaron 1.019 pacientes con media (DE) para: edad 62,7 (5,7) años, puntuación EQ-5D 89,9(13,9), deseo-SFI 3,71 (1,67), erección-SFI 6,11 (3,08), eyaculación-SFI 4,50 (2,06), problemas-SFI 6,85 (3,37), satisfacción sexual-SFI 2,00 (0,99) y mediana IPSS 16 (RI 12-20). Las puntuaciones EQ-5D y SFI fueron inferiores a mayor edad, mayor gravedad de STUI y mayor tamaño prostático (p < 0,01), pero no se encontraron diferencias en cuanto al tiempo en tratamiento con silodosina. En el análisis de regresión múltiple se observó que la puntuación del cuestionario EQ-5D se asoció de forma positiva con las dimensiones satisfacción sexual y deseo del SFI y con la puntuación EVA EQ-5D, y de forma negativa con incapacidad laboral, residencia semi-urbana y comorbididades.

Conclusiones: El deterioro en la función sexual y en la calidad de vida es mayor en los pacientes de mayor edad y en aquellos con STUI graves. Sin embargo, el tratamiento prolongado con silodosina no produce deterioro en la calidad de vida.

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Background
Benign prostate hyperplasia (BPH) is the most common urological disease in men. It is characterized by an increase in size of the prostate, which can cause progressive obstruction of the urinary flow and an increase in the activity of the detrusor muscle. Age is the primary factor associated with the onset of lower urinary tract symptoms (LUTS) related to BPH. Treatment aims to reduce the patients’ symptoms, improve their quality of life and satisfaction and avoid the onset of complications. However, considerable variability has been detected in primary care clinical practice in the healthcare management of patients, which can result in the inefficient use of healthcare resources. For patients with moderate to severe symptoms (IPSS ≥ 8), drug treatment is indicated. In most cases, this treatment consists of alpha-adrenergic blockers (alpha blockers), whose mechanism of action consists of a reduction in smooth muscle tone of the prostate and bladder neck, which improves the symptoms and increases the urinary flow. The efficacy of the various drugs of the alpha-blocker family is similar, although they differ in terms of the onset of adverse effects. Silodosin has shown a better safety profile in the onset of dizziness and orthostatic hypotension; however, the onset of ejaculation problems was more frequent. Nevertheless, it has been reported that the ejaculation problems caused by silodosin are associated with greater improvements in LUTS and causes withdrawal from using the medication in only 2.8–12.6% of patients.

It is important to properly consider the needs of individual patients with BPH, understanding the benefits and adverse effects of the treatments on their lives and assuming that the impact of the disease and the treatment on the patient’s quality of life, and that of their partner, is critical. The medical treatment of urinary symptoms associated with BPH is more effective when the symptoms are properly assessed to determine the dominant component in each patient. Patients prefer long-term relief from symptoms. It is therefore essential to evaluate the patient’s preferences and their sexual satisfaction with the treatment to ensure greater treatment compliance. A previous study conducted by our workgroup showed that older patients with BPH and severe LUTS who were treated with alpha-adrenergic blockers and had been treated for more than a year had a poorer health-related quality of life (HRQL). This study reviews whether the results achieved in patients treated with any drug from the alpha-adrenergic blocker family are reproducible for patients treated with silodosin.

The aim of this study was to evaluate the HRQL and sexual function according to age, symptom severity, prostate size and treatment time of patients with LUTS associated with BPH undergoing drug treatment with silodosin.

Material and methods
This was an observational cross-sectional study, not linked to a drug, of 305 urology practices throughout Spain. Patient enrollment was conducted between March and October 2012. In a single visit, demographic data and the medical history of BPH were collected (including diagnosis, date of diagnosis and starting date of the silodosin therapy). The patients evaluated their general health condition using the...
EQ-5D questionnaire, their sexual function using the Sexual Function Index (SFI) questionnaire and the severity of the BPH symptoms according to the International Prostate Symptom Score (IPSS) questionnaire. The inclusion/exclusion criteria included age between 45 and 70 years and a diagnosis of BPH with moderate–severe symptoms (IPSS > 8). At the time of enrollment, the patient should have been on treatment with silodosin for at least 3 months, agree to participate in the study, have the ability to fill out the aforementioned questionnaires and sign the informed consent.

The IPSS questionnaire for assessing urinary symptoms associated with BPH, which has been validated in Spain, consists of 7 items that assess urinary symptoms and an additional item that assesses quality of life. The total score considers the first 7 items and classifies the symptoms as mild (0–7), moderate (8–19) or severe (20–35).

The EQ-5D questionnaire is a generic HRQL assessment questionnaire, which has been validated for use in Spain, and provides 3 types of information: a description of the HRQL using 5 measures (mobility, personal care, daily activities, pain/discomfort and anxiety/depression), an overall HRQL value and a utility value. The questionnaire includes a visual analog scale (VAS) on the current HRQL, which is also assessed by the patient. Higher values are indicative of a better HRQL.

The SFI questionnaire evaluates sexual function in men and consists of 11 items and 5 measures (sexual impulse, erection, ejaculation, perception of the sexual dysfunction as a problem and overall satisfaction). Higher scores indicate less impact and, therefore, better sexual function.

**Statistical analysis**

The data were recorded using electronic case report forms and analyzed with the statistical analysis programs Stata 10 and SPSS 14.

For the data description, we used absolute and relative frequencies for the qualitative variables and mean and standard deviation (SD) or median and interquartile range, depending on the results of the Kolmogorov–Smirnov normality test, for quantitative variables.

To study the differences in mean scores from the study questionnaires (EQ-5D and SFI), taking into account the variables of interest (that is, group age and moderate–severe severity), we used Student’s t-test with correction for nonhomogeneous variance when necessary, and ANOVA when there was more than 2 groups, with Bonferroni correction to determine a posteriori which groups had differences. In the event that the study variables did not follow a normal distribution, we performed a nonparametric Mann–Whitney U or Kruskal–Wallis test.

Lastly, to evaluate the independent association of the variables of interest on the HRQL (measured by the EQ-5D) and sexual function (measured by the SFI), we performed a multiple linear regression model for HRQL and a Poisson regression model for sexual function, due to the fact that the scores of these questionnaires were fully distributed.

For all analyses, we considered the level of significance to be equal to $\alpha = 0.05$, that is, we used a 95% confidence level as the criterion.

Based on the EQ-5D and SFI scores from a previous study, an expected effect size ($d = 0.35$), a 5% chance of a Type I error, a statistical power of 80%, the groups included in the study and estimated losses of 15%, we calculated that a sample size of 920 patients would be necessary.

**Ethical considerations**

The study was performed according to the requirements laid out in international standards for the implementation of epidemiological studies, as recorded in the International Guidelines for Ethical Review of Epidemiological Studies (Council for the International Organizations of Medical Sciences [CIOMS], Geneva, 1991), as well as the Declaration of Helsinki (Tokyo revision, October 2004). The study was approved by the Clinical Research Ethics Committee of Hospital Clinic i Provincial of Barcelona.

The treatment, communication and transfer of personal data from all participants were conducted under the provisions of the Organic Law 15/1999 of December 13 for the protection of personal data.

**Results**

Data were collected on 1086 patients. By the end of the selection process, 1019 patients who met the inclusion/exclusion criteria were ultimately included. The mean age (SD) of the patients included in the study was 62.7 (±5.7) years, the mean prostate size was 47.0 (±14.5) cm³ and the mean treatment time with silodosin was 9.9 (±7.7) months. The other clinical and demographic characteristics of the patients included in the study are listed in Table 1. The results of the questionnaires completed by the patients are briefly described below.

The median score on the IPSS questionnaire was 16 (interquartile range, 12–20); 720 patients had moderate symptoms (8–19 points) and the remaining 299 had severe symptoms (20–35 points). The mean total score on the EQ-5D quality of life questionnaire was 89.9 (±3.9), and the VAS had an average score of 66.7 (±20.4). For the SFI questionnaire, the mean scores for each of the measures were 3.71 for sexual drive (±1.67), 6.11 for erection (±3.08), 4.50 for ejaculation (±2.06), 6.85 for problems (±3.37) and 2.00 for sexual satisfaction (±0.99).

The mean scores in these questionnaires stratified by age group, symptom severity, treatment time and prostate size are listed in Table 2. While an age ≥60 years, an IPSS score ≥20 and prostate size were associated with a lower score in the EQ-5D questionnaire and VAS and in all the measures of the SFI questionnaire ($p < .001$ for all measures), the treatment time with silodosin (less than 1 year vs. greater than or equal to a year) only resulted in statistically significant differences in the measures of sexual drive and erection on the SFI questionnaire.

In addition, treatment time with silodosin was not associated with a reduction in quality of life as evaluated by the EQ-5D questionnaire and VAS, the SFI measures and the total IPSS score, when analyzed according to the prostate size ($\leq 30$ cm³, 30–40 cm³, 40–50 cm³, >50 cm³). A prostate size $\leq 30$ cm³ was the only measure to have a statistically significant difference in the total IPSS score (mean 14.6
Table 1  Clinical characteristics of BPH and demographic characteristics of the sample included in the study.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Absolute frequency (%)</th>
<th>n = 1019</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;60</td>
<td>287 (28.2)</td>
<td></td>
</tr>
<tr>
<td>&gt;60</td>
<td>732 (71.8)</td>
<td></td>
</tr>
<tr>
<td>Residence</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rural (&lt;5000 inhabitants)</td>
<td>154 (15.1)</td>
<td></td>
</tr>
<tr>
<td>Suburban (5000–19,999 inhabitants)</td>
<td>246 (24.1)</td>
<td></td>
</tr>
<tr>
<td>Urban (≥20,000 inhabitants)</td>
<td>619 (60.8)</td>
<td></td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No formal education</td>
<td>81 (7.9)</td>
<td></td>
</tr>
<tr>
<td>Primary education</td>
<td>386 (37.9)</td>
<td></td>
</tr>
<tr>
<td>Secondary education</td>
<td>377 (37.0)</td>
<td></td>
</tr>
<tr>
<td>Higher education</td>
<td>175 (17.2)</td>
<td></td>
</tr>
<tr>
<td>BPH diagnosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>250 (24.6)</td>
<td></td>
</tr>
<tr>
<td>Adenomatous</td>
<td>768 (75.4)</td>
<td></td>
</tr>
<tr>
<td>Prostate size (cm³)</td>
<td>47.0 (14.5)</td>
<td></td>
</tr>
<tr>
<td>&lt;30</td>
<td>119 (11.7)</td>
<td></td>
</tr>
<tr>
<td>30–40</td>
<td>292 (28.7)</td>
<td></td>
</tr>
<tr>
<td>40–50</td>
<td>277 (27.2)</td>
<td></td>
</tr>
<tr>
<td>&gt;50</td>
<td>331 (32.5)</td>
<td></td>
</tr>
<tr>
<td>PSA level (ng/ml)</td>
<td>2.39 (0.95)</td>
<td></td>
</tr>
<tr>
<td>Treatment time with silodosin (months)</td>
<td>9.9 (7.7)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Comorbidities</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>542 (53.2)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>258 (25.3)</td>
</tr>
<tr>
<td>Constipation</td>
<td>155 (15.2)</td>
</tr>
<tr>
<td>Respiratory diseases</td>
<td>131 (12.9)</td>
</tr>
<tr>
<td>Ischemic heart disease</td>
<td>99 (9.7)</td>
</tr>
<tr>
<td>Reduced mobility</td>
<td>43 (4.2)</td>
</tr>
<tr>
<td>Stroke</td>
<td>22 (2.2)</td>
</tr>
</tbody>
</table>

a  Mean (standard deviation).
b  Each patient can have more than 1 comorbidity.

Discussion

In this study with a sample size greater than 1000 subjects with moderate–high prostate volume and associated comorbidity, the HRQL and the scores in the measure of sexual function in patients with BPH were lower in the oldest group, those with greater LUTS severity and those with the largest prostate size. However, there was no relationship with the treatment time with silodosin, except in the measures of sexual drive and erection. Treatment time with silodosin also had no influence on the quality of life and sexual function when adjusted according to the prostate size. Future studies should assess whether the effect observed on the measures of sexual drive and erection is really due to treatment time with silodosin or to increased prostate size. In a previous study performed in an identical manner with patients treated with alpha-adrenergic blockers for at least 3 months before patient enrollment, the HRQL (also measured with the EQ-5D questionnaire) and all measures of sexual function, except problems, were statistically lower in the patients who had been treated for more than one year. This could be an indicator that silodosin has a greater effect on HRQL in prolonged treatment periods compared with other alpha-adrenergic blockers. This is a relevant factor, given that the recent BPH consensus document considers low quality of life perceived by the patient as an indication for surgery.

In terms of the explanatory model of the EQ-5D questionnaire score, the results are similar to those that have been previously published. Higher scores in the SFI measures of sexual function, sexual drive and sexual satisfaction, as well as higher scores in the EQ-5D VAS represent an improvement in HRQL. Conversely, HRQL decreases with the occurrence of comorbidities, suburban residence and an occupational status of disability. The comorbidities that most decreased HRQL were restrictions of mobility, stroke and respiratory diseases. It is also worth noting that the most prevalent comorbidity in our study’s patient sample (hypertension) appears to have no effect on HRQL; treatment time with silodosin and prostate size also had no effect on HRQL.

The regression models performed to explain the measures of sexual function indicated that all the measures were negatively affected by age; however, HRQL and how it is perceived by the patients positively affects all the measures. Diabetes is the comorbidity that affects the greatest number of measures of sexual function, all except sexual drive. The SFI measure of erection was shown to be affected by a greater number of factors. In addition to the aforementioned age, HRQL and diabetes, erection was also negatively affected in patients diagnosed with hypertension, ischemic heart disease or constipation, as well as in patients with greater prostate size. Retirement appears to negatively affect the measures of sexual drive and sexual satisfaction. Finally, higher education also improves the score in the measure of problems.

As a conclusion, we can state that sexual function impairment and HRQL impairment are greater in older patients...
and in those with severe LUTS. However, prolonged treatment with silodosin does not cause deterioration in HRQL. Lastly, a better sexual function has a positive impact on HRQL, and the presence of concomitant diseases negatively affects HRQL. At the same time, the HRQL perceived by the patient positively affects all measures of sexual function.

**Funding**

This study was funded by Almirall S.A.

**Conflicts of interest**

Dr. Maite Pérez and Dr. Xavier Cortés work for Almirall S.A. The other authors declare that they have no conflicts of interest.

**Appendix A. Supplementary data**

Supplementary material related to this article can be found, in the online version, at http://dx.doi.org/10.1016/j.j.acuroe.2014.02.009.

**References**


10. Roehrborn CG, Kaplan SA, Lepor H, Volinn W. Symptomatic and urodynamic responses in patients with reduced or no seminal
emission during silodosin treatment for LUTS and BPH. Prostate Cancer Prostatic Dis. 2011;14:143–8.


