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AQ1

Changes in Sexual Function for Outpatients With Schizophrenia or Other Psychotic Disorders Treated With Ziprasidone in Clinical Practice Settings

A 3-Month Prospective, Observational Study

To the Editors:

Sexual dysfunction is frequent in patients with schizophrenia treated with antipsychotic drugs.¹ This side effect is associated with low treatment satisfaction² and may impair treatment compliance.³ Although it has great importance, available information describing the association between antipsychotic drugs, including ziprasidone, and sexual dysfunction is limited.⁴ The objective of this study was to assess the effect of ziprasidone on sexual function in patients with schizophrenia.

The present study was a multicenter, noncomparative, and naturalistic study conducted in 9 sites by 13 investigators. After meeting the selection criteria and providing informed consent, patients received open-label treatment with ziprasidone for 3 months. Subjects included sexually active male and female patients, 18 years or older, with a diagnosis of schizophrenia, schizophreniform disorder, schizoaffective disorder, or delusional disorder according to the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*. Exclusion criteria included any contraindication to ziprasidone, coadministration of other antipsychotics, any concurrent medical condition or treatment with well-established negative effects on sexual function, and current use of alcohol or other drugs.

The study was reviewed and approved by the Ethics Committee from

the Hospital Universitario de Salamanca (Spain), was reported to the Spanish Medicines Agency, and was conducted in accordance with the Declaration of Helsinki.

Patients were evaluated at baseline, week 4, and week 12. Psychopathology was assessed with the Brief Psychiatry Rating Scale and the Clinical Global Impression (CGI) scale. Sexual function was evaluated with the PRSexDQ-SALSEX, a questionnaire validated both in patients with depression⁵ and in patients with schizophrenia,⁶ and a CGI addressing sexual functioning. A more detailed description of the outcome measures can be found elsewhere.⁷ Adverse events were assessed at all visits by an open question.

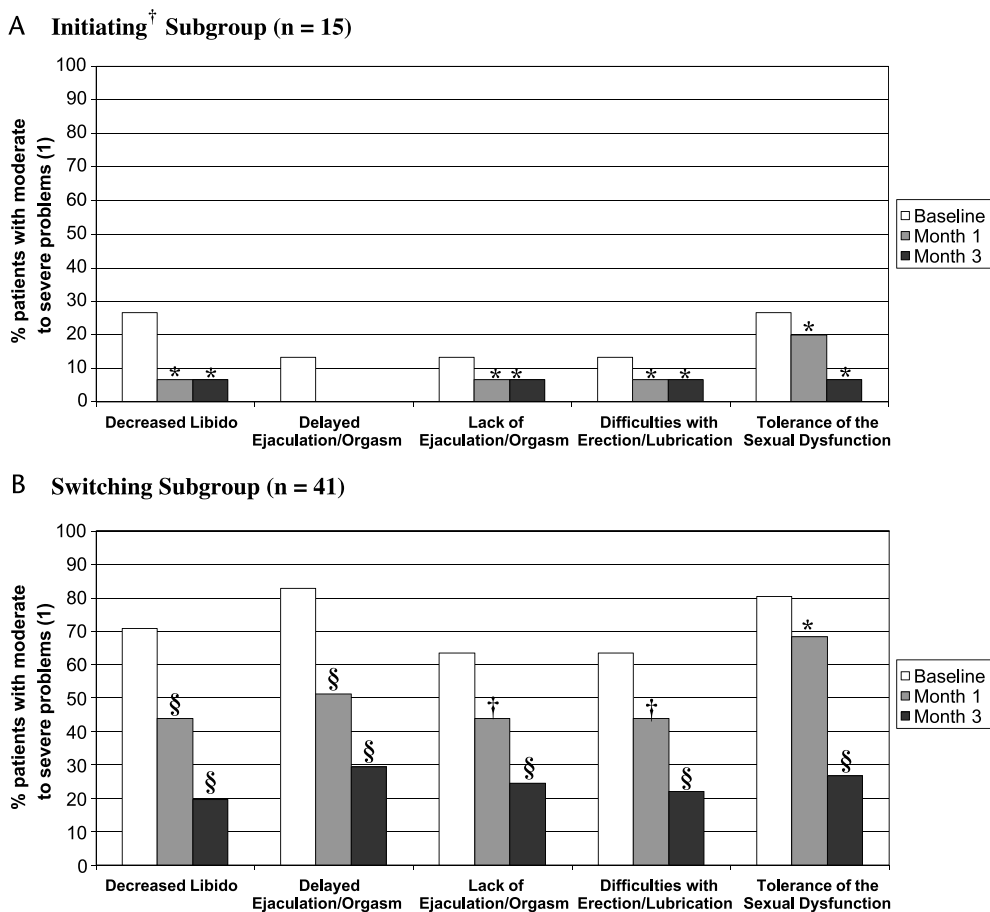
All efficacy analyses were performed in the intention-to-treat (ITT) sample (ie, patients with a ziprasidone prescription and at least 1 postbaseline assessment) using the last-observation-carried-forward method. The analyses were conducted separately for 2 subsets of patients: patients not receiving any antipsychotic drug at the time of the study screening (initiating subgroup) and patients receiving ziprasidone as a substitute for a previous antipsychotic drug (switching subgroup). The safety population consisted of all patients who had received at least 1 ziprasidone dose. In the analysis of the SALSEX questionnaire, intragroup changes in the distribution of responses for each scale dimension were compared using a McNemar test for paired data. Intragroup changes in the SALSEX questionnaire total score were analyzed by a Student *t* test for paired data. All tests were 2 tailed and considered significant when $P < 0.05$.

Fifty-six of the 59 patients included in the study comprised the ITT sample: 41 in the switching subgroup and 15 in the initiating subgroup. Patients included in the study had a mean (SD) age of 34 (10) years, were mostly men (73%) with a diagnosis of schizophrenia (88%), and had a history of long disease duration (10 ± 8 years). Only one third of patients were married or had a stable partner. In the switching group, the most frequent

previous antipsychotic drugs were risperidone ($n = 22$, 54%) and olanzapine ($n = 12$, 29%). The mean (SD) final dose of ziprasidone were 120 (60) and 140 (32) mg/d for the initiating and switching subgroups, respectively.

At study initiation, 2 patients (13%) from the initiating subgroup and 37 patients (90%) from the switching subgroup reported sexual dysfunction of any type. Of these 39 patients, only 14 (36%) spontaneously reported these problems. In the initiating subgroup, a nonsignificant slight decrease in the SALSEX total score (ranging from 0 = no sexual dysfunction to 15 = maximum sexual dysfunction) was observed (3 ± 4.3 vs 1.6 ± 2.4 , $P = 0.240$); in the switching subgroup, a marked and significant decrease of the SALSEX total score was observed in male patients (9.2 ± 3.1 vs 4.2 ± 3.2 , $P < 0.0001$) but was less obvious in female patients (9.7 ± 3.3 vs 5.6 ± 4.1 , $P = 0.022$). At the end of the study, most patients from the initiating subgroup had not experienced any change in (53%) or had slightly improved (33%) their sexual function according to the CGI improvement of sexual function. On the contrary, 50% of patients in the switching group had much or very much improved their sexual function and 24% reported a slight improvement. No significant changes in any dimension were found in the initiating subgroup throughout the study during analysis of the dimensions of the SALSEX questionnaire (Fig. 1A). In the switching subgroup (Fig. 1B), significant improvements were observed in all dimensions of sexual function at the study end point.

Marked and significant decreases in the Brief Psychiatry Rating Scale total score and positive and negative symptoms cluster scores (data not shown) were observed throughout the study in both the initiating and switching subgroups. Thirty-eight patients (64.4%) experienced adverse effects throughout the study. The most frequent adverse effects included increased physical activity level (eg, restlessness and agitation; $n = 14$, 23.7%), disturbances in



*p = NS vs. baseline, †p < 0.05 vs. baseline, §p < 0.001 vs. baseline, McNemar test

FIGURE 1. Sexual functioning throughout the study as measured by the 5 dimensions of the PRSexDQ-SALSEX (ITT-LOCF analysis). A, Initiating[†] subgroup (n = 15). B, Switching subgroup (n = 41). **AQ2**

initiating and maintaining sleep (n = 11, 18.6%), anxiety symptoms (n = 9, 15.3%), and disturbances in consciousness (eg, somnolence) (n = 3, 5.1%). No adverse effects potentially related to hyperprolactinemia (eg, amenorrhea) or sexual dysfunction were reported.

DISCUSSION

Our results suggest that short-term ziprasidone treatment does not have a negative impact on the sexual function of patients with schizophrenia. Furthermore, in both male and female patients with sexual dysfunction related to the use of previous antipsychotic drugs, switching to ziprasidone seemed to be associated with a normalization of sexual function. The lack of impact on sexual function was suggested by results from the initiating subgroup, which showed

no significant changes in the SALSEX total score throughout the study. Additionally, the CGI improvement of sexual function measure confirmed that most patients (87%) from this group indicated no changes or a slight improvement of sexual function. These results are supported by the improvement of sexual function in the switch to ziprasidone patient subgroup.

The improvement of sexual function observed in the switching subgroup suggests that switching to ziprasidone may be a good therapeutic option for the management of antipsychotic-induced sexual dysfunction. However, these results should be considered with caution. The similar and good results over sexual functioning that we observed in a previous study with quetiapine⁷ were not confirmed by a pilot, randomized, and double-blind clinical trial that eval-

uated quetiapine as a substitute for patients with risperidone-related sexual dysfunction.⁸

Our study has several limitations, including the lack of a control group and, due to its observational design, the potential presence of confounding factors. Despite these limitations, our data suggest that ziprasidone does not negatively affect the sexual function of patients with schizophrenia, and that switching to ziprasidone may be a therapeutic option for the management of patients with sexual dysfunction induced by antipsychotic drugs. Both aspects should be confirmed by randomized clinical trials.

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(Valladolid), M. Franco (Zamora), M.T. Gallego (Salamanca), E. Goenaga (Cáceres), F. Gómez (Ávila), C. Iglesias (Asturias), O.M. Holm (Salamanca), N. Prieto (Salamanca), V. Romero (Logroño), S. Ros (Barcelona), I. Rubio (Cáceres), M. Sánchez (Ávila).

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AUTHOR DISCLOSURE INFORMATION

Dr Montejo has been a consultant for Lilly, GlaxoSmithKline, AstraZeneca, and Servier; has received grant research/support from Pfizer, Servier, GlaxoSmithKline, Lilly, Sanofi-Aventis, Lundbeck, and AstraZeneca; has received honoraria from Servier, Glaxo SmithKline, Lilly, SanofiAventis, Lundbeck, AstraZeneca, and Wyeth; and has been on speakers' bureau or advisory boards of Servier, Glaxo SmithKline, Lilly, Sanofi-Aventis, and AstraZeneca.

Dr Rico-Villademoros has served as a freelance consultant for Abbot Labo-

ratories SA, AstraZeneca Farmacéutica Spain, Biometria Médica, Cephalon Pharma SLU, Gilead Sciences, Ingenix Pharmaceutical Services, Laboratorios Casen-Fleet SLU, Pfizer SA, and Sanofi-Aventis SA.

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AQ4

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