International Journal of Impotence Research (2004) 0, 1–3

0955-9930/04 $30.00
www.nature.com/ijir

Original Research

A new atypical antipsychotic: quetiapine-induced sexual dysfunctions

M Atmaca[1]*, M Kuloglu[1] and E Tezcan[1]

[1]*Department of Psychiatry, School of Medicine, Firat University, Elazig, Turkey*

In this paper, we evaluated the new antipsychotic, quetiapine-induced sexual dysfunctions (SDs). The study group consisted of 36 patients with schizophrenia receiving quetiapine. The changes in general sexual functions were assessed by using Arizona Sexual Experience Scale (ASEX) and Udvalg for Kliniske Undersogelser (UKU) Side Effect Rating Scale at baseline and week 4. Also, prolactin (PRL) values were determined at baseline and week 4. There was statistically significant difference with respect to the mean ASEX score at week 4 compared with baseline. The most frequent SD was diminished libido in both male (31.8%) and female subjects (28.6%). No significant correlation was found between ASEX scores and PRL values. The results suggest that SDs are an important problem using even novel antipsychotic, quetiapine.
International Journal of Impotence Research (2004) **0,** 000–000. doi:10.1038/sj.ijir.3901260

Keywords: quetiapine; antipsychotic; sexual dysfunction

Introduction

Antipsychotics are used to treat numerous psychiatric disorders. There is strong evidence that important neurotransmitter systems affected by antipsychotics are involved in sexual functions.[1] Even novel, atypical antipsychotics are not free from such malevolent effects on sexual functions.[2]

Sexual side effects of antipsychotics are important since they reduce the clinical acceptability of these drugs. Although comparable rates of sexual side effects between typical antipsychotic, haloperidol and atypical antipsychotic clozapine have been reported,[2] distinct sexual adverse events might be expected when taking into consideration the difference in receptor-binding profiles between typical and atypical antipsychotics and even among atypical antipsychotics. In general, atypical antipsychotic agents have higher $5\text{-}HT_2 : D_2$ ratio when compared with typical antipsychotics. The main importance of this is that D_2 receptor antagonism may be related to PRL increase and consequently sexual dysfunction.[3] The frequent sexual side effects associated with conventional antipsychotics tend to be dose-related, and the primary underlying mechanism is likely to be the direct dopamine antagonist effect of this type of agent, with some additional indirect effects due to elevated PRL levels.[4] There are only few reports regarding both typical and atypical antipsychotic-associated SDs.[2,5,6] To the best of our knowledge, this is the first report of evaluating quetiapine-induced SDs the newest atypical antipsychotic in Turkey.

Method

A total of 36 heterosexual patients (22 male and 14 female subjects) ranging in age from 20 to 46 y were consecutively recruited to take part in the study. All were schizophrenic according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV).[7] Written informed consent was obtained from the subjects, after full explanation of the entire procedure. The study protocol was approved by the Local Ethics Committee of the Fırat University School of Medicine. All patients had at least 2 weeks drug-free period before the drug study was started. The exclusion criteria were the following: being over 50 y old, not using a reliable method of contraception, not having a steady sexual relationship with a partner, concurrent medical illness affecting sexual function, previous or current alcohol and

*Correspondence: M Atmaca, Firat (Euphrates) Universitesi, Firat Tip Merkezi, Psikiyatri Anabilim Dali, 23119 Elazig, Turkey.
E-mail: matmaca_p@yahoo.com
Accepted 8 April 2003

Gml : Ver 6.0
Template: Ver 1.2.2

Journal: IJIR | ☑ Disk used | Despatch Date: 16/7/2004
Article : npg_ijir_3901260 | Pages: 1–3 | OP: Sudhir Ed: Indira

substance abuse or dependence, the presence of any endocrinological state, receiving treatment with hormones or any other drug capable of interfering with sexual relations, requirement of concomitant drugs except for benzodiazepine derivates, or the presence of pregnancy, lactating or of child-bearing potential. To exclude the organic sexual dysfunctions, the fasting glucose level, urine analysis, complete blood count and sex hormones were obtained.

Quetiapine was started at the dose of 100 mg/day and titrated to 600 mg/day within 5 days. The changes in general sexual functions were assessed by using ASEX,[8] UKU Side Effect Rating Scale,[9] and Positive and Negative Syndrome Scale (PANSS)[10,11] at baseline and week 4. In addition, PRL values were determined at baseline and week 4.

Statistical analysis was performed using the statistical package for social sciences (SPSS/PC 9.05 version, 1998). Wilcoxon's and chi-square tests were used. In addition, a Regression to the Mean Analysis was performed.

Results

All but three patients completed the study. Three patients withdrew from the study due to requirement of additional drugs ($n=2$) or discontinuation because of intolerance ($n=1$). The mean age and duration of illness were 26.9 ± 4.3 and 4.2 ± 3.0 y, respectively. The mean dose of quetiapine was 512.7 ± 68.8 mg/day. The mean ASEX scores at the baseline and week 4 are presented in Figure 1. There was statistically significant difference with respect to the mean total score at week 4 compared with baseline ($r=0.49$, $P<0.05$).

The most frequent SD was diminished libido in both male ($n=7$, 31.8%) and female subjects ($n=4$, 28.6%), following erectile dysfunction in male ($n=5$, 22.7%) and amenorrhea in female subjects ($n=3$, 21.4%) at week 4. With respect to the proportion of SDs, there was a statistically higher rate in male ($n=13$, 59.9%) compared to female subjects ($n=6$, 42.9%) ($P<0.05$). The detailed gender differences in regard to sexual dysfunctions are presented in Table 1. The mean PANSS score was 87.7 ± 5.8, whereas it was 72.1 ± 5.5 at week 4 ($r=0.52$, $P<0.05$). The mean PRL values were 15.7 ± 4.0 ng/ml at baseline and 17.8 ± 5.7 ng/ml at the evaluation of week 4 ($r=0.19$, $P>0.05$). No significant correlations were found between the changes in ASEX scores and the changes in PRL values or those in PANSS scores ($r=0.13$, $P>0.05$ for PRL and $r=0.21$, $P>0.05$ for PANSS).

Discussion

Although this is an open-label investigation on quetiapine-induced SDs, some important conclusions can be extracted from the study. First, the patients enrolled in this study had relatively high ASEX scores at baseline after at least 2 weeks drug-free period. With respect to this subject, it has been reported that in untreated schizophrenic patients, negative symptoms such as anhedonia, lack of interest may contribute to the reduced sexual desire

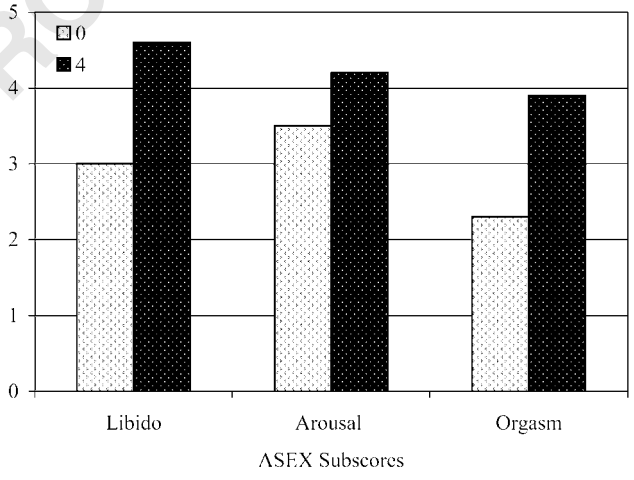

Figure 1 The mean ASEX subscores at baseline and week 4.

Table 1 The gender difference with respect to scale scores

	Male (n = *22*)		*Female* (n = *14*)		*Total* (n = *36*)	
	Baseline	*Week 4*	*Baseline*	*Week 4*	*Baseline*	*Week 4*
ASEX						
Libido	3.1 ± 1.4	4.5 ± 1.8	2.8 ± 0.8	4.8 ± 2.3	3.0 ± 1.1	4.6 ± 2.0
Arousal	3.8 ± 1.6	4.4 ± 2.1	3.1 ± 1.0	3.9 ± 1.5	3.5 ± 1.3	4.2 ± 1.8
Orgasm	2.0 ± 0.7	3.7 ± 1.0	2.5 ± 1.6	4.3 ± 1.5	2.3 ± 0.9	3.9 ± 1.2
PANSS	89.1 ± 6.3	73.7 ± 5.9	85.5 ± 4.9	69.6 ± 5.1	87.7 ± 5.8	72.1 ± 5.5

ASEX, Arizona Sexual Experience Scale; PANSS, Positive and Negative Syndrome Scale.

NPG.IJIR.3901260

and performance.[12] The main result of this study is that in contrast to what would be expected from its mode of action, quetiapine seems to be associated with comparable even higher rates of SDs with the prototypical conventional antipsychotic, haloperidol.[2,6] Quetiapine may be expected to be related to fewer SDs because of its weaker blockade of dopamine (D_2) receptors and its having minimal effect on serum PRL levels, as supported by the present study.[2] However, another atypical antipsychotic, clozapine, which has a similar receptor-binding profile and a similar effect with quetiapine on propensity of causing prolactinemia, has been also reported to have similar even higher rates of SDs when compared with haloperidol.[2,6] Antipsychotic-induced sexual dysfunction may be due to several mechanisms. All antipsychotic agents block dopamine D_2 receptors to varying degrees, causing impaired libido and erection.[13] In addition, nonspecific CNS effects of antipsychotics, such as sedation, can lead to reduced interest in sexual activity and a decrease in sexual functioning. In fact, quetiapine is a sedative atypical antipsychotic, with high affinity for $\alpha 1$ adrenergic and histamine H_1 receptors.[14] Serotonin mechanisms are also important to be considered in discussion of antipsychotic treatment and its relationship to SD. It has been reported that atypical antipsychotic medications produce a downregulation of 5-HT_2 receptors in the brain, but it is also possible that these drugs may produce sexual difficulties as a result of their action upon peripheral serotonin receptors.[15] The findings should be considered as preliminary and subject to some limitations. First of all, the sample is small. In addition, the present study was an open-label study and therefore had the restrictions of such a study design. Thus, comparative studies are needed in order to evaluate the findings of this study. Furthermore, the fact that no control group has been used makes it partly difficult to differentiate what effects are specifically due to the intervention alone.

In conclusion, the present study indicates that SDs are an important problem while using even a novel antipsychotic, quetiapine.

References

1 Gitlin MJ. Psychotropic medications and their effects on sexual function: diagnosis, biology and treatment approaches. *J Clin Psychiatry* 1994; **55**: 406–413.
2 Hummer M *et al.* Sexual disturbances during clozapine and haloperidol treatment for schizophrenia. *Am J Psychiatry* 1999; **156**: 631–633.
3 Hirsch SR, Link CGG, Goldstein JM, Arvanitis LA. ICI 204, 636: a new atypical antipsychotic drug. *Br J Psychiatry* 1996; **29**: 45–56.
4 Gitlin MJ. Psychotropic medications and their effects on sexual function: diagnosis, biology, and treatment approaches. *J Clin Psychiatry* 1994; **55**: 406–413.
5 Peacock L, Solgaard T, Lublin H, Gerlach J. Clozapine versus typical antipsychotics: a retro- and prospective study of extrapyramidal side effects. *Psychopharmacology* 1996; **124**: 188–196.
6 Mullen B, Brar JS, Vagnucci AH, Ganguli R. Frequency of sexual dysfunctions in patients with schizophrenia on haloperidol, clozapine or risperidone. *Schizophr Res* 2001; **48**: 155–158.
7 American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders* 4th edn. American Psychiatric Association Press: Washington, DC, 1994.
8 McGahuey CA *et al.* The Arizona Sexual Experience Scale: validity and reliability. Proceedings of the Annual meeting of the American Psychiatric Association, San Diego, May 17–22, 1997.
9 Lingjaerde O *et al.* The UKU Side Effect Rating Scale: a new comprehensive rating scale for psychotropic drugs and cross-sectional study of side effects in neuroleptic-treated patients. *Acta Psychiatr Scand* 1987; **334**: 1–100.
10 Andreasen NC. *Scale for the assessment of negative symptoms (SANS)* Department of Psychiatry College of Medicine, The University of Iowa, 1983. Q1
11 Andreasen NC. *Scale for the assessment of positive symptoms (SAPS)* Department of Psychiatry College of Medicine, The University of Iowa, 1984. Q2
12 Segraves RT. Psychiatric illness and sexual function. *Int J Impot Res* 1998; **10**: 131–140.
13 Collins AC, Kellner R. Neuroleptics and sexual functioning. *Integr Psychiatry* 1986; **4**: 96–108.
14 Saller CF, Salama AI. Seroquel: biochemical profile of a potential atypical antipsychotic. *Psychopharmacology* 1993; **112**: 285–292.
15 Cutler AJ. Sexual dysfunction and antipsychotic treatment. *Psychoneuroendocrinology* 2003; **28**: 69–82.

NPG.IJIR.3901260