A Randomized Open Label Comparison of the Effects of Risperidone and Haloperidol on Sexual Function

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Objective: Sexual dysfunction in patients who take antipsychotics causes a decline in their quality of life and medication acceptance. Considering the restrictions in cross sectional design of many earlier researches, we used a clinical trial aimed at assessing sexual dysfunction by substituting Risperidone, an atypical antipsychotic drug, with Haloperidol, a typical one .
Method: This clinical trial was conducted on 51 patients who had been using Risperidone with a minimum dose of 2 mg/daily for at least 2 months. The patients were randomly divided into 2 groups. The first group continued taking Risperidone, whereas the second group was given Haloperidol. Sexual function prior to and after the drug substitution was assessed using a sexual questionnaire designed to assess four stages of sexual function .
Results: Compared to those who changed their medication to Haloperidol, the patients who remained on Risperidone therapy suffered from more sexual dysfunction, especially in their tendency towards having sexual activities (P= 0.01), post menstrual sexual activity (P= 0.002), and reaching orgasm in their sexual activities (P= 0.04); however in the Haloperidol group, no significant difference was observed before and after the change in medication .
Conclusion: Although Risperidone and Haloperidol can both disturb patients' sexual function, the side effects of Risperidone are stronger. Hence to prevent the decline of medication acceptance or irregular consumption by patients which may lead to possible relapse, substitution of Risperidone with another drug with fewer side effects on sexual activities is definitely to the advantage of the patients .

Key words: *Adverse effects, Antipsychotic agents, Haloperidol, Risperidone, Sexual dysfunction*

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One of the strongest predictors of patients' unwillingness for drug consumption is their experience of drug side effects. The major side effect of antipsychotic drugs in both sexes is sexual dysfunction which leads to the deterioration of quality of life and a decline in treatment acceptance by the patients. Hence considering the nature of sexual dysfunction and its vital role in the patients' quality of life and their treatment acceptance, selecting a drug with the least side effects should be a priority(1).

Literature reports that both typical and atypical drugs like Haloperidol and Risperidone can affect sexual function adversely (1,2).

The 2006 Knegtering et al study, conducted on 46 patients, compared the effects of Olanzapine and Risperidone on sexual function and reported less sexual dysfunction in patients using the latter(3).

In 2006, Dossendbachm et al simultaneously evaluated the effects of typical and atypical antipsychotics on the sexual function of schizophrenic patients among the patients from the schizophrenia study centers in Austria and Australia, and found that sexual dysfunction in schizophrenic patients leads to deterioration in their life quality and a decline in their treatment acceptance.

Following a one-year period of the treatment, sexual dysfunction was found to be remarkably higher in the Risperidone and Haloperidol groups as compared to the Olanzapine and Queitiapine groups (2). However, the Bobesj et al study conducted in the psychiatry ward of the Spanish Oviedo University-teaching hospital indicated that no meaningful/significant differences in side effects were found /observed between the long-term side effects of typical (Haloperidol) and atypical antipsychotic drugs, including Risperidone (4).

In 2003, in Scotland, Hunter et al, through a systematic review of the data from 1980 to 2002, concluded that Risperidone is more effective than Haloperidol in improving the positive and negative signs, thereby decreasing the possibility of relapse within the first year following the treatment. However, Risperidone had less sexual side effects compared to Haloperidol, demonstrating that Rispridone is more acceptable for treating patients with schizophrenia than Haloperidol (5). Another systematic review conducted by Baggaley et al in England in 2008, reports that antipsychotic drugs are often accompanied by sexual side effects (30-80%), causing a deterioration in the quality of life; they concluded that a limited number of comparative studies have been conducted on the sexual side effects of antipsychotics, particularly the newer antipsychotics

which have not been extensively examined. This review concluded that in ranking order, the relative impact of antipsychotic on sexual function can be summarized as Risperidone, > typical antipsychotics Haloperidol > Olanzapine > Quetiapine > Aripiprazole (1).

In a 2002 prospective study, Wirshing et al compared the sexual dysfunction effects of Clozapine, Risperidone and Haloperidol-fluphenazine, used in a combined regimen and concluded that sexual side effects are prevalent for both typical and atypical drug categories, and they require further clinical consideration (6).

Considering the high prevalence and wide range of Risperidone use and lack of sufficient documented data on the sexual side effects of this drug, compared to typical antipsychotics, we examined the changes in side effects following the replacement of this drug by Haloperidol, a typical antipsychotic medication.

Materials and Methods

This study was approved by the Ethics Committee of Shahid Beheshti University of Medical Sciences. In this randomized clinical trial, after obtaining written informed consent, 64 married patients, aged between 18-48 years were studied. The patients had referred to the Imam Hossein and Ayatollah Taleghani hospitals (admitted or ambulatory) for psychiatric disorders (bipolar mood disorder, schizophrenia or schizoaffective disorder) and were under treatment with the minimum dose of Risperidone (2 mg) for at least two months.

Risperidone dosage was 2-6 mg . After randomization, the first group continued using their previous dose of Risperidone, while Risperidone was replaced by Haloperidol with an equivalent dosage (1mg of Risperidone is considered equivalent to 5mg of haloperidol) for the second group .

The number of patients was determined through the sample volume calculation formula where α=0.05 and β=0.2, considering 30% of the follow up loss. Prior to substituting the medication, approval was obtained from the treating physician.

The patients had no simultaneous medical disorders that could affect sexual function; they were not in the acute phase of their psychiatric disorder and were not taking any other drug that could affect their sexual function. The patients were divided into the two groups (32 patients each), the intervention and control, according to the Random Allocation method and sex blocking (one male and one female group). Risperidone was continued for eight weeks in the control group, whereas for patients of the intervention group, it was replaced by an equivalent dose of Haloperidol for eight weeks, following the physician's advice and obtaining the patients' consent.

In order to examine the sexual function of the patients, a questionnaire was designed based on the combination of the following validated questionnaires, appropriate for patients aged >18 years, containing questions on all four stages of the sexual function (sexual desire, excitement, orgasm and resolution); this questionnaire has been used in another study for which it had been validated(7):

- Arizona sexual experience scale (ASEX)
- Sexual Desires & Interest Inventory Female (SIDI-F)
- Female Sexual Function Index (FSFI)

To evaluate sexual function at the initiation of the study, demographic data were obtained and the questionnaires were filled out by the patients under the supervision of a physician unaware of the type of treatment. Following the follow up and meeting the patients after eight weeks, the questionnaires were again completed.

The statistical software of SPSS version 16 was used for data analysis. After the eight-week study period the patients of both the Risperidone and Haloperidol groups were compared using the Mann-Whitney test. Sign rank test was used for comparing the pre- and post-treatment results of the groups based on questions completed in the questionnaire.

Results

Fifty-one patients, 26 female (50.9%) and 25 male (49.1%), completed this study: 26 from the Risperidone and 25 from the Haloperidol group. The mean age, marriage duration and number of children were 32.5±2.25 years, 10.2±2.68 years and 1.04±0.31, respectively. Regarding literacy levels, 14.6% were below secondary school level, 58.3% at secondary school level and 27.1% at bachelor or higher levels. In the Risperidone group, pre- and post treatment results revealed meaningful differences in answers to six questions (Table 1), showing that patients who had continued to use Risperidone, experienced a more acute decline in their sexual function. For the other questions, there were no meaningful differences between the pre- and post Risperidone consumption results, viz. regarding feeling of disgust towards sexual activity, fear from sexual activity, feeling of pain during sexual activity, unwillingness for sexual activity, other ways to reach orgasm, fear of pregnancy, feeling of guilt in sexual activity, erection dysfunction, and premature ejaculation.

In the group for which Risperidone had been changed to Haloperidol, the pre- and post treatment results showed no significant differences compared to duration of Risperidone consumption, implying that Haloperidol consumption did not deteriorate the sexual function of the group who were previously on Risperidone.

Following the eight-week period of the study, the questionnaires of both groups were compared; responses to three questions showed significant differences, i.e. more sexual side effects for Risperidone; but there were no differences on other questions (Table 2). In fact, tendency towards sexual activity, sexual activity (post menstrual) and reaching orgasm in sexual activity were severely affected by Risperidone in both pre- and post treatment evaluations of the two groups.

Table 1. significant differences before and eight weeks after risperidone consumption

	None (%)		Mild (%)		Moderate (%)		Severe (%)		P
	Pre	post	Pre	post	Pre	post	Pre	post	
Number of sexual activities(weekly)	11.54	30.77	57.69	53.85	23.08	15.38	7.69	-	<0.001
Pain Imagination	84.62	65.38	11.54	26.92	3.85	3.85	-	3.85	0.01
Lubrication at the beginning of sexual activity	11.11	38.89	33.33	55.56	50	5.56	5.56	-	<0.001
Tendency to sexual activity	11.54	30.77	34.62	46.15	30.77	23.08	23.08	-	0.03
Tendency to Sexual Activity(post menstrual)	22.22	55.56	50	44.44	22.22	-	5.56		0.002
Reaching Orgasm in Sexual Activity	19.23	23.08	34.62	42.31	15.38	30.77	- 30.77	3.85	0.01

Table 2. Significant differences in results of haloperidol and risperidone groups, eight weeks after the treatment

	Z	Significant
Tendency to sexual activity	-20592	0001
Tendency to Sexual Activity(post menstural)	-3013	0.002
Reaching Orgasm in Sexual Activity	-20096	0004

Discussion

Considering the study findings, both Risperidone and Haloperidol adversely affect the sexual function of patients, and results indicate more sexual side effects for Risperidone than for Haloperidol. These findings are compatible with the 2006 study of Knegtering et al which also ***r***eported severe deterioration in sexual function in patients treated with Risperidone (3). Our results are also compatible with those of Baggaley, Bobesj et al, and Volavka et al studies which also showed a higher risk of sexual dysfunction for Risperidone, compared to Haloperidol (1,4,8). However, the findings of our study differed from those of Hunter et al, which concluded that sexual side effects of Risperidone did not differ that much compared to those occurring following Haloperidol use(5).

In a prospective study conducted by Wirshing et al, on three groups of patients using Clozapine, Risperidone and a Haloperidol-fluphenazine combined regimen, deterioration of sexual function was observed in all the three groups; most patients under Risperidone or Haloperidol treatment (40-71%) had sexual dysfunction, and libido reduction was significantly lower in the Clozapine group compared to the Risperidone group; erection disorder in the Risperidone group was higher than the Clozapine group and orgasm disorder was significantly lower in the Clozapine group. Results led to the conclusion that sexual side effects are prevalent in both new and typical drug categories, requiring further clinical consideration (6).

The limitations of the study include the manner of patient follow ups as well as the tendency of patients not to raise their complaints relating to sexual dysfunction, as they felt restrained due to cultural beliefs. Another limitation was the open label design, and the fact that we left the choice of the drug brand to be used open to the patient; all the patients preferred to use the Iranian brand of the drug; and the third limitation was that the prolactin levels were not checked.

In both pre- and post treatment evaluations of the two groups, the three conditions of tendency towards sexual activity, sexual activity (post menstrual) and reaching orgasm in sexual activity were greatly affected by Risperidone, leading eventually to the decrease in the acceptance of treatment and irregular consumption of the drugs by patients and consequently relapse, hindering or preventing recovery.

Considering the findings of the present study, Haloperidol, compared to Risperidone, seems to be a better drug in the sample studied. In addition, the increase in the sexual dysfunction of the patients treated by Risperidone makes it necessary to consider other drugs and their side effects. This issue, especially in our country, is of primal importance, due to the cultural limitations affecting people and the impact of the problem discussed on their quality of life.

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