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Evaluation of the effect of typical or Atypical Antipsychotic drug on sexual function in men with schizophrenia

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ABSTRACT

Sexual dysfunction secondary to antipsychotics may decrease the quality of life and therefore is an important item for measuring outcomes. Studies have reported different prevalence of sexual side effects caused by antipsychotic. The aim of this study was to evaluate the effects of typical and atypical antipsychotic drugs on sexual function in men with schizophrenia. A total of 98 schizophrenia men using typical and atypical antipsychotic drugs referred to Farabi Hospital of Kermanshah in 2016 enrolled in the study and BMSFI sexual function questionnaire was completed. The data then entered into SPSS statistical software (version 21) and the scores of each item and total scores were compared between two groups. To analyze the data, the statistical frequency, percentage, mean and standard deviation of test t-test was used. Of the 98 men enrolled in the study, 54 patients treated with typical, and 44 patients were treated with atypical antipsychotics. Sixty-seven men from 98 patients (68.36 percent) had sexual dysfunction. By comparing the average variations in the scores between typical and atypical drugs, a significant difference was only observed in terms of sexual desire between the two groups. But in other areas of sexual dysfunction did not differ significantly between two treatment groups. According to the results of this study, the prevalence of sexual dysfunction in schizophrenic patients treated with antipsychotic drugs is high. So, psychiatrists for treatment of psychological disease, particularly schizophrenia should consider sexual function and change the medication to control it to improve the patient's quality of life, if necessary.

KEYWORDS: *sexual dysfunction, schizophrenia, typical antipsychotic drugs, atypical antipsychotic Drugs*

INTRODUCTION

Schizophrenia is a clinical syndrome including variable but deeply destructive psychopathology that can affect cognition, emotion, perception, and other aspects of behavior [1]. Schizophrenia usually initiates before age 25 and remain stable until the end of life, and no social classes are immune from getting it [1, 2]. The prevalence of schizophrenia in the United States is about one percent. Annually, nearly 0.05 percent of the total population of the United States falls under the treatment of schizophrenia [2]. The prevalence of schizophrenia in men and women is equal, but the onset and course of the disease is different in the two sexes [3]. Schizophrenia starts in men sooner than women [1]. Antipsychotic drugs are the main basis for the treatment of schizophrenia. Such drugs can reduce the symptoms and recurrence rate of schizophrenia. About 70 percent of the patients who are treated with these drugs undergo a state of remission. The drugs utilized in the treatment of schizophrenia benefit from a wide variety of medicinal properties but their common point is postsynaptic dopamine receptor antagonism in the brain.

Antipsychotic drugs can be divided into two broad categories [4]:

Conventional antipsychotic drugs that are also called first-generation antipsychotic drugs or dopamine receptor antagonists.

The newer drugs that are called second-generation antipsychotic drugs or serotonin-dopamine antagonists (SDAs).

All first- and second-generation drugs can raise prolactin level. The long-term increase in release of prolactin leads to the suppression of gonadotropin releasing hormones, and consequently suppression of gonadal hormones. This condition in turn can affect sexual desire and sexual function of patients [5, 6]. Per the DSM-IV-TR, sexual dysfunction is a disorder of sexual response cycle or pain during sexual intercourse [7]. Sexual dysfunction in schizophrenia patients who receive antipsychotic treatment is higher than that of untreated patients [8]. Because the patients, especially those who suffer from schizophrenia, rarely complain of sexual dysfunction, the prevalence of this complication is less taken into account. Sexual dysfunction is a common complication in the patients receiving antipsychotic drug and is the most annoying symptom and side effect leading to a negative impact on health care admissions [9]. Secondary sexual dysfunction caused by antipsychotics may lower the quality of life and therefore is an important measure of treatment outcome [10]. So far, some studies have been performed on the subject that have had conflicting results. The body of research reports different prevalence of sexual side effects caused by antipsychotics. Some studies showed that there are not differences in the two antipsychotic drugs in terms of sexual complications. No comprehensive study in Iran has been yet performed on the effects of typical and atypical antipsychotic drugs on sexual function in the patients with schizophrenia. The current research seeks to present a comparative study of typical and atypical antipsychotic drugs on sexual function in male patients with schizophrenia in order to compare the effects of these drugs and to use the drugs with the minimum side effects on sexual function in patients with schizophrenia to be able to improve the admission of this group of patients and improve their quality of life.

METHODOLOGY

The current research is an analytical-descriptive study. The study population is comprised of all schizophrenia patients referred to Farabi Hospital in Kermanshah in 2014 who were treated with typical and atypical antipsychotic drugs, and 98 patients were selected according to inclusion and exclusion criteria as the sample. Inclusion criteria include all patients with schizophrenia that were diagnosed according to DSM IV-TR criteria by a psychiatrist, the patients who were referred to be treated for the first time, or the ones who at least six months were elapsed since stopping their drug treatment. The patient's age was ranged from 18 to 45 years old. Exclusion criteria include a history of organic diseases such as epilepsy, diabetes, liver or kidney failure, vascular diseases, hypothyroidism, concomitant use of antihypertensive, cardiac, endocrine, thyroid drugs, and some diseases such as depression, anxiety, and drug or medication abuse, need to receive ECT, and unwillingness to participate in the study. After the sample was selected, some explanations on the objectives of the study and implementation procedure were presented to the patients, and a written formal consent to participate in the study was obtained from them, and they were randomly divided into two groups. A group was treated with typical antipsychotic drugs including perphenazine, trifluoperazine, haloperidol, and another group with atypical antipsychotic drugs including olanzapine, risperidone, and aripiprazole. The consumption dose was also recorded to evaluate dose-related sexual dysfunction. BMSFI standard questionnaire was evaluated patients.

Brief Male Sexual Function Inventory (BMSFI):

The questionnaire contains 11 items that measure five aspects of sexual function including libido, erection, ejaculation, how to deal with the problems raised in sexual function in each of the relevant areas, and overall satisfaction. Each item is scored on a 5-option scale. Olery et al. [11] examined psychometric properties of the BSFI on the data obtained from the male subjects in a public medical clinic, and the males who complain of sexual dysfunction. Internal consistency coefficients for the questionnaire was ranged from 0.63 to 0.95 using Cronbach's alpha. Using test and retest procedure, the questionnaire's reliability for the different fields of sexual dysfunction within a period of one month was obtained to be 0.79 to 0.90.

For statistical analysis of the data, paired t-test and chi-square were used. The statistical significance level at all of the tests was considered to be 0.05.

FINDINGS

Out of 98 males participating in the study, 54 (55.1%) were treated with typical antipsychotics, and 44 (44.9%) treated with atypical antipsychotics. The most common medications used were olanzapine and perphenazine. The age range of the all of the males under study was 32.65±6.54 years old (age range of 20 to 45 years). The average age of the men taking typical antipsychotics was 33.93±6.41 years old, and the average age of the receptors of typical antipsychotics was 31.18±6.44. There was no significant difference between the two groups in terms of age (p=0.088). In terms of occupation, 75 patients (76.5%) were unemployed, 10 patients were (10.2%) farmer, 9 patients (2.9%) were rancher, and 4 patients (4.1%) were labor. 22.4% of the patients were illiterate.

Table 1 presents the average drop in the scores relevant to the different areas of male sexual function based on BMSFI. Average scores on all areas was dropped after taking medications for 3 months. By comparing the average variations in the scores between typical and atypical drugs, a significant difference was only observed in terms of sexual desire between the two groups, so that loss of libido in the typical treatment group was higher.

Table-1: Mean different areas of male sexual function scores in the group of typical and atypical

sexual function	Typical	Atypical	P value
Sexual drive	1.37 ± 1.27	0.89 ± 0.81	0.016
Problem assessment	2.13 ± 1.46	2.43 ± 1.79	0.254
Erections	2.39 ± 2.03	2.11± 1.76	0.338
Overall satisfaction	0.57 0.08±	0.41 ± 0.09	0.226
Ejaculations	1.50 ± 0.16	1.41 ± 0.19	0.594
Total score	7.94 ± 4.25	7.70 ± 4.01	0.402

Concerning the patients taking haloperidol, the rate of decline in sexual function was higher in terms of desire and how to deal with the problem, and among the patients taking fluoprazine, such rate was greater in terms of erection, sexual satisfaction, and ejaculation. Overall, the rate of decline in sexual function in haloperidol group was found to be at the highest, and the relevant rate in perphenazine group was the lowest.

Table-2: Mean different areas of male sexual function scores based on the type of drug

Sexual Function	Perphenazine	Haloperidol	Trifluoperazine	Risperidone	Olanzapine
Sexual drive	1.22 ± 1.18	1.67±1.28	1.39±1.22	0.63±0.59	1.03±0.86
Problem assessment	2.01 ± 1.66	2.27±1.17	1.33±0.86	2.40±1.54	2.45±1.93
Erections	2.38 ± 1.91	2.32±2.21	2.44±2.01	2.13±1.12	2.11±2.04
Overall satisfaction	0.59 ± 0.36	0.51±0.06	0.87±00.67	0.62±0.21	0.62±0.21
Ejaculations	1.44± 1.18	1.44±1.24	1.78±1.09	1.41±1.32	1.41±1.32
Total score	7.74±4.52	8.72±4.30	8.01±3.43	7.91±4.61	7.90±4.61

The average drop in the scores relevant to the various fields of male sexual function based on BMSFI after treatment was compared in Table 3 in terms of age group. There was not any significant difference between the males treated with typical and atypical medications in all age groups. In comparing all of the age groups, the average decline in the total score of the sexual function in the male receivers of the typical medications was higher at the age group 26 to 30 years, and among the male users of the atypical medications, this average was greater in the age group older than 40 years old.

Table-3: Mean different areas of male sexual function scores based on age range

Age Range	Sexual Function	Typical	Atypical	P Value
25≤	Sexual drive	1.01 ±0.57	0.44±0.24	0.350
	Problem assessment	1.01±0.43	2.67±1.41	0.024
	Erections	2.57±1.81	1.67±0.68	0.375
	Overall satisfaction	0.43±0.42	0.56±0.24	0.789
	Ejaculations	1.14±0.59	1.22±0.52	0.921
	Total score	6.14±4.37	8.78±6.92	0.396
26-30	Sexual drive	1.89±0.31	1.08±0.18	0.024

	Problem assessment	3.11± 1.16	2.15±1.19	0.254
	Erections	3.11±1.69	2.54±2.18	0.517
	Overall satisfaction	0.56±0.17	0.38±0.18	0.521
	Ejaculations	2.11±0.92	1.77±1.23	0.491
	Total score	10.78±2.53	3.27±7.92	0.060
31-35	Sexual drive	1.01±0.34	1.02± 0.86	0.994
	Problem assessment	1.93±1.68	2.89±2.08	0.238
	Erections	2.00±0.62	1.56±1.33	0.613
	Overall satisfaction	0.71±0.46	0.66±0.22	0.051
	Ejaculations	1.43±0.38	0.44±0.24	0.075
	Total score	7.00±5.08	6.11±1.96	0.624
36-40	Sexual drive	1.50±1.02	0.80±0.29	0.098
	Problem assessment	2.36±1.39	2.30±1.56	0.926
	Erections	2.07±1.61	2.00±0.81	0.925
	Overall satisfaction	0.57±0.17	0.50±0.16	0.777
	Ejaculations	1.29±0.91	1.70±1.25	0.358
	Total score	7.79±4.09	7.30±2.45	0.742
41≥	Sexual drive	1.50±0.47	1.33±0.66	0.865
	Problem assessment	2.01±1.24	2.00±1.57	0.984
	Erections	2.60±1.77	3.67±2.08	0.396
	Overall satisfaction	0.50±0.16	0.57±0.33	0.646
	Ejaculations	1.60±0.96	2.33±1.52	0.239
	Total score	8.20±3.82	9.67±4.72	0.589

According to Table 4, the average decline in the scores relevant to different fields of male sexual function based on BMSFI after typical and atypical treatment at different levels of education showed no significant difference. However, the average decline in the scores relevant to male sexual function at both groups of typical and atypical treatment among the males with education level of diploma and over diploma was lower than that of the other levels of education.

Table-4: Mean different areas of male sexual function scores based on level of education

Education	**Sexual Function**	**Typical**	**Atypical**	**P Value**
Illiterate	Sexual drive	1.13±0.35	0.67±0.42	0.459
	Problem assessment	2.47±1.30	2.01±1.09	0.449
	Erections	2.53±2.03	2.00±0.63	0.541
	Overall satisfaction	0.47±0.13	0.33±0.21	0.599
	Ejaculations	1.40±0.73	1.33±1.03	0.869
	Total score	8.01±4.17	6.33±1.03	0.353
	Sexual drive	1.62±1.29	1.16±0.80	0.140
	Problem assessment	2.04±1.24	2.40±2.04	0.440
	Erections	2.65±2.11	2.52±2.08	0.821
	Overall satisfaction	0.65±0.13	0.40±0.11	0.140

Under diploma	Ejaculations	1.46±1.39	1.88±1.33	0.279
	Total score	8.38±4.14	9.16±4.61	0.531
Diploma and higher	Sexual drive	1.15±0.98	0.46±0.14	0.035
	Problem assessment	1.92±0.56	2.69±1.70	0.304
	Erections	1.69±1.84	1.38±1.19	0.618
	Overall satisfaction	0.54±0.18	0.46±0.24	0.803
	Ejaculations	1.69±1.18	0.54±0.26	0.012
	Total score	7.00±4.74	5.54±1.98	0.316

CONCLUSION

Based on the results obtained from the current research, in terms of sexual function, no significant difference was observed between the two groups taking typical and atypical antipsychotics. Among all of the medications, haloperidol contributed to the maximum level of sexual dysfunction. Uptake of trifluoperazine is associated with more dysfunction in terms of erection, satisfaction, and ejaculation. The results obtained from the studies performed on the incidence of sexual dysfunctions caused by antipsychotic drugs are inconsistent in some cases. In a research performed by Mahmoud et al. (2011) it was shown that, in schizophrenic patients, second-generation (in comparison to first-generation) antipsychotics can significantly improve sexual function [12]. However, the same authors in a more comprehensive study performed in 2012 concluded that among the patients taking first- and second-generation antipsychotic drugs, there is no significant difference in terms of sexual function [13]. The two studies performed in China showed that administration of first-generation antipsychotics is one of the risk factors of sexual dysfunction [6, 14]. However, in another study performed in China, the second-generation antipsychotics were introduced as risk factor of sexual dysfunction [15]. Similar to the current research, Dossenbach et al in their study concluded that sexual dysfunction among the receivers of antipsychotics and risperidone was greater than that of the patients that consumed haloperidol [16]. In addition, the research performed by Oyekanmi et al indicated that the uptake of haloperidol was associated with the highest incidence of sexual dysfunction [17]. The review paper conducted by Baggaley indicated that, among antipsychotic drugs, risperidone and haloperidol had the highest rate of dysfunction disorders among antipsychotics, and aripiprazole had the lowest rate [10]. Unlike the results obtained from the current research, Bobes [9], Mousavi [18], and Nagaroj [19] in their study showed that sexual dysfunction in individuals taking risperidone is greater than that of haloperidol takers. A meta-analysis study performed by Serretti and Chiesa showed that there is an apparent difference between the two categories of the drugs enhancing and decreasing prolactin. Some drugs such as quetiapine, ziprasidone, perphenazine, and aripiprazole are associated with low levels of sexual dysfunction (16-27%), while olanzapine, risperidone, clozapine, and thioridazine are associated with higher rates of sexual dysfunction (40-60%). Antipsychotic drugs are associated with high rates of sexual dysfunction (40-60%) [20]. Antic psychotics with direct and indirect mechanisms can cause sexual dysfunction. Hyperprolactinemia is an important underlying cause of sexual dysfunction in the women and men receiving antipsychotics [16]. Antipsychotics (particularly first-generation antipsychotics, amisulpride, and risperidone) may cause hyperprolactinemia due to blocking D2 dopamine receptors [21]. Atypical antipsychotic drugs due to the effects of drowsiness may adversely affect the sexual activity. This process includes the blockage of dopaminergic and serotonergic receptors (5-HTA2A), antihistaminergic effects (block H1 receptors) and anticholinergic effects

(block muscarinic receptors). In treating the patients taking atypical antipsychotic drugs, symptoms of drowsiness that leads to decreased sexual activity should be taken into account [22, 23]. As aripirazole, sertindole, amisulpiride, and ziprasidone lack any anticholinergic and antihistaminergic effect, they do not show drowsiness symptoms. Thus, these drugs have lesser negative effects on sexual activity [24, 25]. Among various age groups of the patients under study, there was no significant difference between the males treated with typical or atypical drugs. Additionally, based on the results obtained from the current research, better sexual function was observed among the patients with diploma and over. Given that there is no similar comparative study performed on sexual function in the area of schizophrenia therapy in terms of age and education, it was not possible to compare the results obtained from the current research with those of other ones. Based on the results obtained from the current research, the frequency of sexual dysfunction in schizophrenic patients treated with antipsychotic drugs is high. In the research, haloperidol had the most sexual dysfunction among other medications. However, two categories of medications including typical and atypical antipsychotic ones had no significant difference. Thus, among the patients taking haloperidol, if sexual dysfunction leads to a decline in quality of life, it is recommended to change the treatment process and to take the drug that can have fewer sexual side effects. Based on previous studies, sexual problems and issues affect patients' quality of life. Accordingly, in the treatment of psychiatric disorders, especially schizophrenia, psychiatrists should underline sexual problems to be able to control or even change the medication to increase patient's tolerance to medication and enhance patient's quality of life.

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