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ORIGINAL ARTICLE

The effect of bupropion on sexual function in patients with Schizophrenia: A randomized clinical trial

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Abstract
Background and objective: About one percent of the world's population are affected by Schizophrenia. It is assumed that antipsychotic drugs cause sexual dysfunction, but the main mechanism of it, is not specified. Few researches that have addressed this issue showed that there is a relationship between neuroleptics and sexual dysfunction. A number of studies found that bupropion could improve the sexual dysfunction. So the purpose of this study is to investigate the effect of bupropion on sexual function of the patients with Schizophrenia.
Methods: This randomized clinical trial was performed on 40 schizophrenic patients admitted to Kamrani psychiatry clinic in Tehran during 2015–2016. Participants were randomly divided into two experimental and control groups. The experiment group was taken bupropion tablets 150 mg/day and the control group were given placebo for one-month. The sexual performance of participants was studied before and after the intervention by the sexual functioning questionnaire (SFQ). Obtained data were analyzed using the SPSS software with student t-test and chi-square tests.
Results: 40 patients older than 18 year old participated in the study. Before treatment the two groups did not have significant difference based on a general score of SFQ questionnaire, but There was a significant difference between two groups after the intervention. Experiment group (bupropion) showed significant improvement in sexual function. Using bupropion in the experiment group led to significant change in the score of sexual desire, erection and orgasm, but it had no effect on sexual arousal and ejaculation. The associations of ejaculation and orgasm were significance. Using the bupropion changed the erection and orgasm in the two groups of control and experimental.

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Conclusion: This study shows that 150 mg/day dose have considerable effect on sexual dysfunction of patients that are under treatment with anti-psychotic drugs. Also, this drug does not have any special side effects.

Introduction

More than 21 million people are affected by Schizophrenia around the world.[1] Schizophrenia is a mental disorder that its main characteristics are considerable dysfunctions in thought process, educational and occupational performance, disturbed sexual function, hallucinations, delusions, disorganized behavior and the weak emotional responses.[1–3] Symptom onset occurs at the adolescence and its prevalence is about 1 percent of the general population and its diagnosis is based on patient-reported experiences and observed behaviors.[3,4] Schizophrenia prevalence in men is 1.4 times more than women.[5] Patients with Schizophrenia have the 50% more risk for suffering diseases such as major depression, anxiety disorder and substance use disorder during their lifetime.[6]

Bupropion with commercial name of Wellbutrin and Zyban is an atypical antidepressant drug that usually is used to help quit smoking.[7] Causing less sexual dysfunction and weight gain, bupropion can compete with many other regular antidepressant medications. This drug has a good impact on cognition and improves sexual function. Patients taking bupropion have better feeling and can endure it better than other antidepressant medications.[8,9] Bupropion is prescribed for treatment of depression and nicotine addiction and its showed effective outcomes.[7,10] In patients with Schizophrenia, sexual dysfunction will occur as a result of depression, Anti-cholinergic and adrenergic side effects of antipsychotic drugs and smoking.[11–13] Incidence of disorders in sexual desire and in the psychophysiological changes related with the sexual response cycle in men and women is defined as Sexual dysfunctions.[14] The studies showed that sexual dysfunction prevalence in these patients is twice of the general population.[11]

Due to the considerable prevalence of Schizophrenia and the need for treatment of this disease with Antipsychotic drugs, evaluation and management of sexual dysfunction of these patients is an important matter that could improve their quality of life and plays a significant role in patient's adherence to treatment regimen. So, in this study the effect of bupropion on sexual function of the patients with Schizophrenia is studied.

Material and methods

This double blind, randomized clinical trial was performed on chronic Schizophrenia patients admitted to Kamrani psychiatry clinic in Tehran during 2015–2016. The inclusion criteria of participants were: having sex partner, being male, more than 18 years old age, being involved with Schizophrenia or its relapse in the past few years, not having a mood disorder, according to the DSM-IV-TR criterion, no change in patient medications in the last two months of the study start time, not having any other acute illness. Severe medical illnesses, like diabetes, hypertension, severe organ failure and other disorders affecting sexual performance, history of epilepsy and mental retardation were the exclusion criteria.

40 schizophrenic patients participated in the study, were randomly divided into two experimental and control groups based on the two right digits of their medical record number. This numbers were accessible only to authorized individuals who were not involved in the conduct or analysis of the study, until the time of un-blinding. The study designed blinded at the start of the study in the medication dispensing and each scheduled visits. Participants in the experiment group were taken bupropion tablets 150 mg daily and placebo tablets with the same size and color that were indistinguishable with the matching bupropions were given to the control group for one-month period of observation. Also all participants were to remain blinded to study until ending of the double-blind clinical data. The sexual performance of participants was studied before and after the intervention by the sexual functioning questionnaire (SFQ) which its purpose is to assess the effects of medication treatment on sexual function that after factor analysis and validity and reliability in Persian was divided into 5 groups of sexual desire, sexual arousal, erection, ejaculation and orgasm. Cronbach's alpha values were above the 0.70 threshold for all domains demonstrated high level of internal consistency reliability. *R* values for Pearson's correlation coefficient were from 0.81 to 0.91.[15] Obtained data were analyzed using the SPSS software with student t-test and chi-square tests.

Results

40 patients with different stages of the disorder, older than 18year old participated in the study. The different stages did not influence on the final results. The patients divided into control and experimental groups and compared based on the sexual function questionnaire. Before treatment the two groups did not have significant difference based on a general score of Sexual Functioning Questionnaire (SFQ) questionnaire. There was a significant difference between two groups after the intervention. Experiment group (bupropion) showed significant improvement in sexual function (Table 1).

Table 1 comparison of the SFQ questionnaire score before and after the treatment with Bupropion and placebo.

Study stages	Mean(±SD)		*p* value
	Placebo	Bupropion	
Before treatment	6.90 ± 2.44	5.05 ± 3.21	0.25
After treatment	8.10 ± 1.86	6.55 ± 2.81	0.02
p-value	0.08	0.04	

Using a placebo in the control group led to significant change in the erection score, but had no effect on the rest of the items. On the other hands, treatment with bupropion significantly changed the score of sexual desire, erection and orgasm, but had no effect on sexual arousal and ejaculation. Before the treatment the two groups were not in significant association in ejaculation and arousal but the associations of ejaculation and orgasm were significance. Using the bupropion changed the erection and orgasm in the two groups of control and experimental (Table 2).

Discussion

Schizophrenia is a disabling disease and antipsychotic drugs as the cornerstone of its treatment may cause sexual disability that increases the patient problems. Some studies have shown that an antidepressant drug bupropion can attenuate this disability.[16–19] To test this hypothesis in our study, 40 patients with Schizophrenia older than 18 years old were studied in two groups of placebo and bupropion.

The research showed that the bupropion has a significant positive impact on sexual dysfunction of patients compared to placebo. The results showed that the greatest effect of bupropion was on the erection and orgasm subscales and no significant changes showed in libido, sexual arousal and ejaculation before and after the study.

Studies related to effect of bupropion on the sexual performance of schizophrenic patients are scant, however the studies over this issue showed that it is better to prescribe bupropion for Schizophrenia patients to avoid sexual dysfunction.[12,20] The studies that investigate the mechanism of bupropion action, showed that this drug affects orgasm and could cause delays in orgasm and the improvement of ejaculation in men who have premature ejaculation problems.

A study has shown that using antidepressant drug could worsen the sexual dysfunction and by changing the drug with bupropion the orgasm will be improved. The study has shown that using the bupropion can be used in purpose of treatment of orgasm disorder.[21] These results are consistent with our study and it is shown that bupropion has a significant association with erection and orgasm, however bupropion was without effect on libido and sexual arousal.

In this study we used 150 mg bupropion per day, another study used 150 mg twice a day (300 mg) and obtained similar results to ours. The study showed that 300 mg bupropion had more effect on decreasing sexual dysfunctionality[11] however another study had used a 75 mg dose per day and obtained the similar results too.[16] In another study the standard therapeutic dose of bupropion (150 mg/day for the first 3 days, followed by 300 mg/day) administered orally to investigate the improvement of symptoms of Schizophrenia and it concluded the efficiency of the medication.[22] This can make it difficult to determine an appropriate dose for treatment of patient's sexual dysfunction. The mentioned studies did not mention that whether the effect of bupropion is related to dose or not and besides did not determine the amount of dose the side effect occurs.

Nevertheless, some studies that investigated the bupropion side effects in Schizophrenia patients showed that its side effects are negligible also we did not find any side effect related to taking bupropion. In a study in 2014 it was found that bupropion as a norepinephrine dopamine reuptake inhibitor, caused psychosis in a patient that had used bupropion for smoking cessation. This study considered the possibility of seizures and psychosis is likely to bupropion.[12]

Another study showed that bupropion cause elimination of psychotic symptoms and also worse the symptoms.[23] A study showed that the bupropion is psychogenic and patients who had these symptoms along with bupropion had taken other dopaminergic drugs. Also the study has concluded that mentioned side effect were transient and gone after discontinuation of the drug.[24]

So the results obtained from the studies, shows using bupropion must be wary and there is an urgent need for more studies to clarify the mechanism of the medicine. The strength of this study is that, the randomized clinical design is the leading strength of this study. Besides, the psychiatric health care system in Iran is based on Government, ensuring a representative sample of patients with Schizophrenia.

Table 2 comparison of different subgroups of SFQ questionnaire score between control and experimental group.

Variables	Mean(±SD)					
	Control group		*p* value	Experimental group		*p* value
	Before treatment	After placebo		Before treatment	After Bupropion	
Sexual desire	–	–		3.00 ± 0.7	1.4 ± 0.54	0.01
Sexual arousal	1.15 ± 0.81	1.10 ± 0.64	0.77	1.21 ± 0.69	1.14 ± 0.36	0.67
Erection	4.37 ± 1.45	3.37 ± 1.4	0.04	4.14 ± 1.06	1.57 ± 0.53	0.002
Ejaculation	0.30 ± 0.47	0.35 ± 0.48	0.57	0.92 ± 0.61	0.35 ± 0.48	0.13
Orgasm	1.50 ± 0.68	1.70 ± 0.73	0.38	0.90 ± 0.85	2.55 ± 0.88	0.001

There were some limitations in this study that may cause the results of this study non-generalizable. First was the few number of samples, even though we've held explanation sessions for all patients and all patients were given a full explanation, the conception of patients from the questionnaire may be different from the practitioner conception so the answers of the patient may not be accurate. Another limitation is that most of the questionnaires are translated to Persian language and may have had a lower cultural adaptation specially in sexual matters so that the majority of respondents to this study generally did not totally respond any answer to some questionnaire items.

Another limitation of this study was time limits on the duration of the study so that it made us unable to trace bupropion effects on patients in medium-term and long-term. The last point is that different doses of the drug to achieve minimum effective dose with minimal side effects has not been investigated that is important because of the effect of bupropion on dopamine pathways.

So we propose doing more controlled studies with larger sample size and longer time of follow-ups to have results with higher accuracy and efficiency and also these studies should be done with simple questionnaires and for Psychiatric patients that among them are patients with low literacy so that the results will be more accurate.

Also, several studies with a different usage of bupropion doses should be done to find the minimum effective dose of bupropion and to what extent can raise the dose of the drug to prevent the serious side effects such as psychosis and seizure.

Conclusion

This study shows that a daily 150 mg dose has considerable effect on sexual dysfunction patients with Schizophrenia that are under treatment with anti-psychotic drugs. Also, this drug does not have any special side effects.

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Authors contributions

Study design: OR. Data synthesis: MSN and BA. Drafting the manuscript: MAP and FF. Critical revision of the manuscript: OR and MSN.

Conflict of interests

All authors have no conflicts of interest to be declared.

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