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THE EFFECT OF OLANZAPINE AND SERTRALINE ON PERSONALITY DISORDER IN PATIENTS WITH METHADONE MAINTENANCE THERAPY

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SUMMARY

Background: *Various drugs have been suggested for treatment of Borderline Personality Disorder (BPD)-a disabling disease affecting two percent of the general population. If a drug could alleviate a wide range of symptoms, it would be more suitable. In these disorders drug addiction is very common. This fact makes the symptoms complicated and the treatment more difficult.*

Subjects and methods: *This study is designed to evaluate the effect of Olanzapine and Sertraline in patients suffering from personality disorders who are on methadone maintenance therapy. This study is a clinical trial. 120 males and females were chosen for methadone maintenance therapy through interview by a psychiatrist based on DSM-IV-TR diagnostic criteria for BPD. Afterwards they were randomly divided into two groups. These groups separately received Olanzapine (5-10 mg daily) and Sertraline (50-100 mg daily) therapy. The SCL-90 questionnaire was filled by all participants before treatment and at the 4^{th}, 8^{th} and 12^{th} weeks of treatment.*

Results: *According to this clinical trial, Olanzapine and Sertraline are effective in ameliorating symptoms of depression, anxiety and aggression, reducing sensitivity in interpersonal relationships and alleviating obsessive symptoms, pessimistic behaviors and somatization disorders in patients with personality disorders on methadone maintenance therapy.*

Conclusion: *As result of this study it appears that Olanzapine and Sertraline are definitely effective in alleviating symptoms of patients with personality disorder, prescribing theses drugs are recommended for these patients.*

Key words: *borderline personality disorder - methadone maintenance therapy – Olanzapine - Sertraline*

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INTRODUCTION

Co-existing mental disorders among substance abusers, especially Heroin, is a therapeutic-predictive factor. Cluster B personality disorders are among the most common co-morbidities (35-60%) with the worst prognosis. The treatment of these co occurring diseases can lead to improved patient function, stability in methadone maintenance therapy and improvement of symptoms such as aggression, depression and self-mutilation. Increase in methadone dosage in theses patients in comparison with patients without co occurring disorders, does not ameliorate symptoms of personality disorders and often may cause them to discontinue their methadone therapy and consequent recurrence of drug addiction. In the present study, we attempted to evaluate the effect of Olanzapine and Sertraline on these patients (Skodol et al. 1999).

The more broadly a drug can cover the spectrum of symptoms, the more appropriate it can be considered. Substance abuse is often in close correlation with other psychiatric disorders such as anxiety disorder and personality disorders (especially cluster B-Borderline and anti social personality disorders). Diagnosis and treatment of comorbid conditions in substance abusers has been considered during the past 10 (Frei & Rehm 2002).

Unraveling the relationship between drug abuse and other psychiatric disorders is fundamental in order to clarify the type of treatment and prognosis. One of the factors that can help physicians to identify substance abusers with a higher chance of recurrence is the presence of any co occurring psychiatric disorder. In this way, high-risk patients can be managed more appropriately (Darke et al. 2004; Sullivan et al. 2005). Understanding the correlation between psychiatric disorders and substance abuse is helpful in the selection of a better treatment as well as in prevention. Frontal and peri-frontal lobe dysfunctions can lead to impairment of self-assessment and self-control. This fact indicates that there may be a relationship between substance abuse and personality disorders (Chakroun et al. 2004; Kathleen & Rajita 2005). A research study in 2003 showed that men with psychiatric disorders such as antisocial personality disorders or depression are more prone to a drug abuse (Gerra et al. 2004).The results of a study in 1999 designed to evaluate the co occurrence of BPD and substance abuse demonstrated that patients suffering from BPD who are not on any

kind of treatment are more likely to become drug abusers (Gerra et al. 2006).

Patients suffering from psychological disorders and a co-occurring substance abuse problem should receive simultaneous treatment for both disorders. These parallel treatments can cure the main problem and also help patients to stop taking illicit drugs. This would not only prevent disease recurrence, but also would alleviate detrimental symptoms. Most rehabilitation centers have programs to decrease psychiatric symptoms in addition to their plans to help patients to stop drugs (Centre for Addiction and Mental Health, 2009). The co occurrence of cluster B personality disorders and heroin abuse is reported to be 35-60%. BPD is characterized by a widespread disturbance in interpersonal relationships, mood and self-image in addition to symptoms of aggression and instability. Although psychotherapy has been useful to improve patient function, there is no doubt in the effectiveness of drug therapy in ameliorating symptoms related to the personality (Bellino et al. 2008). Psychopathologies which are considered as treatment goals are mood dis-regulation, aggressive behavior and cognitive symptoms. Antidepressants and mood stabilizers have been used for the treatment of the first two problems and anti psychotics are used to treat cognitive symptoms (Skodol et al. 1999).

SUBJECTS AND METHODS

This study is a clinical trial. The patients being investigated were all suffering from BPD and on methadone maintenance therapy (MMT). The diagnosis was confirmed by an expert psychiatrist according to DSM-IV-TR criteria. The induction and stabilization processes of their MMT were completed successfully. In spite of adjustment of methadone dose, the symptoms of aggression, depression and self-mutilation continued. The patients did not suffer from any kind of axis I disorders or other somatic disorders such as hepatitis or AIDS.

According to the sample size formula, 120 males and females on MMT with a diagnosis of BPD were chosen and randomly placed in two groups in which they received either Olanzapine (5-10 mg daily) or Sertraline (50-100 mg daily). This clinical trial was granted an approval from Medical Ethics Committee at Lorestan Medical University on 12/04/2007. All participants consented to this trial. All data was gathered through interviewing by a psychiatrist using the SCL-90 questionnaire. This standard questionnaire evaluates the following nine items: somatization, depression, anxiety, obsession and aggression, hypersensitivity in interpersonal relationship, pessimistic behavior, psychotic symptoms and phobias. The SCL-90 questionnaire was filled in by all participants before treatment and in 4^{th}, 8^{th} and 12^{th} weeks of treatment.

In addition to the nine-item covered in the questionnaire other items such as self-mutilation behaviors, dose of methadone and number of negative urine samples in 4^{th}, 8^{th} and 12^{th} weeks of treatment were used to compare these two groups. Data was processed by SPSS software. Descriptive statistics and repeated measure of Friedman's test were used in order to describe frequencies and to compare data respectively.

RESULTS

Among the patients in the Sertraline group, there were 83.3% females and 16.7% males with a mean age of 28 years. 45% of them were single, 43.3% were divorced or widows and the rest (11.7%) were married. In regard to education, 56.7% were uneducated, 33.3% and 8.3% had high-school diploma and higher education respectively.

In the Olanzapine group, there were 81.7% females and 18.3% males with a mean age of 26 years. 36.7% of them were single, 45% were divorced or widows and the rest (18.3%) were married. In regard to education, 6.7% were uneducated, 48.3% had some kind of education (below high school diploma). 36.7% and 8.3% had high-school diploma and higher education, respectively. The mean duration of addiction was 3.3 and 2.2 years in Sertraline and Olanzapine groups, respectively.

In evaluation of SCL-90 questionnaire before treatment in the sertraline group the mean scores of the nine items were as follows: somatization disorders 2.18, OCD 1.35, hypersensitivity in interpersonal relationship 3.30, depression 2.61, anxiety 2.45, aggression 3.26, phobias 1.89, paranoia 2.07, and psychotic symptoms 1.42. In the Olanzapine group the mean scores of the similar items were: somatization disorders 2.18, OCD 1.33, hypersensitivity in interpersonal relationships 3.30, depression 2.64, anxiety 2.43, aggression 3.28, phobias 1.76, paranoia 2.05, and psychotic symptoms 1.63.

The mean scores in the first, second and the third month of treatment reduced in both groups. According to the statistical tests, there was a statistically significant difference in the mean scores of both groups before and after treatment in the 1^{st}, 2^{nd}, and 3^{rd} months of treatment (Table 1).

Similarly, comparison of both drugs in regard to decreasing symptoms of depression and anxiety, demonstrated that both drugs can generally ameliorate depression and anxiety in a 12-week treatment ($P<0.05$), nevertheless, sertraline was more effective in decreasing symptoms of depression ($P=0.017$) while olanzapine was more useful for anxiety ($P=0.00$) (Table 1).

Both drugs were capable of decreasing hypersensitivity in interpersonal relationships and aggression ($P<0.05$). Olanzapine was more useful in decreasing aggression ($P=0.025$) and sertraline was more effective

in decreasing hypersensitivity in interpersonal relationships (P=0.015) (Table 1).

Paranoia symptoms more effectively decreased by olanzapine (P=0.04) (Table 1). Both drugs could effectively decrease obsession and somatization symptoms. Sertraline was more effective than olanzapine in ameliorating obsession (P=0.016) but there was no difference in decreasing somatization symptoms between both drugs (P=0.9) (Table 1).

Table 1. Mean scores of the nine items in SCL-90 questionnaire in different study phases (before treatment, 4, 8, and 12 weeks after treatment) in olanzapine and sertraline groups

Study phase / Symptom	Before treatment Mean± SD		4 weeks after treatment Mean± SD		8 weeks after treatment Mean± SD		12 weeks after treatment Mean± SD		P-value
	Sertraline group	Olanzapine group	Sertraline group	Olanzapine group	Sertraline group	Olanzapine group	Sertraline group	Olanzapine group	0.000*
Depression	2.61±0.48	2.64±0.47	2.36±0.45	2.43±0.44	2.05±0.47	2.32±0.40	1.82±0.43	2.19±0.39	
Anxiety	2.45±0.53	2.43±0.49	2.32±0.52	2.01±0.53	2.23±0.55	1.79±0.50	2.14±0.56	1.56±0.46	
Aggression	3.26±0.50	3.28±0.47	2.90±0.49	2.74±0.44	2.63±0.47	2.40±0.40	2.38±0.46	2.05±0.39	
Hypersensitivity in interpersonal relation	3.30±0.50	3.30±0.50	2.99±0.47	2.87±0.54	2.78±0.43	2.50±0.53	2.56±0.44	2.14±0.44	
Obsession	1.35±0.50	1.33±0.49	1.18±0.43	1.27±0.48	1.08±0.39	1.24±0.46	0.97±0.34	1.17±0.47	
Paranoia	2.07±0.65	2.05±0.65	1.93±0.58	1.68±0.56	1.85±0.55	1.47±0.47	1.74±0.53	1.25±0.43	
Somatization	2.18±0.50	2.18±0.50	1.96±0.45	1.96±0.47	1.80±0.45	1.80±0.45	1.60±0.41	1.60±0.41	
Psychosis	1.42±0.60	1.63±0.59	1.48±1.25	1.36±0.52	1.28±0.52	1.18±0.44	1.21±0.49	1.05±0.39	
Phobia	1.89±0.65	1.47±0.65	1.70±0.59	1.62±0.65	1.60±0.58	1.60±0.58	1.47±0.55	1.54±0.60	

SD: Standard Deviation; *There was a significant difference in mean scores of both groups (olanzapine and sertraline) before and after treatment in the 1st, 2nd, and 3rd months of treatment

At the end of 12 weeks of treatment, there was no difference between these two groups in rate of negative urine samples (P=0.07). In regard to self mutilation, there was a significant difference (P<0.001). In the olanzapine group, self mutilation behaviors were reduced significantly in comparison to the sertraline group. The mean methadone dose in the olanzapine group was 9.7 and 7.6 before and after treatment, respectively. In the sertraline group, the mean methadone dose was 9.3 and 8.7 before and after treatment, respectively.

DISCUSSION

According to the results of this clinical trial, it seems that sertraline and olanzapine are effective in ameliorating symptoms of depression, anxiety and aggression, reducing hypersensitivity in interpersonal relationships and alleviating obsessive symptoms, pessimistic behaviors and somatization disorders in patients with BPD who are on methadone maintenance therapy. As olanzapine, in comparison to sertraline, was shown to be more effective in many tasks such as reducing symptoms of anxiety, hypersensitivity, aggression, paranoia, depression and obsession, it is preferred. In one double-blinded study by Linehan in 2008, olanzapine was added to psychotherapy. The study demonstrated that olanzapine can effectively reduce aggression in patients (Linehan et al. 2008).

Another clinical trial designed to clarify the effects of various drugs on BPD in 2008, showed that among mood stabilizers and anti-depressants, serotonin-dopamine antagonists are be preferred (Bellino et al. 2008). In another investigation on patients suffering from BPD with severe aggressive behavior, one single intramuscular injection of olanzapine definitely reduced aggression so that only 16% of them required an additional injection.

The effect of single fluoxetine or olanzapine therapy compared to combination therapy in BPD was investigated in a study in 2004. Results showed that using combination therapy will lead to a better outcome. Moreover, in 2004 the superiority of olanzapine to placebo in the treatment of BPD was reported (Akerele & Levin 2007). Additionally, in 2001 a low-dose of olanzapine was reported to reduce self-mutilation behaviours (Hough 2001). In a study in 2001 on female patients suffering from BPD, olanzapine (5-10 mg daily) was shown to alleviate a wide range of symptoms such as mood and cognition symptoms, self-mutilation like behaviours and interpersonal relationship abnormalities (Zanarini & Frankenberg 2001). In a study in 2001, the effects of Sertraline and imipramine were compared in patients with BPD and disthymia. Results showed that disthymia and personality problems were ameliorated (Hellerstein et al. 2000). In another study in 2002, the therapeutic effects of fluoxetine on BPD were investigated. Although it was effective on mood changes, no effect was shown on aggression and hypersensitivity (Compton et al. 2003). Gerra demonstrated the effect of olanzapine on aggression in heroin dependent patients in 2006. Olanzapine led to decreased aggression (Akerele & Levin 2007). Additionally, in

another study in 2007 a comparison between the effects of olanzapine and risperidone on heroin addicts suffering from schizophrenia showed that olanzapine is potentially more useful for the treatment of both problems (Gerra et al. 2007). According to the previous studies and this clinical trial showing that olanzapine is preferable to sertraline; psychiatrists should consider serotonin-dopamine antagonists as the main therapy or in combination with other drugs for treating BPD patients on Methadone therapy.

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