



ISSN No: 2319-5886

International Journal of Medical Research & Health Sciences, 2016, 5, 9S:282-287

The effect of adding Pregabalin to Conventional Treatment in schizophrenia Patients, for improving Positive, negative and general symptoms of These Patient

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ABSTRACT

Schizophrenia is a complex and heterogeneous disorder, with multiple, and varying symptoms. For this very reason it cannot be distinguished based on inherent disorder process, effects of medication therapy, or continuous long-term hospitalization. To date, much effort has been made to identify drugs, effective in the treatment of its symptoms. Yet, despite great progress made in this path, treatment of these symptoms has not had any significant success. Thus, the aim of the present study is to examine the effect of adding the drug Pregabalin to the customary drugs of the patients with schizophrenia for improvement in positive, negative, and general signs of these patients. The method used, in this study, was quasi-experimental. The type of objective was functional, having pre-test – post-test design, with a control group. The population, in the study, consisted of 60 schizophrenic patients, hospitalized in the serenity center, who had been diagnosed according to the standards of DSM – 5, and were placed on a fixed dose, of customary medications, for a minimum of 2 months. 30 individuals were selected according to random table, and, on that basis, were placed in two groups of test and control, with 15 members each. The measurement instrument used was PANSS. Pre-test was performed by having all 30 patients filling out the PANSS questionnaire. Then, Pregabalin (50 mg.) was administered, to the test group, two times a day, for a period of 6 weeks. No medication was added to that of the control group. Following a two-week period, both groups were reassessed using PANSS test. The obtained results were analyzed using covariance analysis, using SPSS software. Results of the study indicated that adding Pregabalin did not result in improvement in any of the symptoms (positive, negative, general, agitation, anxiety, and depression) in schizophrenia patients. The study results indicated that although symptoms (positive, negative, general, agitation, anxiety, and depression) were lowered in patients with schizophrenia, but this decline was not significant, and no significant difference was observed between the two groups of test and control.

Key words: schizophrenia, Pregabalin, positive and negative symptoms, general symptoms

INTRODUCTION

A group of disorders in which the protagonist fall completely scrambled, distorted reality and a person will find favor with schizophrenia is functioning in everyday life. The disorder affects about 1% of the population, the incidence is similar in men and women, usually in their late teens and early adulthood has become apparent. Starting in most cases was between 15 and 35 years of age (Hylgard, 2006), based on positive and negative symptoms of schizophrenia are divided into two types 1 and 2. In patients with type 1 mainly positive symptoms that include hallucinations, delusions and strange behavior and impaired thinking form, the structure of the brain CT scan is normal and relatively good response to treatment and in patients with predominantly negative symptoms of type 2

are slowing emotional states, aphasia, passivity, apathy. There is a lack of attention and structural brain abnormalities seen on the CT scan and response to treatment is not a good time (Parsa Moin, 2010). Fortunately, in recent years, with the changes that occurred in the field of research and treatment of schizophrenia. At the heart of many patients and families glimmer of hope is the spark. However, existing drugs used to treat these patients was associated with only partial results in improving psychotic symptoms and the effect of these drugs on the symptoms of schizophrenia is positive. This means that the severity of delusions and hallucinations may reduce or completely prevent them. People are stimulated to calm patients and disturbing and aggressive behaviors decrease. Most of the withdrawal apathy and other negative symptoms are less effective. Therefore, finding ways to improve and reduce the effective treatment of mental health issues is the inability of these patients (Tayebi, 2009).

Schizophrenia is as a result of very high activity of dopaminergic. The most famous enhancing drugs dopaminergic activity amphetamines. Excessive release of dopamine in people is strongly positively associated with psychotic symptoms of schizophrenia (Sadock et al, 2015). The effects of antipsychotic drugs in this way are that these drugs bind to dopamine receptors. Of adhering to these receptors, inhibit dopamine. When dopamine is blocked, positive symptoms are also blocked, which resulted in significant improvement in cognitive and behavioral. Chlorpromazine and haloperidol while it seems to affect only the positive symptoms, negative symptoms with clozapine treatment success and seem to be in a place where other treatments are immaterial, the drug is effective (Breslin, 1992; quoted in Roznahan et al, 2008). Antipsychotic drugs have unpleasant side effects often cause patients to stop taking them. For example, among the side effects of chlorpromazine (Torazin) as this include dry mouth and throat, drowsiness, visual disturbances, increased or decreased weight, menstrual disorders, constipation and depression (Roznahan et al, 2008).

Drugs mentioned in previous research mainly on positive symptoms, but unfortunately the effect on the negative symptoms and cognitive symptoms and schizophrenia in particular have considerable influence. In other words, these drugs increase the cost of disorders that cause disability and they do not cure the disease, however, these drugs have serious side effects and sometimes annoying. It given that drug treatment for negative symptoms and cognitive needs to try new drugs are still not ideal (Poormohammad, 2013). The results Nunes et al (2012) as the effect of pregabalin on behavioral changes induced by ketamine in rats showed that pregabalin effects of ketamine could be useful in return. The results showed that pregabalin could be used as the adjuvant in the treatment of behavioral changes as a result of schizophrenia considered. The results of some research in the journal Biological Psychiatry world was published in 2012, adding pregabalin medications to reduce symptoms of schizophrenia, positive and negative symptoms of schizophrenia was advised. The results also Englisch et al (2012) in his study of schizophrenia patients with pregabalin showed strengthen add pregabalin in the treatment of schizophrenia and other drugs that can reduce the positive symptoms, negative and general help these patients.

Is an anticonvulsant drug pregabalin in neuropathic pain and as an adjunctive therapy in partial seizures in adults. The drug such as gabapentin, the voltage-dependent calcium channels and causes the release of neurotransmitters in the cerebrospinal fluid attached, such as glutamate and noradrenaline. Gabapentin, pregabalin, is similar in terms of pharmacological. The drug appears to inhibit the release of excitatory neurotransmitters too, and thereby exerts its medicinal properties. The drug increases levels of GABA in neurons, and combining its drive shaft combining gabapentin six times and its half-life is longer (Sadock et al, 2015). Therefore, and due to research activities in this area in this research question is whether pregabalin in improving positive symptoms, negative and schizophrenia affect public or not?

MATERIALS AND METHODS

Research Methodology

The control variable, quasi-experimental and terms of purpose, is applied. Scheme used in this study pretest - posttest control group. Pretest - posttest control group is composed of two groups. Both groups were measured twice. The first measure by implementing a pre-test before treatment, and the second measurement was performed after the treatment period required.

The population, sample size and sampling

The study sample consists of all schizophrenic patients at the center of the 60 people who were relaxed entry criteria, 45 patients (according to DSM-5 criteria for schizophrenia, were detected on a fixed dose of common drugs for at least 2 months old) had to study. In terms of the location of available sampling and sample selection (schizophrenic patients) were randomized as follows:

Of which 60 had schizophrenia patients Inclusion criteria for the study were 45 people and based on randomly selected 30 patients in two groups of 15 individuals were placed on the same basis. In this study, the minimum number of samples was used. The sample size consisted of 30 patients with schizophrenia. 15 patients were in the experimental group and 15 patients in the control group.

Measuring tool

The instrument used in this study, positive and negative symptoms of schizophrenia PANSS (Positive and Negative Syndrome Scale). The questionnaire has 30 questions and 5 elements and subjects over a five-item scale for even, occasionally, medium, high and very high responds to it. These factors include negative symptom questionnaire (questions 1 to 9) symptoms (questions 10 to 15), positive symptoms (questions 16 and 21), signs of agitation (questions 21 to 25) and the symptoms of anxiety and depression (questions 26 to 30). The first questionnaire by Kay, Opler & Fiszbein (1987) for comprehensive evaluation of the symptoms of schizophrenia was made. However, much research has been done about it. In 1990, the square and to identify the factor authentication PANSS, it carried out on 240 patients with schizophrenia and positive and negative syndromes identified two factors that specific values in order of 7.08 and 3.74, which could explain 36 percent of the total variance of schizophrenia. In this study, Cronbach's alpha for this scale was obtained 0.95 is acceptable (Ghamari Givi *et al.*, 2010).

Research method

Among the schizophrenic patients relaxation center that meets the criteria of DSM-5 were detected, 60 patients who met the study inclusion criteria, 45 patients out of the 45 cases, 30 were selected based on random numbers table and accordingly divided in 15 groups. Selected patients by a psychiatrist and a clinical psychologist experienced by the scale (PANSS) (for negative and positive symptoms and general psychopathology of schizophrenia) at baseline were evaluated. Pregabalin 50 mg, 2 times a day for 6 weeks was added to the experimental group and control group members, there was no drug added. After a 2-week period in both groups by test PANSS, were re-evaluated. Research data based on quantitative data (numbers) were collected, to analyze the data; SPSS software version 21 was used.

RESULTS

All the research data examined descriptively. Described data in two parts is done. The first part describes the demographic variables and then describes the research variables.

Table 1: Demographic characteristics of subjects in each group

Variables	Variable levels	Examination group		Control group	
		Pretest (N = 15)	Posttest (N = 14)	Pretest (N = 15)	Posttest (N = 14)
Age (M ± SD)	does not have	14.783 ± 48.60	15.141 ± 49.21	10.183 ± 42.60	9.819 ± 43.57
Education (prevalence)	Low Diploma	7	6	8	7
	Diploma	7	7	5	5
	Associate Degree	0	0	2	2
	Bachelor	1	1	0	0
Marital status (frequency)	Single	11	11	11	10
	Married	3	2	1	1
	Divorced	1	1	3	3

Table 2 shows the mean and standard deviation positive symptoms, negative, public, agitation, anxiety and depression in patients with schizophrenia show two experimental and control groups.

Table 2: describes the variables using mean and standard deviation

Variables	Examination group		Control group	
	Pretest (N = 15)	Posttest (N = 14)	Pretest (N = 15)	Posttest (N = 14)
Negative Symptoms of Schizophrenia	5.240 ± 20.80	4.999 ± 13.93	8.053 ± 21	5.244 ± 14.43
Constitutional symptoms of schizophrenia	4.507 ± 18.20	4.940 ± 12.36	5.725 ± 16.73	4.448 ± 13.36
Positive symptoms of schizophrenia	6.556 ± 14.53	3.483 ± 8.86	5.557 ± 13.80	4.046 ± 10.71
Stimulate the symptoms of schizophrenia	1.952 ± 7.33	1.787 ± 6.50	2.473 ± 8.60	3.006 ± 7.50
Symptoms of anxiety and depression in patients with schizophrenia	5.071 ± 11	2.786 ± 7.93	4.938 ± 10.33	2.585 ± 7.71

In Table 3 Kolmogorov-Smirnov test results shows the distribution of positive symptoms, negative, public, agitation, anxiety and depression in patients with schizophrenia groups (control and test) is normal (0.05 < p).

Table 3: Kolmogorov - Smirnov Results

Variables	Group	P	
		Pre-test	Posttest
Negative Symptoms of Schizophrenia Constitutional symptoms of schizophrenia	Control	0.891	0.762
	Experiment	0.940	0.501
Positive symptoms of schizophrenia Stimulate the symptoms of schizophrenia	Control	0.884	0.609
	Experiment	0.688	0.341
Symptoms of anxiety and depression in patients with schizophrenia Variables	Control	0.468	0.845
	Experiment	0.266	0.492
Negative Symptoms of Schizophrenia	Control	0.877	0.186
	Experiment	0.806	0.461
Constitutional symptoms of schizophrenia	Control	0.323	0.753
	Experiment	0.654	0.618

In Table 4 Levin results show that assuming there variances for two experimental and control groups ($0.05 < p$).

Table 4: results of the homogeneity of variances

Variables	Group	Levene	Sig.
Negative Symptoms of Schizophrenia	Control	0.649	0.436
	Experiment	1.681	0.219
Constitutional symptoms of schizophrenia Positive symptoms of schizophrenia	Control	0.047	0.832
	Experiment	0.601	0.451
Stimulate the symptoms of schizophrenia	Control	0.306	0.590
	Experiment	4.402	0.058
Variables	Control	4.354	0.059
	Experiment	1.829	0.201
Negative Symptoms of Schizophrenia	Control	0.623	0.445
	Experiment	0.008	0.932

Now, according to adhere to the default of covariance, we study the Inferential statistics.

Table 5 Results of the analysis of covariance to the positive symptoms of schizophrenia is given.

Table 5: Table analysis of covariance to the positive symptoms of schizophrenia

Source	Total Square Type III	df	average of squares	F	Sig.	Eta Chi minor
Modified	25.018	2	12.509	0.846	0.441	0.063
Intercept	374.774	1	374.774	25.343	0.001	0.503
pretest positive signs	0.875	1	0.875	0.059	0.810	0.002
Group	24.602	1	24.602	1.664	0.209	0.062
Error	369.696	25	14.788			
Total	3076	28				
Total modified	394.714	27				

The solid line shows the random variable adjuvant (pre-test positive symptoms) are significantly dependent variable (post-test negative symptoms) are related. The next line indicates that the group has no significant effect on the dependent variable. After adjustment for pretest scores, significant effect between subjects factor (partial Eta squared = 0.062, 0.209 = significance level, 1.664 = F) groups. Thus, according to the results of this table, pregabalin improves the positive symptoms of schizophrenia are not.

Table 6 Results of the analysis of covariance for negative symptoms of schizophrenia is given.

Table 6: analysis of covariance for the negative symptoms of schizophrenia patients

Source	Total Square Type III	df	average of squares	F	Sig.	Eta Chi minor
Modified	123.974	2	61.987	2.767	0.082	0.181
Intercept	150.244	1	150.244	6.706	0.016	0.211
pretest positive signs	122.224	1	122.224	5.455	0.028	0.179
Group	0.374	1	0.374	0.017	0.898	0.001
Error	560.133	25	22.405			
Total	6313	28				
Total modified	684.107	27				

The solid line shows the random variable adjuvant (pre-test negative symptoms) was significantly dependent variable (post-test negative symptoms) are related. The next line indicates that the group has no significant effect on the dependent variable. After adjustment for pretest scores, significant effect between subjects factor (partial Eta

squared = 0.001, 0.898 = significance level, 0.017 = F) group. Thus, according to the results of this table, pregabalin improves the negative symptoms of schizophrenia.

Table 7 Results of the analysis of covariance for Constitutional symptoms of schizophrenia is given.

Table 7: Table analysis of covariance for Constitutional symptoms of schizophrenia

Source	Total Square Type III	df	average of squares	F	Sig.	Eta Chi minor
Modified	41.082	2	20.541	0.950	0.400	0.71/0
Intercept	173.548	1	173.548	8.029	0.009	0.243
pretest positive signs	34.082	1	34.082	1.577	0.221	0.059
Group	10.779	1	10.779	0.499	0.487	0.020
Error	540.347	25	21.614			
Total	5210	28				
Total modified	581.429	27				

The solid line shows the random variable adjuvant (pre-test symptoms) was significantly dependent variable (post-test negative symptoms) are related. The next line indicates that the group has no significant effect on the dependent variable. After adjustment for pretest scores, significant effect between subjects factor (0.020 = partial Eta square, significance level = 0.487, 0.499 = F) group. Thus, according to this study, pregabalin improves symptoms in patients with schizophrenia.

Table 8 Results of the analysis of covariance for signs of agitation in patients with schizophrenia is given.

Table 8: Table analysis of covariance for signs of agitation in patients with schizophrenia

Source	Total Square Type III	df	average of squares	F	Sig.	Eta Chi minor
Modified	19.630	2	9.815	1.676	0.207	0.118
Intercept	42.917	1	42.917	7.330	0.012	0.227
pretest positive signs	12.630	1	12.630	2.157	0.154	0.079
Group	2.586	1	2.586	0.442	0.512	0.017
Error	146.370	25	5.855			
Total	1538	28				
Total modified	166	27				

The solid line shows the random variable adjuvant (pre-test excitation signals) are significantly dependent variable (post-test negative symptoms) are related. The next line indicates that the group has no significant effect on the dependent variable. After adjustment for pretest scores, significant effect between subjects factor (partial Eta squared = 0.017, 0.512 = significance level, 0.442 = F) group. Thus, according to this study, pregabalin improves symptoms of schizophrenia patients are not motivated.

Table 9 Results of the analysis of covariance for symptoms of anxiety and depression in patients with schizophrenia is given.

Table 9: Table analysis of covariance for symptoms of anxiety and depression in patients with schizophrenia

Table 9 Results of the analysis of covariance for symptoms of anxiety and depression in patients with schizophrenia is given.

Table 9: Table analysis of covariance for symptoms of anxiety and depression in patients with schizophrenia

Source	Total Square Type III	df	average of squares	F	Sig.	Eta Chi minor
Modified	3.775	2	1.888	0.256	0.776	0.020
Intercept	227.876	1	227.876	30.906	0.001	0.553
pretest positive signs	3.454	1	3.454	0.468	0.500	0.018
Group	0.371	1	0.371	0.050	0.824	0.002
Error	184.332	25	7.373			
Total	1901	28				
Total modified	188.107	27				

The solid line shows the random variable adjuvant (Pre-test anxiety and depressive symptoms) was significantly dependent variable (post-test negative symptoms) are related. The next line indicates that the group has no significant effect on the dependent variable. After adjustment for Pre-test scores, significant effect between subjects factor (partial Eta squared = 0.002, 0.824 = significance level, 0.050 = F) group. Thus, according to this study, pregabalin improves symptoms of anxiety and depression in patients with schizophrenia.

CONCLUSION

The aim of this study was to evaluate the effect of the drug pregabalin in patients with schizophrenia drugs to improve the positive symptoms, negative and general patients. Subjects of this study, 30 patients with schizophrenia (according to DSM-5 criteria were diagnosed) that a fixed dose of common drugs for at least two months. The cases of all schizophrenic patients at the center of peace, based on a random numbers table and on the basis of 15 people in two groups (control and test) were assigned. However, research continues because of the death of one person control group and experimental group were due to the withdrawal of one of the 14-member, research and finished with 28. Selected patients by a psychiatrist and a clinical psychologist experienced by the scale (PANSS) to examine research hypotheses at baseline were examined. 50 mg pregabalin, 2 times a day for 6 weeks was added to the experimental group and control group members, there was no drug added. After a 2-week period in both groups by test PANSS, were re-evaluated. The results showed that although the positive symptoms scores in both experimental and control groups reduced, but this reduction was not statistically significant. The results also showed that although there are negative symptoms after adding the drug pregabalin but the differences between the experimental and control groups was not statistically significant. The results showed that although symptoms of schizophrenia in the post-test in both groups were reduced but this decline is not significant and there is no meaningful difference in symptoms between the two groups means. Results showed signs of agitation in schizophrenic patients in the post-test, although slightly down but the differences are not significant and pregabalin improves symptoms of schizophrenia patients are not motivated. In the end, the result of the effect of adding drugs to improve the symptoms of anxiety and depression in patients with schizophrenia showed that pregabalin. Although the amount of these symptoms at post-test and improvement can be seen below but this decline is not significant and meaningful difference between experimental and control groups in symptoms of anxiety and depression is observed. In general explained that the results of these hypotheses is not in line with past research it can be noted that patients in the center (relaxation) of patients had chronic who has spent the acute phase of the disease and we also had some ability to control the research criteria.

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