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Research Article

Role of antioxidants in the management of Schizophrenia: a Randomized Control Trail

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ABSTRACT

Objectives: To explore the role and compare the effects of antioxidants (vitamin C & E) in the management of schizophrenia.

Materials & Methods: 105 patients were selected and assigned into 03 groups by simple random method. For 08 weeks, group-1 was intervened with 500 mg vitamin C tablet on daily basis, Group-2 received 600 IU vitamin E twice daily and Group-3 was administered with a placebo capsule daily. PANSS scale was used to assess the severity of schizophrenia before and after intervention. Demographic information was collected by using a structured questionnaire.

Results: Paired T-test was applied to measure the mean difference of before and after intervention, which was found significant in 1st group symptoms as (P-value=0.299) and Two-way ANOVA was applied for comparison of three groups which is statistically significant (p-value <0.05).There was no major difference in frequency of food intake among the three groups, before and after intervention None of the subjects was using vitamins supplements.

Conclusion: The role of selected antioxidants as added treatment with antipsychotics was significant and improved the schizophrenia symptoms in 1st and 2nd group as compared to 3rd.

Recommendations: Antioxidants can be confidently prescribed as added treatment in the management of schizophrenia. Further studies on other antioxidants are recommended to explore their effect on schizophrenia.

Keywords: Antioxidant; Schizophrenia; Positive symptoms; Negative symptoms; Oxidative stress

INTRODUCTION

Schizophrenia is one of the leading mental disorders. The global burden of schizophrenia is on the rise. Certain psychological factors like stressful and emotional life events, physiological reasons such as oxidative stress, immune system activation and genetic disorders play a significant role in escalated prevalence of schizophrenia. [1]According to World Health Organization fact sheet (April-2018) twenty one million people have been affected from schizophrenia around the globe. The prevalence rate of schizophrenia in Pakistan has been observed as 1.5/100 [2]. The incidence is on the higher side in men than women and age of onset in men is early as well [3]. Peak age for onset of schizophrenia range from 20-28 years among men and 26–32 years among women [4]. Childhood onset is very rare [5]. For the diagnosis of schizophrenia, psychotic symptoms must be prominently present for at least a month. These symptoms are also related to decrease in social and occupational functioning. The symptoms of schizophrenia vary from person to person, but are broadly classified into positive and negative symptoms. The positive symptoms imply adding signs which are not normally present but appear in schizophrenic patients such as hallucinations and delusions. Hallucination can be one or more of all five senses like visual, auditory, olfactory, gustatory, and tactile. However, most common hallucination is experienced in the auditory sense [6]. Whenever, delusions directed to converted thought such as misinterpretations of one's perceptions or experiences. Furthermore, behavioral deviations commonly present with disorganized speech and distortions in behavior. While, negative symptoms are the behaviors normally present but are absent or diminished in a person with schizophrenia such as apathy or flat mood, loss of pleasure, and poverty of speech. Moreover, speech content may have reduced complexity or it becomes empty [7]. Diagnosis of schizophrenia is only made on clinical assessment. Positive and Negative Symptoms Scale (PANSS) is widely used by psychiatrists for schizophrenia diagnosis [8].

Despite an advancement in therapeutic interventions, still recov-

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ery is compromised as schizophrenia affects between 0.5-1.5% of the world's population [7]. The effects of this disease are devastating as the illness tends to be deteriorating with increased disability, elevated personal and societal burden which may have negative effects on academic and vocational capabilities [9]. Survival of schizophrenia patients is likely to be poorer in developing countries due to late diagnosis and limited access to timely and standardized treatment [10]. Reduced levels of vitamins and resultant oxidative stress has been implicated in the pathophysiology of schizophrenia and can have domino effect on psychiatric symptoms in many people. Patients with psychiatric disorders having vitamins deficiencies are often presented with more warning signs and decreased effect of antipsychotic drugs [11]. The treatment of schizophrenia, by dopamine D2 receptors antagonists is reported inadequate compounded with unfavorable effects [12]. Whereas, use of Vitamin C & E as add on treatment has been found effective in improving the psychopathology of chronic-medicated schizophrenic patients [13]. There is also an evidence that antioxidants like vitamin C and E, Omega a-3 fatty acid, Melatonin, Hydroxyl Tyrosol enhanced neuroprotection[14]. Furthermore, supplementation of vitamin C and E adjuvant antipsychotic therapy in the management of psychotic disorders like schizophrenia has also been proved effective as decrease in the severity of symptoms is observed in certain studies [15].

Another study demonstrated that long-term use of vitamin C and E had better impact on cognitive functions of the subjects as compared to subjects who had never used vitamin C or E [16]. Moreover, in a randomized, controlled trial, it was recognized that the baseline plasma ascorbic acid was considerably reversed in study group than the control group. The researchers of the study also stated that symptomatic outcomes were notably improved in study group [17]. Another; double blind placebo controlled 8 weeks study also revealed that use of antioxidant vitamin C 500mg once a day with antipsychotic drugs remained effective [18]. While, deficiency of Vitamin C deteriorated the symptoms of schizophrenia. However, use of this vitamin in large doses improved the condition of patients with schizophrenia.

Although the results of previous studies conducted worldwide are promising but still controversial in dissimilar background. Thus, the current study was first in its nature in Pakistan which was intended to assess the role of antioxidants (Vitamin C and E) in the management of schizophrenia & to compare the effects of vitamin C and E in the management of schizophrenic patients.

MATERIALS AND METHODS

Study Design and Duration

Randomized Control Trial (RCT)

Duration: Eight weeks

Sampling Technique

Simple Random Lottery Method

Inclusion Criteria

All diagnosed schizophrenic patients 20-50 years of age who visited department of psychiatry and behavioral sciences King Edward medical university Lahore was included.

Exclusion Criteria

Patients having any other pathological condition like hypertension, hyperlipidemia and cardiac disorders were excluded.

Sample Size

105 patients who fulfilled inclusion & exclusion criteria were enrolled

Study Population

All patients diagnosed with Schizophrenia

Study Setting

Department of psychiatry & behavioural sciences, King Edward medical university Lahore

Randomization

From April 27, 2017 to May 15, 2017, total 105 patients diagnosed with schizophrenia by psychiatrist according to diagnostic statistical manual 4th edition text revision (DSM-iv-TR) were selected. Participants were divided into three groups, 35 patients in each (1st group (Vitamin C), 2nd group (Vitamin E) and 3rd group (Placebo group).

Clinical Assessment and Research Tool

Subjects were selected on first visit according to inclusion and exclusion criteria. Structured questionnaire was used for participant's demographic information. Information was collected by face to face interview in local language. Positive and Negative Syndrome Scale (PANSS) was used to measure symptoms of schizophrenia. Evaluations were performed before and after intervention by using PANSS.

Supplementation with Selected Antioxidants (Vitamin C and E) and placebo

1st group was supplemented with Tablet Vitamin C 500mg once a day. 2nd group was given 600 IU vitamin E capsules twice daily and3rd group was administered with500mg paraffin oil capsule once daily.

RESULTS

The data was collected in the light of major objectives i.e. to assess the role of vitamin C and E and comparisons of this role in the management of schizophrenia Paired T test was applied to measure the mean difference of findings of before and after intervention.

Vitamin C group pre and post intervention PANSS Positive, negative and general psychopathology symptoms

Level of Significance=($p< 0.05$) reveals mean differences between vitamin C group PANSS positive, negative & general psychopathology symptoms(pre-intervention and post intervention). Paired T test found significant difference in all three groups as vitamin C group PANSS positive symptoms paired mean difference was 11.73 ± 6.51 (P value 0.000); mean difference of Vitamin C group PANSS negative symptoms was 12.83+3.591(P value .000) and the paired mean difference of general psychopathological symptoms was17.23+11.349(P value 0 .000)

Vitamin E pre and post intervention PANSS positive, negative and general psychopathology symptoms

Level of Significance=($p< 0.05$) reveals mean differences between vitamin E group PANSS positive, negative & general psychopathology Symptoms (pre-intervention and post intervention).

Paired T test found significant difference in all three groups as vitamin E group PANSS positive symptoms paired mean difference was13.25 ± 5.11 (P value 0.000); mean difference of Vitamin E group PANSS negative symptoms was10.58 ± 4.264(P value 0.000) and the paired mean difference of general psychopathological symptoms was12.51 ± 9.01 (P=value 0.000).

Placebo pre and post intervention PANSS positive, negative and general psychopathology symptoms

Level of Significance=(p< =0.05) reveals mean differences of Placebo group PANSS positive, negative & general psychopathology Symptoms (pre-intervention and post intervention). Paired T test found significant difference in placebo group PANSS positive symptoms as paired Mean difference was 2.363 ± 4.35 (P value >.004).While, the mean difference of placebo group PANSS negative symptoms and PANSS general psychopathological was found insignificant as Paired T test found insignificant difference for PANSS negative symptoms with Mean ± SD 2.30 ± 5.264 (P value >0.017) and for PANSS general psychopathological Mean ± SD 1.72 ± 9.401 (P value>0.299).

Comparison between pre and post vitamin C and E PANSS positive, negative and gen. psychopathological symptoms

reveals comparison between vitamin C and E groups, vitamin C is found more effective in PANSS negative and general psychopathological symptoms decline as compare to vitamin E with paired mean differences 12.83 ± 3.591, 10.58 ± 4.264 and17.23 ± 11.34, and 12.51 ± 9.014 respectively. But vitamin E is found to be significant in PANSS positive symptoms reduction with paired mean difference 13.25 ± 5.111 as compared to vitamin C with paired mean difference11.73 ± 6.51.

Statistical determination of dependence among three groups (1st, vitamin c) (2nd vitamin e) and (3rd, placebo)

Table 1 shows that the statistical significance of independent variables in the two-way analysis of variance using the Wald statistic. Vitamin C & E were statistically significantly different from placebo (p-value < 0.05). Whereas, Vitamin E & C were not found statistically significantly different from each other (p-value > 0.05).

Table 1: Analysis of Vitamin C Group Pre & Post Intervention PANSS Positive, negative &general psychopathology Symptoms.

GROUP	Paired samples statistics	Paired difference	Sig. (2-tailed)
	Mean ±S.D	Mean +SD	
Vitamin C pre-intervention PANSS positive symptoms score ranking .7-49	24.43+7.242	11.73+6.51	0
Vitamin C post-intervention PANSS positive symptoms score ranking.7-49 01-07-1949	12.70+3.761		
Vitamin C pre-intervention PANSS negative symptoms score ranking 01-07-1949	24.36+4.958	12.83+3.59	0
Vitamin C post-intervention PANSS negative symptoms score ranking 7-49	11.53+2.944		
Vitamin C pre-intervention psychopathology scores,16-112	39.93+16.1638	17.23+11.35	0
Vitamin C pre-intervention PANSS General	22.70+6.696		
Vitamin C post-intervention PANSS General psychopathology scores,16-112			

DISCUSSION

There is increasing evidence that oxidative stress is associated with major neuro-psychiatric disorders. Evidence-based interventions play an important role to restructure oxidative damage for improving clinical manifestation. Earlier international studies confirmed that use of antioxidants with antipsychotic drugs enhances neuro-protection and have favorable effects on cognitive function.[16]Although previous literature has provided paramount evidence about the effective use of antioxidants as add on treatment of schizophrenia but still there was a dire need of conducting research in demanding areas like Pakistan where the treatment options and compliance, and psycho-social attributes of population are different than other advanced countries. The current study proved the positive role of antioxidants (vitamin C and E) in the management of schizophrenia.

In current study PANSS (Positive and Negative Symptoms Scale) was used to measure the severity of schizophrenic symptoms before and after intervention of selected antioxidants. Paired T test was applied, and mean differences was found significant in vitamin C&E group's PANSS positive, negative & general Psychopathological Symptoms. While, in Placebo group mean difference was found insignificant in negative symptoms and general psychopathological symptoms but in positive symptoms mean difference remained significant.

Thus, the current study provided evidence that supplementation of vitamin C and E with antipsychotic drugs in the management of schizophrenia are effective in decreasing the severity of schizophrenia symptoms.

The results of current study are aligned with previous study13that

found significant association between vitamin C& E with schizophrenia symptoms as severity of symptom decreased after intervention of selected antioxidants. Another RCT [20] also supported the findings of present study as it explored that vitamins (C+E) improved the recovery. In addition, the results of current study are also in line with previous literature19documenting that Vitamin C found to be effective in the management of schizophrenia as deficiency of Vitamin C deteriorated the symptoms of schizophrenia. Similarly, the results of current study are also supported by previous RCT 21thatdiscovered positive effects of vitamin E supplementation in patients treated with haloperidol depot injection.

In comparison of Vitamin C and E group, Vitamin C group PANSS scores had greater mean difference of before and after intervention. Although, the findings of current study represented that the use of Vitamin C & E in combination with antipsychotic drugs reduced severity of schizophrenic symptoms, but Vitamin C showed greater effects as compared to Vitamin E. Previous literature has also endorsed the reduction of an oxidative stress and better outcomes of schizophrenia in Vitamin C supplementation as compared to Vitamin E in term of clinical manifestation [19,20].

CONCLUSION

The antioxidants (Vitamin C and E) as add on treatment with antipsychotics was found effective as supplementation of the two improved the PANSS positive, negative, and psychopathological symptoms of schizophrenia and effect of vitamin C was even better in reducing an oxidative stress and improving health status.

DISCLAIMER

None.

CONFLICTS OF INTEREST

None.

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