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EFFECTS OF ANTIPSYCHOTIC DRUGS ALONE VERSUS ANTIPSYCHOTIC DRUGS IN COMBINATION WITH VITAMIN D AND VITAMIN E ON LIPID PROFILE LEVELS OF PSYCHIATRIC DISORDER PATIENTS-----A RANDOMIZED CONTROLLED TRIAL.

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ABSTRACT

BACKGROUND: A psychological disorder poses a greater risk of all-cause of deaths at earlier stages of life[1]. According to epidemiological research, people with mental illnesses have a 7 to 24 year lower life expectancy, which is a bigger toll than heavy smoking**. METHODOLOGY:** The study had comprised of n=140 individuals who had mental problems and were deficient in both vitamin D and vitamin E. All individuals had been taking antipsychotic drugs on a consistent basis for at least two months previous to the commencement of the research, and their antipsychotic doses remained constant throughout the study. **RESULTS**: The analyses of the findings had revealed that participants in the Risperidone group had substantially higher levels of Total Cholesterol after antidepressant administration (235.26±35.37 vs. 157.09±16.34 mg/dL; $p<0.0001$). When compared to other treatment groups, the mean value of Total Cholesterol was considerably lower ($p<0.05$) in the group receiving Quetiapine coupled with Vitamin E and Vitamin D. Regarding efficacy, the treatment groups receiving Olanzapine, Risperidone, Quetiapine, Olanzapine combined with Vitamin E and Vitamin D, and Risperidone combined with Vitamin E and Vitamin D did not show any significant effects on the Total Cholesterol levels of patients (208.06±34.32 vs. 229.31±37.59 vs. 178.86±25.23 vs. 178.11±20.72 mg/dL, respectively). **CONCLUSION:** In conclusion, the study's findings demonstrated that risperidone usage was related with higher levels of total cholesterol and lower levels of high-density lipoprotein (HDL) compared to the control group. When quetiapine was coupled with vitamins E and D, total cholesterol and low-density lipoprotein (LDL) levels were significantly reduced. Furthermore, when individuals in the risperidone group were given with vitamin E and vitamin D, their triglyceride levels were lower.

KEYWORDS: Dyslipidemia, antipsychotic agents and vitamins

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INTRODUCTION

Psychological disorders pose a greater risk of all-cause of deaths at earlier stages of life[1]. According to epidemiological research, people with mental illnesses have a 7 to 24 year lower life expectancy, which is a bigger toll than heavy smoking[2]. Physical comorbidities, particularly cardiovascular diseases (CVDs), are responsible for approximately 60% of the higher mortality found in mental patients[3-4]. Various mental illnesses, such as depression, schizophrenia, bipolar disorder (BD), and anxiety disorder, have been linked to dramatically elevated risks of CVDs and related comorbidities such diabetes, stroke, and obesity[5]. To assess the risk increased risk of CVDs among psychiatric illness patients a concept of metabolic syndrome (MetS) was

developed to help doctors identify and manage people at high risk of cardiovascular disease (CVD) [6]. MetS is defined by a number of characteristics, including abdominal obesity (central obesity), high blood pressure, low levels of high-density lipoprotein cholesterol (HDL-C), raised triglycerides, and hyperglycemia (high blood sugar levels) [7-8]. A recent meta-analysis found that the prevalence of metabolic syndrome (MetS) is 58% greater in those with mental problems than in the general population[9]. Clinical researches on the relationship between blood lipid levels and depression have revealed a variety of relationships. Low levels of high-density lipoprotein (HDL) cholesterol, for example, have been connected to long-term depression symptoms, whilst high triglycerides, total cholesterol, and low-density lipoprotein (LDL) cholesterol have been linked to depression itself[10]. In contrast, it has been observed in another study that low levels of total cholesterol and LDL cholesterol was found in patients with depression and acute suicidality tendencies[11-13]. Lower LDL cholesterol has also been identified as a risk factor for depressive symptoms in older individuals. Studies have provided evidences that antipsychotic drug usage has been associated with metabolic adverse effects such as considerable weight gain, glucose intolerance, and hyperlipidemia. These adverse effects add to an elevated risk of cerebrovascular disease (CVD) occurrences in a group already at high risk of CV complications that lead to mortality[14-15]. Further it has also been evident from recent researches that the use of antipsychotic medicines raises blood triglyceride (TG) and total cholesterol (TC), with the TG concentrations having a greater influence. Elevated serum TG appears to be the most important element in the dyslipidemias linked with antipsychotic drug usage[16]. Studies have provided favorable evidences on the role of Vitamin D supplementation in reducing blood total cholesterol, LDL cholesterol, and triglyceride levels, but it does not appear to effect HDL cholesterol levels. Individuals with hypercholesterolemia and vitamin D deficiency, particularly those at high risk of cardiovascular disease, may benefit from vitamin D supplementation[17]. Further on the other hand literatures revealed no marked effect of vitamin E on lipid profile levels but the antioxidant effects of Vitamin E protects against neurodegenerative diseases[18]. Hence can be used as a potential agent to prevent the progression of psychiatric diseases and limit the sides effects associated with the intake of psychiatric drugs. It is therefore the present is aimed to identify the effects of using antipsychotic drugs alone versus antipsychotic drugs in combination with Vitamin D and Vitamin E on lipid Profile levels of Psychiatric Disorder patients.

METHODOLOGY

To explore the effects of Vitamin D and Vitamin E supplementation on psychiatric improvement in people with mental health issues, a Randomized Control Trial (RCT) design was used. The study was conducted over a two-month period at the Jinnah Postgraduate Medical Center's Basic Medical Sciences Institute (BMSI). The study had comprised of n=140 individuals who had mental problems and were deficient in both vitamin D and vitamin E. All individuals had been taking antipsychotic drugs on a consistent basis for at least two months previous to the commencement of the research, and their antipsychotic doses remained constant throughout the study.

Study Group

Group 1: Outpatient clinic controls (20 age- and gender-matched controls).
Group 2: Risperidone (2 mg/day) treatment group.
Group 3: Olanzapine (10 mg/day) treatment group.
Group 4: Quetiapine (50-100 mg/day) treatment group.
Group 5: Vitamin D + E + Risperidone treatment group.
Group 6: The vitamin D + vitamin E plus olanzapine treatment group.
Group 7: Vitamin D + Vitamin E + Quetiapine treatment group.

For two months, all groups got the recommended therapy. Patient compliance sheets and regular phone calls were used to guarantee treatment adherence.

Inclusion/ Exclusion Criteria

- Those using antipsychotic medications such quetiapine, olanzapine, or risperidone.
- Participants who are between the ages of 20 – 70 years are both sex male and female. Participants who are taking a combination of one or two antipsychotics.
- Participants who were under antipsychotic therapy and not diagnosed with type 2 diabetes mellitus.

Exclusion Criteria:

- Patients at mental hospitals are mostly women who are either pregnant or nursing.

- Patients who were taking anticonvulsants, ketoconazole, or corticosteroids, or who had a history of other mental or neurologic illnesses, as well as those who used phosphor, calcium, as well as vitamin D supplements or teriparatide, were not included in the study.
- Participants were also ruled out if they had preexisting conditions including renal or hepatic failure, or a parathyroid disease.

Outcome Measure

Lipid Profile

The lipid profile components (total cholesterol, triglycerides, HDL cholesterol and LDL cholesterol, were measured using a BioVision Lipid Assay Kit. Blood samples were acquired from research participants in accordance with the appropriate ethical rules and protocols. The blood samples were processed to separate the serum or plasma containing the lipid components of interest.

Ethical Consideration

The researchers took great care to ensure the participants' physical, mental, social, and spiritual well-being, as well as their rights and dignity, and that no harm was done during the study. The confidentiality and privacy of the participants' information were strictly protected, and each subject gave informed consent before to participating in the study.

RESULTS

The analyses of the findings had revealed that participants in the Risperidone group had substantially higher levels of Total Cholesterol after antidepressant administration (235.26±35.37 vs. 157.09±16.34 mg/dL; p<0.0001). When compared to other treatment groups, the mean value of Total Cholesterol was considerably lower (p<0.05) in the group receiving Quetiapine coupled with Vitamin E and Vitamin D. Regarding efficacy, the treatment groups receiving Olanzapine, Risperidone, Quetiapine, Olanzapine combined with Vitamin E and Vitamin D, and Risperidone combined with Vitamin E and Vitamin D did not show any significant effects on the Total Cholesterol levels of patients (208.06±34.32 vs. 229.31±37.59 vs. 178.86±25.23 vs. 178.11±20.72 mg/dL, respectively). Further an analysis of variance revealed that individuals taking the antidepressant Risperidone in conjunction with Vitamin E and Vitamin D had substantially lower triglyceride levels than those receiving a placebo (164.28±18.09 vs. 151.74±11.85 mg/dL; p<0.0001). When compared to other treatment groups, the Risperidone + Vitamin E + Vitamin D group had a substantially lower mean value of triglycerides (p<0.05). In terms of efficacy, treatment with Olanzapine, Risperidone, Quetiapine, Olanzapine combined with Vitamin E and Vitamin D, and Quetiapine combined with Vitamin E and Vitamin D had no significant effects on patients' triglyceride levels (208.06±34.32 vs. 229.31±37.59 vs. 178.86±25.23 vs. 178.11±20.72 mg/dL. On the levels of High Density Lipoprotein (HDL) Risperidone group showed substantially lower levels of HDL (46.31±3.90 vs. 50.57±4.31 mg/dL; p<0.00001) compared to those in the Control group. When compared to the other treatment groups, the Risperidone group had a substantially lower mean HDL value (p<0.05). Treatment with Olanzapine, Quetiapine, Olanzapine combined with Vitamin E and Vitamin D, Risperidone combined with Vitamin E and Vitamin D, and Quetiapine combined with Vitamin E and Vitamin D had no significant effect on patients' High-Density Lipoprotein (HDL) levels (53.51±4.38 vs. 46.60±4.44 vs. 46.71±3.10 vs. 53.45±4.32 vs 54.60±4.59 mg/dL, respectively. In addition to that the LDL levels of patients in Group Risperidone were significantly lower than those in Group Control after taking antidepressants (141.62±7.40 mg/dL vs 134.42±9.32 mg/dL; p<0.00001) due to the effects of the former. The mean value of Low-density lipoprotein (LDL) was significantly reduced (P-value <0.05) in Group (Quetiapine + Vitamin E+ Vitamin D) than other treatment Groups. In terms of efficacy, treatment with Groups (Olanzapine), (Quetiapine), (Olanzapine + Vitamin E + Vitamin D) and (Risperidone + Vitamin E+ Vitamin D) did not show any effect with regards to the Low-density lipoprotein (HDL) of patients (140.57±8.41 Vs 142.17±7.08 vs 134.31±4.50 vs 132.60±6.06 mg/dL) respectively. The effects on Very low-density lipoprotein (VLDL) levels were not significantly different between the Risperidone and Control groups after treatment with antidepressants (p=0.292; 23.374.69 vs. 22.026.14 mg/dL, respectively). The mean value of Very low-density lipoprotein (VLDL) was not significantly reduced (P-value >0.05) in Group (Quetiapine + Vitamin E+ Vitamin D) than other treatment Groups.In terms of efficacy, treatment with Groups (Olanzapine), (Quetiapine), (Olanzapine + Vitamin E + Vitamin D) and (Risperidone + Vitamin E+ Vitamin D) did not show any effect with regards to the Very low-density lipoprotein (VLDL) of patients

(22.71±5.65 Vs 24.25±4.96 vs 22.45±3.96 vs 22.25±3.11 mg/dL) respectively as shown in table 1

Table 1 Effects of antipsychotic drugs in combination with vitamin D and Vitamin E on lipid Profile levels

Variables	Control Mean ± SD	Olanzapine Mean ± SD	Risperidone Mean ± SD	Quetiapine Mean ± SD	Olanzapine + Vitamin E + Vitamin D Mean ± SD	Risperidone + Vitamin E+ Vitamin D Mean ± SD	Quetiapine + Vitamin E+ Vitamin D Mean ± SD	p-value
Total Cholesterol (mg/dl)	157.09±16.34	208.06±34.32	235.26±35.37	229.31±37.59	178.86±25.23	178.11±20.72	177.37±14.72	p<0.005
Triglycerides (mg/dl)	164.28±18.09	173.68±13.70	175.94±9.87	178.60±9.43	153.40±10.23	151.74±11.85	151.94±10.21	p<0.005
HDL (mg/dl)	50.57±4.31	46.60±4.44	46.31±3.90	46.71±3.10	53.45±4.32	53.51±4.38	54.60±4.59	p<0.005
LDL (mg/dl)	134.42±9.32	140.57±8.41	141.62±7.40	142.17±7.08	134.31±4.50	132.60±6.06	131.25±5.07	p<0.005
VLDL (mg/dl)	22.02±6.14	22.71±5.65	23.37±4.69	24.25±4.96	22.45±3.96	22.25±3.11	21.74±2.75	p<0.005

DISCUSSION

The study's findings provided evidences that risperidone patients had greater levels of total cholesterol and lower levels of high-density lipoprotein (HDL) compared to the control group. The combination of quetiapine with vitamins E and D, on the other hand, resulted in a considerable decrease in total cholesterol and LDL levels. Furthermore, when supplemented with vitamin E and vitamin D, participants in the risperidone group had decreased triglyceride levels. The study found no significant impact on lipid profiles in individuals receiving olanzapine, quetiapine, or antipsychotics combined with vitamin E and vitamin D. These findings show that different combinations of antipsychotic medicines and vitamin supplements may have different impacts on lipid profiles in people with mental illnesses. The findings of previous literature that was aimed to examine the risk of dyslipidemia (abnormal lipid levels) linked with second-generation antipsychotics versus first-generation antipsychotics in people with severe mental illness. The results of 18 relevant research revealed conflicting correlations between second-generation and first-generation antipsychotics and dyslipidemia[19]. The effects Clozapine, olanzapine, and risperidone revealed moderately higher correlations with dyslipidemia when compared to first-generation antipsychotics. Clozapine was also linked to higher triglyceride levels. However, there was a lot of variation among the trials[19]. There were no statistically significant increases in cholesterol or triglycerides when olanzapine and risperidone were compared to haloperidol. It was concluded that that comparing the metabolic risks of second-generation versus first-generation antipsychotics as a group may have limited clinical utility, and that it is more important to consider the metabolic risks of specific antipsychotics rather than grouping them into broad categories. In another study the combine effects of Olanzapine with Vitamin D was assessed as Olanzapine an antipsychotic drug increases the risk of dyslipidemia and when it was administered in combination with vitamin D supplements it was found that the risk of developing Olanzapine induced dyslipidemia was significantly reduced among Schizophrenic patients[20]. Similarly a narrative review that was performed to looks at the possible function of vitamin E in the treatment of major depressive disorder (MDD). The review examines the role of inflammation, oxidative stress, and nitrosative stress in the pathogenesis of MDD, as well as clinical and preclinical findings that relate vitamin E to this mental illness[21]. Clinical investigations have found a link between low vitamin E levels and MDD symptoms, with vitamin E exhibiting favorable effects on oxidative and inflammatory indicators, which may help to alleviate depressed symptoms. Preclinical investigations have also shown vitamin E's antidepressant-like effect, suggesting its potential in moderating oxidative stress and neuroinflammation[21]. However, further study is required to evaluate the usefulness of vitamin E as an adjuvant in the treatment of MDD[21].

The randomized controlled design of the study determining the effects of vitamin D and vitamin E supplementation on psychiatric improvement in patients with mental health issues helps minimize bias and demonstrate causal links. The study also included a broad sample of n=140 patients with mental diseases, which increased the generalizability of the findings. The uses of standardized antipsychotic doses, as well as the addition of a control group, improve the study's design even more. The use of patient compliance sheets and regular phone conversations maintained patient compliance, lowering the risk of treatment non-adherence. On the other hands limitations include the study's very short duration (two months), which may restrict the capacity to capture long-term effects of the therapies. Furthermore, there was no placebo group in the trial, which may have offered a better comparison to evaluate the effects of vitamin supplementation. The sample size for each therapy group was also small, which may have reduced statistical power and limited the findings' generalizability. Furthermore, the study only looked at lipid profiles and did not look at other psychological outcomes or possible side effects of the therapies. Prospective investigations must navigate through these constraints in order to acquire a fuller knowledge of how both vitamin D & supplements containing vitamin E affect psychological disorders.

Conclusion

The findings from the research showed that when analysed in comparison to those in the control group, risperidone use was associated with a decrease in levels of high-density lipoprotein (HDL) & higher levels of total cholesterol. When quetiapine was coupled with vitamins E and D, total cholesterol and low-density lipoprotein (LDL) levels were significantly reduced. Furthermore, when individuals in the risperidone group were given with vitamin E and vitamin D, their triglyceride levels were lower. Individuals receiving olanzapine, quetiapine, or antipsychotics in combination with vitamin E and vitamin D had no significant changes on their lipid profiles. These findings imply that different antipsychotic drug and vitamin supplement combinations may have variable effects on lipid profiles in people with mental disorders. Long-term effects and potential adverse effects of these therapies, as well as other psychological outcomes, should be investigated in future study.

ETHICS APPROVAL: The ERC gave ethical review approval.

CONSENT TO PARTICIPATE: written and verbal consent was taken from subjects and next of kin.

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