Effect of probiotics on olanzapine-induced metabolic syndrome in Wistar albino rats

Mushraf Syed (✉ syed.mushraf@manipal.edu)
Melaka Manipal Medical College  https://orcid.org/0000-0001-9168-5735

Veena Nayak
Kasturba Medical College Manipal

Research Article

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Abstract

**Purpose:** Olanzapine is the most viable second-generation antipsychotic (SGA) used in the treatment of schizophrenia and at the same time, it is the most notorious SGA to cause metabolic syndrome (MS). The target of this study is to assess the adequacy of probiotics in fighting the unfriendly impacts of olanzapine treatment such as weight gain, hyperlipidemia, and hyperglycemia in the olanzapine-induced MS model in rodents.

**Methods:** Thirty-six Wistar rodents were haphazardly separated into six groups (n=6). The groups were treated for a month as follows: Group-I: Normal saline 1 ml/kg/day orally, Group-II: olanzapine 2 mg/kg/day i.p., Group-III: probiotic-VSL#3: 0.6 g/kg/day orally, Group-IV: VSL#3: 1.2 g/kg/day orally, Group-V: olanzapine 2 mg/kg/day i.p. + VSL#3: 0.6 g/kg/day orally, and Group-VI: olanzapine 2 mg/kg/day i.p. + VSL#3: 1.2 g/kg/day orally. Bodyweight, fasting blood glucose (FBG), and lipid profile was assessed at baseline and consequently at the end of each week. Data were analyzed by applying repeated measures ANOVA, followed by post-hoc Bonferroni test. P-value <0.05 was considered statistically significant.

**Results:** There was a noteworthy increment in the total cholesterol and triglycerides level after olanzapine treatment (P<0.01), and similarly a decline in the total cholesterol and triglycerides level in the probiotic treated groups (p < 0.05). There was a decrease in weight increase and FBG levels instigated by olanzapine in the probiotic-treated groups.

**Conclusion:** Probiotics forestalled the advancement of hyperlipidemia and decreased the weight addition and increment in FBG levels initiated by olanzapine. A long-haul evaluation should be directed to additionally assess the impact of probiotics on MS and their plausible mechanism.

Introduction

Atypical/Second-Generation Antipsychotics (SGAs) are the mainstay of treatment in most psychotic disorders.[1] Among the SGAs, olanzapine (OLZ) is more efficacious than other SGAs in terms of improving the general mental state and reducing associated depressive and anxiety symptoms.[1-4] SGAs have been associated with initiating and aggravating metabolic syndromes such as obesity (increased BMI), diabetes, and hyperlipidemia.[4] Among the SGAs, even though OLZ is more efficacious than other SGAs, it also has the maximum potential to cause MS.[5-8] Obesity is observed to be a precursor for MS, and treating it with physical activities, counseling for behavioral reforms, calorie-restricted diets, administration of drugs for weight loss, as well as surgery for weight loss can be the key aspects in the management and control of MS. However, strategies like physical exercise and behavior reforms require strong mind control and are difficult to adopt by patients who are mentally ill. Diet modification strategies are also found to be less effective. On the contrary, the existing pharmacological management has its drawback of adverse side-effects and high cost of treatment.[9]
Probiotics are live microorganisms, generally regarded as safe, which when administered in adequate amounts confer health benefits on the host.\textsuperscript{[10]} It is the probiotic component of the gut microbiota that plays a crucial role in the maintenance of general homeostasis and health.\textsuperscript{[11]} The two key members of this group include \textit{Lactobacilli} and \textit{Bifidobacteria}.\textsuperscript{[11-12]} With oral supplementation of probiotics manipulating the gut, the microbiota has proved to be a crucial strategy against high-fat-diet (HFD) induced MS.\textsuperscript{[12]} Various strains of beneficial microorganisms have been used alone or a lot more as cocktails, and have shown promising results to combat metabolic complications like obesity, insulin resistance, and/or hepatic steatosis in HFD-fed rodents. These strains include \textit{Bifidobacterium} spp., \textit{Lactobacillus} spp., \textit{Streptococcus thermophilus}, \textit{Bacteroides uniformis}, and \textit{Akkermansia muciniphila}.\textsuperscript{[13-21]}

VSL\#3 probiotics, a multistrain cocktail containing \textit{Streptococcus thermophilus} and a few types of lactobacilli and bifidobacteria, are found to advance the arrival of the hormone GLP-1, bringing about decreased food consumption and improved glucose resistance. The VSL\#3-initiated changes were related to an expansion in the levels of SCFAs, which leads to the release of GLP-1 from intestinal L-cells, proposing a potential mechanism for the VSL\#3-related effects.\textsuperscript{[22]}

Notwithstanding, little is known about the impact of probiotics, on antipsychotic-induced MS.\textsuperscript{[23]} Thus, in the current situation, the advancement of dietary methodologies, i.e., planning natural food items with probiotics and prebiotics that regulate MS will be a financially savvy approach without the dread of unfavorable effects on health.

**Materials And Methods**

The study was done for over 28 days, after getting the permission of the Institutional Animal Ethics Committee, MAHE, Manipal.

**Animal selection**

A sum of 36 adult male Wistar albino rats, each weighing 150-250 grams were acquired. Male rodents were picked over female rodents as the latter's estrous cycles meddle in initiating the MS. All rodents were housed in the central creature research office, Manipal, at room temperature (23 ± 2°C) with 12 hours of light: dark environment. They were given standard research centre feed and water. The study was carried out as per the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA) guidelines.

**Drugs, reagents, and other materials:** A fine powder of olanzapine was blended in with a little volume (0.1 ml) of glacial acetic acid, and later made to volume utilizing normal saline.\textsuperscript{[24]} Probiotic VSL\#3 (manufactured in India by Sun Pharmaceutical Ind. Ltd.) is a freeze-dried pharmaceutical probiotic preparation containing 112.5 billion CFU/capsule (a mix of \textit{Streptococcus thermophiles, Bifidobacterium longum}/lactis, \textit{Bifidobacterium breve, Bifidobacterium infantis, Lactobacillus acidophilus, Lactobacillus
*plantarum, Lactobacillus paracasei, Lactobacillus delbrueckii subsp. bulgaricus* was bought from the drug store and made to volume with an ample volume of normal saline.\[22-23\] Reagents for the biochemical test (serum lipid profile) were purchased from Aspen Laboratories Pvt Ltd. Computerized glucometer and testing strips (from AccuChek), centrifuge, and semiautomatic analyzer from the Department of Pharmacology, Kasturba Medical College, Manipal Academy of Higher Education, Manipal were used.

**Selection of dose of medications:** The dose (2 mg/kg/day), term (a month), and route (intraperitoneal – i.p.) of olanzapine were picked depending on past investigations that indicated positive induction of MS in female Wistar rodents with this regimen.\[24\] VSL#3 dose by chose by converting the adult human dose of a mean 70 kg man into rat dose using the standard dose conversion formula.\[25\] The VSL#3 capsules were stored at 2 to 8°C before administration and were dissolved in normal saline just before administering to the rats.\[22-24\]

**Experimental groups:** Thirty-six rats were randomly divided into six groups (n=6), as shown in figure 1.

**Group I** - Rats received normal saline, 1 ml/kg/day orally for four weeks as a single daily dose.

**Group II** - Rats received olanzapine, 2 mg/kg/day i.p. for four weeks as a single daily dose.

**Group III** - Rats received VSL#3 (Dose I), 0.6 gm/kg/day for four weeks orally as a single daily dose.

**Group IV** - Rats received VSL#3 (Dose II), 1.2 gm/kg/day for four weeks orally as a single daily dose.

**Group V** - Rats received olanzapine, 2 mg/kg/day i.p. + VSL#3 (Dose I), 0.6 g/kg/day orally for four weeks as a single daily dose.

**Group VI** - Rats received olanzapine, 2 mg/kg/day i.p. + VSL#3 (Dose II), 1.2 g/kg/day orally for four weeks as a single daily dose.

**Parameters assessed**

- **Total body weight:** Baseline weight was measured before the commencement of the doses, and at the end of each week for four weeks, and values were noted in grams.\[24\]

- **Fasting blood glucose:** Rats were fasted overnight (for 12 h) and blood glucose levels were measured by taking blood from tail pricks using a digital glucometer before the dosing started (as baseline) and once a week thereafter for four weeks. All values were noted down in mg/dL.\[28\]

- **Serum lipid profile:** Venous blood was acquired from all rats from the retro-orbital venous plexus for assessment of lipid parameters – total cholesterol, HDL, and triglycerides. The blood was centrifuged, and the serum was exposed to a semiautomatic analyzer (utilizing the reagent kits standard procedure). All the values were noted down in mg/dl. This assessment was done at baseline and the finish of every week from that point for four weeks.\[24\]
• **Estimation of total cholesterol**: 10 μl of test serum sample was added to 1000 μl of the testing reagent, blended well, and incubated for ten minutes at 37°C. The absorbance was compared against the reagent blank. To get the estimation of total cholesterol, the absorbance of the test was divided by absorbance of standard and multiplied by the calibrator concentration factor.

• **Estimation of HDL**: 50 μl of test serum sample was added to 1 ml of the testing reagent, blended well, and incubated for ten minutes at 37°C. The absorbance was perused at 505 nm. To get the estimation of HDL, the absorbance of the test sample was divided by absorbance of standard and multiplied by the calibrator concentration factor, and two.

• **Estimation of triglycerides**: 50 μl of test serum test was added to 1 ml of the testing reagent, blended well, and incubated for ten minutes at 37°C. The absorbance was perused at 505 nm. To get the estimation of HDL, the absorbance of the sample was divided by absorbance of standard and multiplied by the calibrator concentration factor, and two.

• **Statistical analysis**: The data obtained was analyzed using IBM Statistical Package for Social Sciences (SPSS) v. 20.0. The significance of differences within the groups at a various time focuses was evaluated by applying repeated measures of One-way Analysis of Variance (ANOVA), trailed by the post-hoc Bonferroni test. All experimental groups were compared against the control and standard groups to finish up the outcomes. The p-value of less than 0.05 was considered statistically significant.

**Results**

The present study demonstrated the effects of various groups on body weight, total cholesterol, triglycerides, HDL cholesterol, and blood glucose levels as shown below.

1. **Effect on body weight**

The body weight was measured at baseline and the end of every week for four weeks. At baseline, the bodyweight of all the groups was comparable. After four weeks, there was a significant increase in the body weight in the OLZ treated group (250 ± 7.82), when compared to the baseline (211.67 ± 12.24) (p<0.001). There were no significant changes in body weight at four weeks in the groups treated with probiotics when compared to baseline. Intergroup comparison showed a significant increase (p<0.001) in the bodyweight of the group treated with olanzapine when compared to the control group at the end of week four. There was a decrease in the weight of the animals treated with probiotics (237.6 ± 1.5, 195.2 ± 9.38, 177.75 ± 7.02, 227.33 ± 11.56) when compared to the olanzapine treated group (250 ± 10, 211.67 ± 12.24, 230 ± 0, 200 ± 0, 180 ± 4.89, 232 ± 11.13), though not statistically significant. The mean ±SEM of the animals treated with probiotic (dose I) was 237.6 ± 1.5 (baseline value 230), probiotic (dose II) 195.2 ± 9.38 (baseline value 200), and that of olanzapine was 250 ± 7.82, though there was a decrease in weight, it was not statistically significant.

**Table 1: Bodyweight comparison of the different experimental groups**
| S. No. | Group               | Baseline body weight in grams (Mean ± SEM) | Bodyweight in grams (Mean ± SEM) at the end of 1 week | Bodyweight in grams (Mean ± SEM) at the end of 2 weeks | Bodyweight in grams (Mean ± SEM) at the end of 3 weeks | Bodyweight in grams (Mean ± SEM) at the end of 4 weeks |
|-------|---------------------|------------------------------------------|---------------------------------------------------------|-------------------------------------------------------|------------------------------------------------------|------------------------------------------------------|
| 1     | Normal control      | 246.67 ± 6.67                            | 254 ± 6.22                                              | 255.5 ± 6.04                                          | 260 ± 5.81                                           | 263. ± 5.83                                          |
| 2     | Olanzapine          | 211.67 ± 13.76                           | 231.83 ± 12.36                                          | 238.17 ± 9.8 *                                       | 244.33 ± 7.20                                       | 250 ± 5.46 ***                                      |
| 3     | Probiotic dose-I    | 230 ± 0                                  | 232.67 ± 1.81                                          | 235.5 ± 2.87                                          | 241 ± 2.39                                           | 237.17 ± 2.91                                      |
| 4     | Probiotic dose-II   | 200 ± 0                                  | 199.17 ± 0.9***                                        | 199.17 ± 0.98***                                     | 193.5±1.33***                                       | 195 ± 0.93 ***                                     |
| 5     | Olanzapine + probiotic dose-I | 180 ± 4.47 | 211.50 ± 1.96                                          | 175.83 ± 2.80***#                                     | 174.50 ± 2.71###                                   | 177.33 ± 1.81###                                  |
| 6     | Olanzapine + probiotic dose-II | 235 ± 9.57 | 224.83 ± 7.03                                          | 215.50 ± 6.23 *                                      | 217.33 ± 8.04*                                      | 222.83 ± 7.40***                                   |

[n – number of animals in each group] (* denotes p<0.05 versus control group; *** denotes p<0.001 versus control group; # denotes p<0.05 versus olanzapine group; ### denotes p<0.001 versus olanzapine group).

2. Effect of probiotics on total cholesterol, triglycerides, HDL-cholesterol

Table 2: Total cholesterol level comparison of the different experimental groups
**Table 3: Triglycerides level comparison of the different experimental groups**

| S. No. | Group                  | "Baseline total cholesterol level in mg/dL (Mean ± SEM)" | "Total cholesterol level in mg/dL (Mean ± SEM) at the end of 1 week" | "Total cholesterol level in mg/dL (Mean ± SEM) at the end of 2 weeks" | "Total cholesterol level in mg/dL (Mean ± SEM) at the end of 3 weeks" | "Total cholesterol level in mg/dL (Mean ± SEM) at the end of 4 weeks" |
|--------|------------------------|---------------------------------------------------------|-----------------------------------------------------------------|------------------------------------------------------------------|------------------------------------------------------------------|------------------------------------------------------------------|
| 1      | Normal control         | 45.59 ± 1.24                                           | 45.26 ± 0.43                                                    | 53.12 ± 0.91                                                     | 51.06 ± 0.9                                                      | 52.93 ± 1.13                                                     |
| 2      | Olanzapine             | 45.84 ± 0.74                                           | 70.28 ± 1.27***                                                 | 78.89 ± 1.9*                                                    | 85.64 ± 1.59***                                                  | 98.84 ± 0.87***                                                  |
| 3      | Probiotic dose-I       | 45.56 ± 1.41                                           | 47.36 ± 1.27###                                                 | 73.99 ± 1.6                                                     | 63.9 ± 1.4                                                      | 63.53 ± 1.07###                                                 |
| 4      | Probiotic dose-II      | 45.29 ± 0.75                                           | 52.03 ± 0.93                                                   | 73.49 ± 1.6                                                     | 65.77 ± 1.24                                                    | 54.54 ± 1.05###                                                 |
| 5      | Olanzapine + probiotic dose-I | 45.09 ± 1.09                          | 51.78 ± 1.48                                                   | 70.13 ± 1.9                                                    | 61.15 ± 1.65                                                    | 54.73 ± 0.74###                                                 |
| 6      | Olanzapine + probiotic dose-II | 45.53 ± 0.79                          | 51.35 ± 1.6                                                    | 64.23 ± 1.06                                                   | 58.67 ± 0.78                                                    | 48.37 ± 0.77###                                                 |

[n – number of animals in each group; SEM – Standard Error of Mean] (* denotes p<0.05 versus normal control group; *** denotes p<0.001 versus control group; ### denotes p<0.001 versus olanzapine standard group, p-value calculated by One-way ANOVA followed by post hoc Bonferroni test]

There was a statistically significant increase in total cholesterol levels at the end of the first, third, fourth week (p<0.001), and second week (p<0.05) when compared with the control group as shown in figure 2. There were statistically significant differences (p<0.001) of decrease in total cholesterol levels at the end of four weeks when probiotics were given alone (both low and high dose) and along with olanzapine therapy when compared with the olanzapine group (p<0.001). There was a statistically significant decrease (p<0.001) in total cholesterol levels at the end of the first week when probiotics were given alone at a low dose.
Table 4: HDL-cholesterol level comparison of the different experimental groups
| S. No. | Group                        | Baseline HDL level in mg/dL (Mean ± SEM) | HDL level in mg/dL (Mean ± SEM) at the end of 1 week | HDL level in mg/dL (Mean ± SEM) at the end of 2 weeks | HDL level in mg/dL (Mean ± SEM) at the end of 3 weeks | HDL level in mg/dL (Mean ± SEM) at the end of 4 weeks |
|--------|------------------------------|------------------------------------------|-----------------------------------------------------|-----------------------------------------------------|-----------------------------------------------------|-----------------------------------------------------|
| 1      | Normal control               | 75.21 ± 1.51                             | 76.33 ± 1.62                                        | 76.33 ± 1.42                                        | 81.25 ± 1.78                                        | 81.72 ± 1.21                                        |
| 2      | Olanzapine                   | 76.91 ± 1.04                             | 56.41 ± 1.94                                        | 56.56 ± 1.33                                        | 58.47 ± 1.74                                        | 71.39 ± 2.27                                        |
| 3      | Probiotic dose-I             | 76.70 ± 1.21                             | 128.64 ± 1.61** ‡‡‡                                       | 99.45 ± 1.67                                        | 96.9 ± 1.97                                        | 87.99 ± 1.86                                        |
| 4      | Probiotic dose-II            | 77.27 ± 1.20                             | 117.15 ± 1.72* ‡‡‡                                     | 92.19 ± 1.41                                        | 89.64 ± 1.87                                        | 94.26 ± 2.38                                        |
| 5      | Olanzapine + probiotic dose-I| 77.98 ± 1.39                             | 97.56 ± 1.74‡                                        | 98.97 ± 2.25                                        | 100.57 ± 1.82                                      | 113.29 ± 2.1 ‡‡‡                                    |
| 6      | Olanzapine + probiotic dose-II| 79.68 ± 1.41                             | 91.22 ± 1.37                                         | 95.64 ± 1.84                                        | 87.87 ± 1.47                                        | 88.28 ± 1.91‡                                       |

[n – number of animals in each group; SEM – Standard Error of Mean] (* denotes p<0.05 versus control group; *** denotes p<0.001 versus control group; ‡ denotes p<0.05 versus olanzapine standard group; ‡‡‡ denotes p<0.001 versus olanzapine standard group; p-value calculated by One-way ANOVA followed by post hoc Bonferroni test]

There was an increase in the HDL levels of probiotics (groups 3 and 4) at the end of the first week when compared with the olanzapine group (p<0.001) as shown in figure 4. There was an increase in HDL levels in group 3 (p<0.001) and group 4 (p<0.05) when compared with the control group. There was a statistical increase in the HDL levels in group 5 (p<0.001) and group 6 (p<0.05) when compared with the olanzapine group.

3. Effect on fasting blood glucose levels

In figure 5, FBG levels of the baseline and at the end of the fourth-week treatment of rats of all the different experimental groups are shown. The values are noted down in mg/dl. There was an increase in the FBG level observed after treatment with olanzapine and probiotics at the end of the fourth week when compared with the baseline FBG level, but it was not statistically significant.

Discussion
Metabolic syndrome is a cluster of cardiovascular diseases, and various risk factors such as an increase in blood pressure, insulin resistance, and blood coagulability cause an increase in obesity and neutral fat, and LDL-C, decreases in HDL-C, and the effect of dyslipidemia.[29] Olanzapine is an SGA; it is used in the present study to induce metabolic syndrome at the dose of 2mg/kg.[27]

The study showed that with olanzapine treatment, there was a statistically significant (p<0.001) increase in body weight, total cholesterol, and triglycerides levels which is suggestive of metabolic syndrome.

Mechanism of OLZ induced MS- The histamine H₁ receptor antagonism promotes feeding in rodents. The metabolic complications with olanzapine therapy begin with increased appetite and weight gain, and progress to obesity, insulin resistance, and dyslipidemia with an increase in fasting triglyceride levels. Ultimately, hyperinsulinemia advances to pancreatic β-cell failure, prediabetes, and then diabetes. Once diabetes is established, the risk for cardiovascular events is further increased, as is the risk of premature death.[30]

In the present study, probiotics when given alone in low and high doses and along with olanzapine therapy, decreased bodyweight, total cholesterol, and triglycerides levels at the end of four weeks. Probiotics alone in low dose and along with olanzapine therapy, decreased the lipid profile at the end of every week, with p<0.001 at the end of the fourth week. There was also an increase in the HDL cholesterol level even with the first and fourth weeks of administration of probiotics.

Past investigations indicated that probiotics directly introduce beneficial bacteria, for example, Lactobacilli and Bifidobacteria into the gut.[31] Supplementation of probiotics was found to improve increased lipid profile levels in HFD fed rodents and humans.[32-33] The outcomes from the past studies have demonstrated a reduction in plasma cholesterol and triglycerides levels. Bile acid deconjugation by probiotics and cholesterol bonding has additionally been proposed as likely components of bringing down cholesterol by probiotics.[34] Probiotics may change cholesterol into coprostanol, which is straightforwardly excreted through feces.[35] They have viably restored gut barrier function, decreased intestinal inflammation, and saved the intestinal microstructure in HFD fed rodents.[36] Probiotics likewise re-established gut barrier dysfunction and diminished concentrations of circulating glucocorticoids and pro-inflammatory cytokines. These cytokines weaken the integrity of the blood-brain barrier and allow conceivably pathogenic or inflammatory components. Probiotics additionally increment anti-inflammatory cytokines, which upgrade the integrity of the blood-brain barrier, the gut barrier, and decrease inflammation.[31] Another investigation demonstrated that Lactobacilli species are fit for strengthening the epithelial boundary and may forestall lipopolysaccharide-interceded inflammation and hyperglycemia.[37]

Dysbiosis is a state portrayed by alteration in microbiota composition, a change in bacterial metabolic action, or potentially a more local distribution of microorganism communities. Intestinal dysbiosis is vital in the comprehension of the pathophysiology of a few metabolic diseases, including obesity and T2D.[34] The gut microbiota is overwhelmed by two phyla, Firmicutes and Bacteroidetes, which characterize about
90% of the apparent multitude of bacterial species in the gut. Many vital studies have exhibited that the control of the gut microbiota and its metabolic pathways can influence the host's adiposity and metabolism. Gordon and associates utilizing germ-free (which lack microbiota) mice showed that they have 40% less fat versus fat in normally raised mice, and are impervious to diet-induced obesity. They additionally found that obese mice have an 'obesity-related microbiome' comprising of corresponding movements in the two most bountiful phyla of microorganisms—firmicutes (expanded) and bacteriodetes (diminished), comparative outcomes were shown by another investigation where rodents were given HFD, it diminished Bacteroidetes. They also gave produced mounting proof suggestive of alterations in the gut microbiome as a vital factor in the prevalence of obesity.

Supplementation of probiotics prevented the development of hyperlipidemia and hyperglycemia induced by olanzapine in the Wistar albino rats. There was a clinical difference observed in the gain of body weight of the rats treated with probiotics and olanzapine treated groups for four weeks, which was statistically not significant, which could be attributed to their dietary pattern.

Limitations

- Long-term studies to evaluate the effects of probiotics on olanzapine-induced metabolic syndrome should have been done.
- The effect of different SGAs in inducing metabolic syndrome needs to be assessed.

Long-term studies need to be done to check for a change in the weight gain and lipid profile by both olanzapine and probiotics on rats. Further evaluation of the gut hormones level, short-chain fatty acids, and enteroendocrine neurotransmitters could give an insight into the pathophysiology leading to change in the lipid profile and weight gain in rats treated with olanzapine and probiotics administered to counteract the olanzapine-induced MS.

Declarations

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Author Contribution Statement
**MS:** conceived and designed research, conducted experiments, analyzed data, wrote the manuscript

**VN:** conceived and designed research, contributed new reagents or analytical tools, wrote the manuscript

All authors read and approved the manuscript and all data were generated in-house and that no paper mill was used.

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**Figures**
36 male Wistar albino rats

**Group I**: Normal saline: 1 ml/kg/day orally for 28 days

**Group II**: Olanzapine: 2 mg/kg/day i.p. for 28 days

**Group III**: VSL#3 (Dose I): 0.6 gm/kg/day for 28 day’s

**Group IV**: VSL#3 (Dose II): 1.2 gm/kg/day for 28 days

**Group V**: Olanzapine: 2 mg/kg/day i.p. + VSL#3 (Dose I): 0.6 g/kg/day for 28 day’s

**Group VI**: Olanzapine: 2 mg/kg/day i.p. + VSL#3 (Dose II): 1.2 g/kg/day for 28 days

**Figure 1**

Experimental groups

**Total cholesterol levels at the end of 4 weeks treatment**

| Treatment groups                  | Total cholesterol levels in mg/dl |
|-----------------------------------|----------------------------------|
| Normal control                    | 50.00 ± 5.00                     |
| Olanzapine (OLZ)                  | 80.00 ± 5.00*                    |
| Probiotic dose-1                  | 70.00 ± 5.00                     |
| Probiotic dose-2                  | 70.00 ± 5.00#                    |
| Probiotic dose 1+OLZ              | 60.00 ± 5.00#                    |
| Probiotic dose 2+OLZ              | 60.00 ± 5.00#                    |

**Figure 2**

Total cholesterol levels in the different experimental groups at the end of 4th week. Inter-group comparison of total serum cholesterol levels. * p < 0.001, olanzapine vs control; # p < 0.001, probiotic
Figure 3

Triglyceride levels in the different experimental groups at the end of 4th week. Inter-group comparison of triglyceride levels. * p < 0.05, olanzapine vs control group; # p < 0.001 probiotics (low and high dose) alone and along with olanzapine vs olanzapine group; p-value calculated by One-way ANOVA followed by post-hoc Bonferroni test).
Figure 4

HDL-cholesterol levels in the different experimental groups at the end of 4th week. Inter-group comparison of HDL cholesterol levels. * p<0.001, probiotic low dose + olanzapine vs olanzapine; # p<0.05, probiotic high dose + olanzapine vs olanzapine; p-value calculated by One-way ANOVA followed by post-hoc Bonferroni test).
Figure 5

Fasting blood glucose levels from baseline to end of 4th week

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Rawdata.xlsx