RESEARCH PAPER

Effect of Olanzapine on High Fat Diet Induced Weight Gain in Zebrafish Model

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Introduction: Olanzapine is a first line antipsychotic drug that is often used in treatment of psychiatric illness as it has low risk of extra pyramidal symptoms compared to other antipsychotic drugs[1]. The model used was zebra fishes (ZF) where it is 70% similar to human genetic structure and has more favorable ethical procedure compared to higher order animals[2]. Thereby, Olanzapine was tested on the ZF to identify any weight gain potential. **Method:** A Danio Rerio model were used where high fat diet were given to ZB for 28 days. **Result & Discussion:** There is significant weigh gain difference between control and test group (one way ANOVA, $p < 0.0005$, $F = 8.573$). In 0.5uM olanzapine, ZF has a behavior of hyperphagia, aggressive behavior and increased in weight gain however, in 5uM olanzapine, the ZF has the highest weight gain with no aggressive behavior observed. In LC 50, 60uM has lowest survival rate and 15uM has highest survival rate. There were interactions found with D2, 5-HT2A, HT2 , A1, & M3 receptors thus, leading to alternation of Leptin, adiponectin and ghrelin level[3]. **Conclusion:** In summary, olanzapine does induce weight gain together with high fat diet in zebrafish by increasing the appetite of zebrafish provide evidence supporting the validity of this model for olanzapineinduced obesity.

KEYWORDS: Danio Rerio (Zebrafish), Olanzapine induce weight gain, LC50 on Zebrafish, High fat diet

How to cite this article: Nilugal KC, Kakadiya J. Effect of Olanzapine on High Fat Diet Induced Weight Gain in Zebrafish Model. Int J Drug Deliv Technol. 2026;16(16s): 739-747. DOI: 10.25258/ijddt.16.16s.79

INTRODUCTION

In the case of human illnesses, we can also divide them into two categories, physical illness and mental illness. Physical illness is when there's an illness that has been caused due to the damage or failure of an organ, such as brain injuries or kidney failure. On the other hand, mental illness is a group of brain-based conditions that affect an individual and his/her emotions, thinking and behavior. Psychiatric illnesses, as they are known, disrupt daily activities due to alterations or differences in brain function caused by imbalances in brain chemicals. Common mental illnesses include depression, schizophrenia, bipolar disorder, and autism.

Depression is the most common mental disorder in the world affecting an estimated 280 million people4. Tragically, more than 700,000 persons choose death by suicide each year as a result of depression. Symptoms of depression include the following: constant feelings of sadness, feelings of emotional illness, negative thoughts, lack of interest or pleasure in activities, hopelessness for at least two weeks. Other symptoms may include disturbed sleep or appetite, tiredness and problems with concentration[4].

Bipolar disorder, which afflicts about 48 million people around the world, involves a series of alternating manic and depressive episodes followed by periods during which a person is in normal mood. It is a mental disorder when the people are unable to control their mood differences, energy levels as well as capabilities of performing day-to-day tasks[4].

Diagnosed in about 24 million people worldwide, schizophrenia is less common but has enormous effects on its victims. The causes of schizophrenia are not yet fully understood, but it's characterized by poor reception of reality by an individual, hallucinations, delusions, disorder of thought and behavior that can lead to confusion between reality and dreams[4].

Olanzapine is a second-generation atypical antipsychotic drug and is widely used for the treatment of a variety of mental disorders, such as schizophrenia, mania, autism, and bipolar disorder[1]. It acts on the receptors for serotonin (5-HT) and dopamine (D2) by inhibiting the action of dopamine binding to D2 receptors and enhancing binding of serotonin-to-serotonin receptor 5-HT2A and 5-HT2C[3]. Olanzapine also interacts with the alpha and muscarinic receptors but to a greater extent

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with 5-HT receptors than dopamine receptors.

Despite its effectiveness in treating mental illnesses, olanzapine has the potential of causing metabolic dysfunctions such as weight gain, which are significant adverse effects. Weight gain is the biggest cause for concern with patients with schizophrenia showing a mean weight gain of around 3.3 kg in 8 weeks from the administration of olanzapine[5]. Olanzapine can also cause other abnormalities of the metabolism, such as hyperglycemia, hyperinsulinemia, dyslipidemia, and increased risk of type 2 diabetes mellitus and cardiovascular complications[6].

Taking into account the effect of these atypical antipsychotic drugs on weight gain and the metabolic syndrome, research using the zebrafish as a model organism becomes necessary. Zebrafish (Danio rerio) has a genome that is ~70% similar to human genome, where 84% of their genes are similar to the human diseases[2]. Additional advantages of measuring zebrafish are that they produce many embryos per week, they grow quickly, and they develop outside the female's body[7]. These characteristics make them perfect for studying various aspects of research, including, the relationship of olanzapine and the factors contributing to weight gain.

In the research experiment, the zebra fish will be exposed to different concentrations of olanzapine in the water and eat a high-fat diet to cause significant weight gain. By using this model, the goal is to simulate a clinical environment better and get a better understanding of the mechanisms underlying antipsychotic drug-induced weight gain.

Olanzapine is an important treatment option for patients with psychotic conditions because of its efficacy in treating symptoms of hallucinations, mania and depression. It offers patients more rational and positive thinking and behavior and has a lesser risk of extrapyramidal symptoms in comparison to other drugs in this group. However, the concern about the weight gain and metabolic syndrome due to olanzapine prescription still has a high rate because of the growing morbidity and mortality rates as a result of secondary diseases.

In summary, the use of zebrafish as a model organism offers a useful tool to study the relationship between olanzapine and weight gain in a more precise and relevant way. Understanding the mechanisms involved can help reduce the fatality rate preserved in the individuals with mental illnesses, particularly schizophrenia, and address the problems associated with metabolic dysfunctions produced by anti-psychotic drugs.

METHODOLOGY

Study Design

The general objective of this research is to study the potential of using zebrafish as an alternative animal model to study the effects of olanzapine and high fat diet-induced obesity. Specifically, the study will be aimed at determining if olanzapine, a drug, and a high-fat diet given to zebrafish causes abnormalities related to weight gain and behavior. Additionally, the research aims to test underlying mechanisms by which olanzapine contributes to the weight gain in Zebrafish focuses on energy expenditure and nutrient utilization. By solving such objectives, the aim of the study is to get some insights on the relationship of olanzapine, high-fat diet and obesity in the areas of zebrafish as a model organism. Understanding the mechanisms behind olanzapine-induced weight gain in this model can contribute to the understanding of the metabolic effects of antipsychotic drugs, which can lead to the development of future treatments for mental illness with fewer metabolic side effects.

Chemicals/ Reagent / Apparatus

Olanzapine (5mg), Dry weight Artemia diet, 0.9% normal saline solution, 4% paraformaldehyde, 0.03% tricaine (sigma-Aldrish, St Louis, MO, USA) solution, 4% formalin, Oil Red O (Wako), Distilled water, fresh water , 0.1% DMSO , 3ml syringe with needle, 10ml syringe with needle , fish tank with biological filter, Tap water and charcoal filtering, fluorescence microscope (MZ 16F, Leica, Tokyo, Japan), GFP2 filter, cryostat, Stereoscopic microscope, UV lamps, Inverted microscope, Fish nets, pH meter, Petri dish , Strainer, 96-Well, Razor blades or a scrubbing sponge, Zebrafish (Danio rerio)

Purchasing of Zebrafish

72 healthy female adult zebrafish weighing 220±20mg are targeted in this study, the zebrafish bodyweight will be weight and record once in 3 days interval and they will be feed with respective food diet for 2 months. The zebrafish will be procured from animal house after obtaining the approval of Animal Ethics and Control Committee (AECC) of Management and Science University (MSU). Animals will be maintained in a standard room condition (at 28˚C under 14-h light: 10-h dark cycle and water condition of environmental quality was maintained according to an established protocol.)[7]. After allowing 2 weeks adaption, the zebrafish will be assigned randomly into 12 group and the study will be conducted according to the current guidelines for the care of the laboratory animals and all the protocols will be performed under the guidance from Animal Ethics and Control Committee of Management and Science University, Shah Alam.

LC50 test:

4 concentrations (15uM, 30uM, 45uM and 60uM) with 2 controls (1%DMSO and Tape water) are use in the toxicity test on Zebrafish larvae in 96 Well Plate. 3 Trials have been done each trails undergoing 7 days[8].

Breeding:

Zebrafish embryo have been breeding in lab, these tanks are equipped with suitable substrates, such as marbles or mesh, for the zebrafish to lay their eggs on. To induce breeding behaviour, a balance of male to female zebrafish is kept in the tanks for breeding. The male zebrafish establish territories and display courtship behaviors to attract the females, the male and female zebrafish will be separated via a partition for 14H in dark cycle and the partition is removed after that, allowing both fishes match for 1H. After 1H, the eggs have been collected and be place in a Petri dish (30 eggs in 1 dish), the Petri dish be observed and placed in an incubator with 28ºC for 24H. The fertilized, alive embryo will be transfer into 96 Well plate. Observation of the zebrafish embryo will be done for 7 days.

Olanzapine induced weight gain

In this study, a total of 24 healthy female adult zebrafish (w 210+-10 mg) were selected and raised in controlled environmental conditions. The zebrafish were kept in tanks at a temperature of 28˚C with a 14-hour light and 10-hour dark cycle. The water quality in the tanks was carefully maintained. The body weight of the zebrafish was recorded every 3 days, and their food intake was monitored daily for a period of one month.

The design of the study included 4 groups with 6 zebrafish in each group. The groups were as follows: Group 1 served as the control and consisted of zebrafish fed a high-fat diet and treated with 0.5% DMSO and system water. Group 2 and Group 3

were also fed a high-fat diet but were additionally treated with 0.5µM olanzapine, with Group 3 receiving a higher concentration of 5µM olanzapine. The olanzapine tablets were crushed into a fine powder, and the desired amount was dissolved in the fish tanks along with a 0.5% DMSO solution. The dissolved olanzapine was then added to the water system in the tanks.

Measuring Zebrafish weight:

To measure the weight of the zebrafish, a separate fish tank was used. The weight of the beaker containing water was recorded as (X), and then the target zebrafish was transferred into the beaker. The weight of the beaker with the zebrafish was then measured as (Y), and the net weight of the zebrafish (Z) was calculated as X - Y = Z.

Statistic:

Data analysis was performed using SPSS Version 23. The data is presented as mean +- SEM and statistical analysis was performed with one-way analysis of variance, called ANOVA, and thereafter the Tukey test. Statistical significance was taken at a 0.05 level. Before conducting the study, animal ethics and control committee (AECC) of Management and Science University (MSU) was obtained. The ethical treatment of the animals was assured throughout the study and proper care was given to ensure that unnecessary suffering of the zebrafish was avoided.

In sum, the present study included the utilization of 24 female adult zebrafish in order to evaluate the effects of olanzapine and a high fat diet on weight gain as well as behavior. The zebrafish were separated in four groups and their weights were monitored during a one-month period. Olanzapine was given to the animals by mixing crushed tablets in the fish tanks. Data analysis was carried out through the use of statistical methods and also the study was conducted within the guidelines of ethics to ensure the well-being of the zebrafish.

RESULTS

LC 50 test

The survival rate of zebrafish embryos across different olanzapine concentrations over 7 days is presented in Table 1.

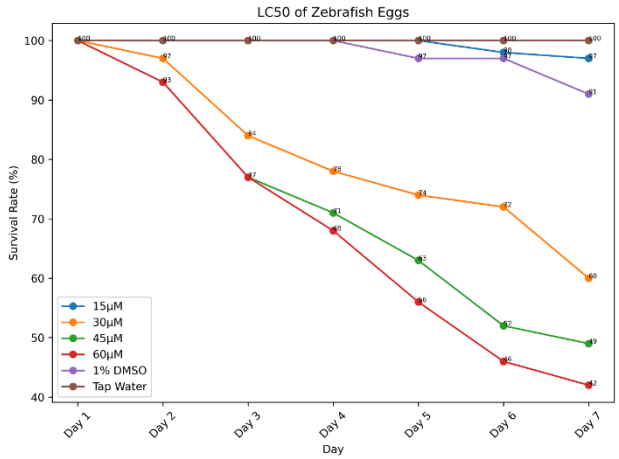
Table 1. Survival rate (%) of zebrafish embryos (LC50 analysis)

Day	15µM	30µM	45µM	60µM	1% DMSO	Tap Water
Day 1	100	100	100	100	100	100
Day 2	100	97	93	93	100	100
Day 3	100	84	77	77	100	100
Day 4	100	78	71	68	100	100
Day 5	100	74	63	56	97	100
Day 6	98	72	52	46	97	100
Day 7	97	60	49	42	91	100

The temporal trend of survival decline with increasing concentration is further illustrated in **Figure 1**.

Figure 1. LC50 toxicity analysis of olanzapine in zebrafish embryos

Line graph representing survival rates of zebrafish embryos over 7 days at different olanzapine concentrations, demonstrating dose-dependent toxicity.



The LC50 values were used in the current study to determine the toxicity of a substance to a zebrafish. The survival rates of the zebrafish were recorded for several days at various concentrations of the substance. At 15uM, the zebrafish had 100% surviving, so there were no significant toxic effects. However, at 30uM, 45uM, and 60uM, the level of survival progressively declined; i.e. increasing levels of toxicity. The average survival rates ranged from 100% to 57% for 30uM concentration, 100% to 47% for 45uM concentration and 100% to 40% for 60uM concentration. In comparison, the survival rate of the zebrafish exposed to 1% of DMSO with tap water (control groups) was very high with 100% to 90%, and 100% to 93%, respectively, showing no significant toxic effects. On the whole, the results confirm a concentration-dependent toxic effect on the zebrafish, the higher the concentration, the larger the reduction in survival rate through time. These results underscore the value of knowing the possible toxicity of substances on zebrafish and their value in evaluating their safety in research and environmental setting.

Olanzapine induced weight gain & Food Intake

The progression of zebrafish body weight over the experimental period is summarized in Table 2.

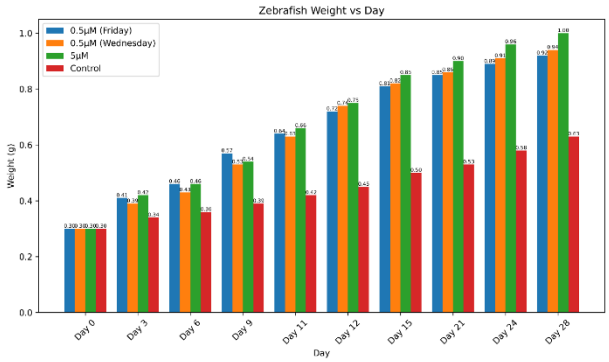
Table 2. Zebrafish weight progression over 28 days

Day	0.5µM (Friday)	0.5µM (Wednesday)	5µM	Control
Day 0	0.30	0.30	0.30	0.30
Day 3	0.41	0.39	0.42	0.34
Day 6	0.46	0.43	0.46	0.36
Day 9	0.57	0.53	0.54	0.39
Day 11	0.64	0.63	0.66	0.42
Day 12	0.72	0.74	0.75	0.45
Day 15	0.81	0.82	0.85	0.50
Day 21	0.85	0.86	0.90	0.53
Day 24	0.89	0.91	0.96	0.58
Day 28	0.92	0.94	1.00	0.63

The longitudinal trend of weight gain across treatment groups is graphically represented in Figure 2.

Figure 2. Effect of olanzapine on zebrafish weight over time

Bar graph showing the progression of zebrafish body weight over 28 days under different concentrations of olanzapine and control conditions.



The variation in food intake among different treatment groups is detailed in Table 3.

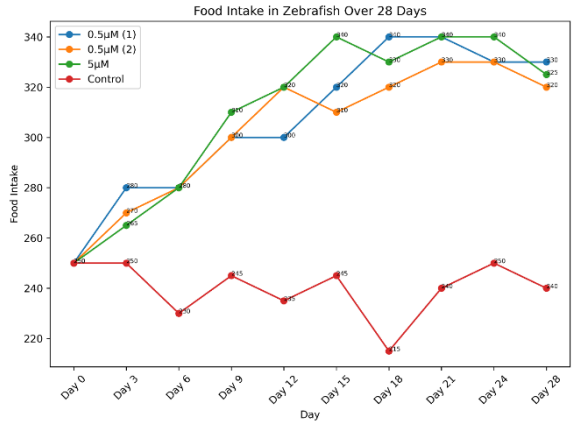
Table 3. Food intake of zebrafish over 28 days

Day	0.5µM (1)	0.5µM (2)	5µM	Control
Day 0	250	250	250	250
Day 3	280	270	265	250
Day 6	280	280	280	230
Day 9	300	300	310	245
Day 12	300	320	320	235
Day 15	320	310	340	245
Day 18	340	320	330	215
Day 21	340	330	340	240
Day 24	330	330	340	250
Day 28	330	320	325	240

Changes in feeding behavior over time are illustrated in Figure 3.

Figure 3. Food intake patterns in zebrafish during 28-day treatment

Line graph illustrating changes in food consumption across different treatment groups, indicating increased appetite in olanzapine-treated zebrafish.



The goal of this study was to examine the effects of treatment with olanzapine on weight increase and food consumption in the zebrafish. Four sets of zebrafish were considered, 0.5uM (1), 0.5uM (2), 5uM and a control group.

The weight of the zebrafish treated with olanzapine 5uM had the most weight gain overall - overall mean weight was 0.5438g. This group showed a significant increase in the weight when compared to the control group which had a mean weight of 0.3163g. The weight gain ratio was calculated by using each treatment group compared to the control group to expound on the effect of olanzapine on weight gain. The weight gain ratio of the 5uM group was determined as 1.719, which is a huge weight gain compared with that of the control group.

In comparison the two groups with 0.5uM of olanzapine had slightly reduced overall mean weights. The mean weight of the 0.5uM (2) group was found to be 0.5284g, whereas the mean weight of the 0.5uM (1) group was a little less at 0.5181g. Despite these differences, both 0.5uM groups showed higher ratios of weight gain than the control group with a value of 1.670 and 1.638, respectively. These results suggest that even at lower concentrations, olanzapine has the potential for weight gain induction in zebrafish.

To analyze the weight gain progression through time, it monitored the weight of the zebrafish in the 0.5uM (1) group for 28 days. A line graph was plotted to draw the weight gain pattern. From Day 0 to Day 3, there was a significant change in weight indicating rapid growth during the first period of the experiment.

This early gain of weight was associated with hyperphagia and elevated feeding behavior as observed in the fish.

After Day 3, the weight gain of the 0.5uM (1) group remained steady, but more moderate. Whereas from Day 3 to Day 28 the line graph reflected a gradual, upward trend showing sustained increase in weight over time. This stable increase indicates that the zebrafish in the 0.5uM (1) group was responsive to the olanzapine treatment so that they continued to grow throughout the duration of the experiment.

Food intake was also monitored throughout the experiment in order to examine the association between olanzapine treatment and feeding behavior. The data from food intakes showed varying diets for the different treatment groups over the period of 28 days. The zebrafish that were treated with the 0.5uM (1) resulted in hyperphagia, and an increased food intake as early as day 3. These fish were aggressive when feeding times arrived, they would fight in order to feed and were more irritable. The food intake ratio, compared with the food intake of every treatment group to the control group, showed that the 0.5uM (1) group had a ratio of 1.253 (higher food intake than the control group).

Similarly, the olanzapine treated zebrafish which was treated with 0.5uM (2) and 5uM also exhibited higher food intake than the control group. However, feeding behavior of these two groups differed from that of 0.5uM (1) group. The 0.5uM (2) fish showed a slightly less food intake ratio with 1.237, which implies a moderately increased appetite. The 5uM group, on the other hand, fell on the higher side of the food intake ratio at a ratio of 1.267, having the greatest amount of food intake amongst all the treatment groups. Interestingly, the fish in 5uM group had a more relaxed behavior and slower swimming movements, which would indicate a lack of association between increasing food intake and aggressive behavior or food fights.

In conclusion, olanzapine treatment in zebrafish resulted in loss of weight and changes in feeding behavior. The zebrafish treated with higher concentrations of olanzapine showed higher weight gain, and even the concentrations that were lower than this amount of olanzapine showed weight gain compared to the control group. The progression of weight gain had periods of rapid growth with prolonged weight increase over time. The food intake data showed that the appetite is increased in the olanzapine treated groups, with different aggressiveness levels towards feeding. These results offer important insights into the effect of olanzapine on weight regulation and feeding behavior in zebrafish to highlight the potential value of this species as a model to study the mechanisms underlying antipsychotic-induced weight gain;

Behavior of Zebrafish

The results suggest that olanzapine treatment in zebrafish causes significant weight gain, altered food intake and differentiated behavioral alterations. The 5uM concentration resulted in the greatest weight gain and food consumption with higher food intake and aggressive feeding behavior of the 0.5uM treated fish. These findings are important for understanding the impact of olanzapine on weight management and behavior in zebrafish and raise important implications of olanzapine use in clinical settings.

One Way Anova

The descriptive statistical parameters of zebrafish weight across groups are presented in Table 4.

Table 4. Descriptive statistics of zebrafish weight (weight1)

Group	N	Mean	Std. Deviation	Std. Error	95% CI Lower	95% CI Upper	Minimum	Maximum
1	10	0.528313	0.1590878	0.0503080	0.414508	0.642118	0.2067	0.7239
2	10	0.518100	0.1807986	0.0571735	0.388764	0.647436	0.2084	0.7447
3	10	0.543004	0.1953001	0.0617593	0.403295	0.682713	0.2009	0.7991
4	10	0.237450	0.0636047	0.0201136	0.191950	0.282950	0.2000	0.4150
Total	40	0.456717	0.1990900	0.0314789	0.393045	0.520389	0.2000	0.7991

The results of one-way ANOVA assessing differences between groups are shown in Table 5.

Table 2. One-way ANOVA analysis of zebrafish weight

Source	Sum of Squares	df	Mean Square	F	p-value
Between Groups	0.644	3	0.215	8.573	< 0.001
Within Groups	0.902	36	0.025	—	—
Total	1.546	39	—	—	—
F(3,36) = 8.573, p < 0.001 indicates a **statistically significant difference** between groups.					
"There was a significant effect of treatment on weight, F(3,36) = 8.573, p < 0.001."					

The statistical analysis confirms a significant difference in weight gain between groups. The statistical analysis with one way ANOVA showed the significant difference of weight increase in the experimental groups. The F value of 8.573 was greater than the critical range and so the null hypothesis was rejected. The indicator of the sum of squares values indicated statistically significant differences in the groups within and between groups. The DF for the analysis came to 3 and 36 (totaling 39 DF). The calculation of the mean squares produced a between group mean square of 0.215 and an in group mean square of 0.025. The calculated F showed a highly significant difference between the groups with <0.001 level of significance.

DISCUSSION

Olanzapine LC 50 test using Zebrafish embryo

The results of the LC50 test showed that the acute toxicity of olanzapine on zebrafish embryos is relatively low, as high rates of survival were recorded under an assay concentration value of 60uM. The falling survival rates with increasing concentrations of olanzapine suggests concentration-dependent adverse effects on embryo viability. The control groups (i.e., 1% DMSO and tap water) had higher survival rates, indicating that the effects noted were specific to olanzapine exposure. However, the LC50 only measures immediate toxicity and fails to give any information on potential sublethal or long-term developmental effects. Stronger studies are needed to determine the effects of olanzapine on embryonic development and its consequences. An understanding of the toxicity profile of olanzapine is important to the next set of experiments conducted in adult zebrafish and high-fat diet-induced weight gain as this guarantees the safety and reliability of the study.

Observation/ condition of embryo at/ at LC 50

The results of the observations of varying egg formation and heart rate in the olanzapine LC50 test show some insights into the effects of olanzapine to zebrafish egg formation and survival. The appearance of early coagulation, late coagulation and an unhealthy-larvae, suggests that olanzapine is having a significant impact on the viability of the egg. Additionally, effects on heart rates were observed to suggest possible cardiotoxicity of olanzapine on zebrafish eggs. Further research is necessary to determine the mechanisms for these effects, as well as long term consequences of exposure to olanzapine and the effect on the development of zebrafish. These results add to the understanding of the risks of olanzapine and form a basis for further studies on olanzapine's effects on weight gain in the zebrafish model[8].

Olanzapine induced weight gain in adult female zebrafish

The study investigated the exposure of olanzapine to weight gain in zebrafish. The results showed that olanzapine significantly caused weight gain in comparison with the control group. The weight gain

ratios were also robust evidence for the significant influence of olanzapine on weight control. These findings are compatible with previous research done in zebrafish, other animal models and humans, which attests to the relevance of the study.

The study investigated the mechanisms responsible for olanzapine weight gain. Olanzapine acts on the neurotransmitters which comprise dopamine and serotonin, the receptors associated with the regulation of appetite. The antagonistic effect of olanzapine on dopamine D2 receptors is likely to be responsible for the increase in appetite and food intake that results in weight gain[3]. Olanzapine also has a specific effect on serotonin receptors, in particular, the 5-HT2C receptor, that is involved in the regulation of appetite[9]. Disruption of such systems by olanzapine can disrupt normal feeding behavior and energy homeostasis and in turn lead to weight gain.

In addition, olanzapine has also been found to affect adipokine concentrations, especially adiponectin. Decreased levels of adiponectin in association with olanzapine treatment were associated with increased adiposity and impaired glucose metabolism contributing to weight gain and metabolic abnormalities[10]. The changes in the gut- brain axis and release of appetite-regulating hormones, such as ghrelin are also possible. Elevated ghrelin levels induced by olanzapine could increase the search for food and calorie intake leading to further weight gain[11].

Comparisons with other experiments motivating on zebra fish and different varieties of animals give more insights. Studies on the effects of other atypical antipsychotic medications such as risperidone have shown weight gain, also dose-dependent, similar to olanzapine. Furthermore, the results of studies in rodents have found that olanzapine worsens weight gain in animals when they are fed a high-fat diet[12]. This is similar to the current study of the effect of olanzapine on weight gain induced by a high-fat diet in the zebrafish, reinforcing the evidence for the role of olanzapine in promoting weight gain.

Overall, this study adds to the knowledge of effects of olanzapine on weight gain in zebrafish. The results underscore how potent olanzapine is with respect to weight control and offer a glimpse of how it works with respect to the underlying mechanisms involving neurotransmitter systems, adipokine level and appetite-regulating hormones. The consistency of these results with past studies in different species adds some validity to the results. Further study is needed to investigate the long-term consequences and possible mitigating strategies of olanzapine induced weight gain.

One Way Anova

The results of the one-way analysis of variance (ANOVA) is an interesting source of information about the statistical differences of the experimental groups in weight gain. The analysis showed a significant difference in weight gain between the groups which shows the treatments had an effect on the changes in weight observed.

The significance test of the F ratio ($F = 8.573$, $p < 0.001$) shows that there are different levels of weight gain among the experimental groups. This suggests that olanzapine administration had a significant effect on weight gain in high- fat diet exposed zebrafish. Post-hoc tests may be performed to determine between specific groups which are found to significantly differ from one another.

Further analysis of the sum of squares indicated that between group variability (SS between = 0.644) represented a high proportion of the total variability (SS total = 1.546). This means that the impact of the treatments on weight gain was significant. The values for the mean square (MS between = 0.215, MS within = 0.025) give further proof of the significant differences between the groups.

These findings suggest that the administration of olanzapine in the high-fat-dieted zebrafish found that the animals were significantly heavier than the non-treated ones. The observed increase in weight could potentially be attributed to a number of factors associated with the pharmacological properties of olanzapine.

Olanzapine is known to act on the various several neurotransmitter receptors such as serotonin and dopamine receptors. By blocking dopamine from binding with the D2 receptors and increasing serotonin binding with 5-HT2A and 5-HT2C receptors, the balance of these types of neurotransmitters is disrupted by olanzapine. This change in neurotransmitter activity is one such change that may have played a role in the observed weight gain of our zebrafish model.

It is worth noting that the doses of olanzapine used in this study were 0.5uM (1), 0.5uM (2), and 5uM, representing different concentrations of the drug. The specific mechanisms by which olanzapine induces weight gain in zebrafish exposed to a high- fat diet are not yet fully understood, but it is possible that the effects are dose-dependent.

Interestingly, the weight gain observed in zebrafish exposed to the lower concentrations of olanzapine (0.5uM (1) and 0.5uM (2)) was not significantly different from the group exposed to the higher concentration (5uM). This implies that even at lower concentrations, olanzapine can have a significant impact on the weight gain of zebrafish.

The present study used adult female zebrafish with an average weight of 200mg ± 10mg. However, it is important to bear in mind that gender and age may be important influences on olanzapine-induced weight gain. Previous studies have suggested that females may be more susceptible to olanzapine weight gain than males. Further investigations can investigate the gender-

dependent effects of olanzapine in Zebrafish.

Additionally, the underlying mechanisms of the olanzapine-induced weight gain in zebrafish is not fully described. It is conceivable that olanzapine could affect appetite and calorie intake and change the endocrine or metabolic regulation of body weight. These things might be responsible for the weight gain that is seen.

The results of our research have implications on the clinical application of olanzapine in the treatment of mental disorders in humans since weight gain is a frequent side effect found in association with its use. The zebrafish model used in the study is a useful tool to further explore the mechanism behind the olanzapine-induced weight gain and find ways to reduce the effects of olanzapine.

To sum up, our study proves that the administration of olanzapine in zebrafish under a high-fat regimen has a significant role in weight gain. The significant outcomes of one-way analysis of variance support the potential role of olanzapine in weight gain and the need for further research to understand the specific mechanisms involved. Understanding these mechanisms may help in the development of interventions to reduce the weight gain associated with olanzapine treatment and the overall approach to the management of mental disorders in patients.

CONCLUSION

Understanding the relationship of olanzapine and high-fat, diet-induced weight gain is important in light of mental illness treatment. Olanzapine, which is commonly prescribed for the treatment of schizophrenia and bipolar disorder, leads to major weight gain and metabolic imbalance. This weight gain can result in metabolic disorders, cardiovascular diseases and psychological consequences themselves. Persistent weight gain makes the problem of mental illness even more burdensome for a sufferer.

Understanding the process of this is important for helping to devise methods of reducing weight gain. Researchers can determine targets for interventions, such as dietary changes, lifestyle changes and the use of specific medications. Understanding the factors that can contribute to weight gain helps in making the treatment decision and personalized treatment. Close follow-up, exercise, diet advice, and use of favorable weight profile antipsychotics are potential measures.

Optimizing mental health treatment balances the benefits and harm of treatment. By preventing weight gain, patients will have better outcomes, improved quality of life and less long-term health risks. Skin Cancer: identifying risks and applying interventions to provide effective and individualized care while minimizing negative consequences.

Overall, knowledge of the relationship between olanzapine and high-fat diet-induced weight gain is extremely important for elucidating the best way to treat mental illness. By acknowledging risks and applying the right interventions, healthcare providers can guarantee effective and personalized care and reduce negative impacts on weight and metabolic health.

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