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Effects of Oral Administration of Monosodium Glutamate (MSG) on Obesity in Male Wistar Rats (*Rattus Norvegicus*)

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ABSTRACT

Background: Monosodium glutamate (MSG) is one of the most widely employed food enhancers. Although the umami compound, controversy persists regarding the effects of MSG intake on body weight. Chronic MSG intake may result in excessive body weight gain and obesity. Consumption of MSG result in organ damage, cardiovascular disease, oxidative stress, and also risk factors for obesity. This study aims to determine the effect of oral MSG on obesity in adult male Wistar rats (*Rattus norvegicus*). **Methods:** This true experimental study used the post-test control group design. Twenty-four adult male Wistar rats were randomly divided into four groups: control (received distilled water), Group 1 (MSG 0.378 mg/gr BW), Group 2 (0.756 mg/gr BW) and Group 3 (1.512 mg/gr BW). The obesity parameter was obtained by the Lee index. Kruskal-Wallis test follows by Mann-Whitney test were used to compare the Lee index between groups. **Results:** Lee's index mean for each group was 358.4%, 314.1%, 287.8%, and 320.9%, respectively. The Kruskal Wallis test showed a significant difference in the Lee index between groups ($p = 0.043$). A follow-up test using Mann-Whitney found a significant difference between group 2 and the control group ($p = 0.043$, $p < 0.05$). The mean of Lee index of group 2 was 70.51% lower than the control group. **Conclusion:** This study concluded that Lee index was not increased in MSG-treated rats than in the control group after oral MSG intervention for 21 days.

1. Introduction

Monosodium glutamate (MSG) is a flavour enhancer that increases sweetness and saltiness and reduces sour and bitter tastes in food products.¹ L-glutamate binds to receptors in the taste buds and stimulates the distinctive umami taste provided by MSG. The use of Monosodium Glutamate (MSG) in food is increasing due to fast food popularity. The Food and Agriculture Organization (FAO) and the World Health Organization (WHO) stated that MSG as a food flavour enhancer with an acceptable daily intake (ADI) is 0-120 mg/kg^{1,2}. Excessive and continuous MSG consumption increases the activity of α -ketoglutarate, nitric oxide synthase,

and protein kinase C, causing increased lipid peroxidation. This condition leads to an increase in the risk of obesity³.

Administration of MSG to neonatal rats causes damage to the ventromedial hypothalamic nucleus and arcuate nucleus, leading to obesity due to impaired energy metabolism⁴ and decreased sympathetic and thermogenic activity of brown adipose tissue / BAT⁵. Besides, there is also damage to the cholinergic infundibular system in the hypothalamus. The hypoactivity of this system causes the accumulation of choline resulting in metabolic disorders, namely an

increase in phospholipid synthesis/transport in obese mice⁶.

The role of MSG, as a food additive, in the global obesity epidemic is still unclear. This study aims to investigate the effect of oral MSG on obesity in male Wistar rats (*Rattus norvegicus*).

2. Methods

This true experimental laboratory study used the Post-test control group design. Twenty-four adults male Wistar rats were randomly divided into four groups, and the experimental group were supplemented with MSG. MSG doses used in this research were acceptable daily intake (ADI) doses that WHO / FDA has approved (60 mg/kg BW) and converted into doses of experimental animals. The control group were received distilled water. Group 1, 2, and 3 were administered oral MSG solution at 0.378 mg/gr BW; 0.756 mg/gr BW and 1.512 mg/gr BW, respectively, on a daily basis for twenty-one days. After this period, the animals were sacrificed. The animal protocol was approved by the Research Ethics Committee of the Faculty of Medicine of Syiah Kuala University.

The obesity parameter was estimated according to the Lee index for each animal. This index consists of

dividing the cubicle root of the weight in grams by the naso-anal length in millimetres multiplied by 1000. With normal body composition in rats, the Lee index is 295 to 310, a value of ≤ 300 was classified as normal. Rats with values > 300 were classified as obese. Lee et al. explained that calculating the obesity index in experimental animals such as mice was carried out using several methods, including the Röhler index, Lee index, and TM index⁷.

Data were analyzed with computer software and presented as the mean \pm standard deviation (SD) for Lee Index (LI). Kruskal-Wallis test follows by Mann-Whitney test were used to compare the variables between groups. The difference between groups was defined as statistically significant when a p-value < 0.05 .

3. Results

The control group had the highest Lee index score, while the lowest mean of Lee Index was found in group 2. The Kruskal-Wallis test showed a difference in the mean Lee index between groups. The follow-up test results of the Mann-Whitney test showed a significant difference in the Lee index between the control group and group 2 ($p = 0.043$); the mean Lee index score in group 2 was 70.51 lower than the control group. Lee Index (LI) for each group shown in Table 1.

Table 1. Lee index difference in Control and Experimental Groups

	Group	Median	Minimum	Maximum	Mean \pm Sd	P
Lee's Index (g/cm)	Control	390.18	298.81	406.27	358.40 \pm 43.84	0.043*
	Group 1	320.77	261.18	360.56	314.19 \pm 37.31	
	Group 2	289.50	272.31	300.00	287.89 \pm 10.74	
	Group 3	322.93	322.31	370.03	320.97 \pm 41.97	

*Kruskall-Wallis test. Values are statistically significant at $p < 0.05$. SD = standard deviation, $n = 6$.

4. Discussion

Our study showed that the mean value of Lee's index of the treatment group was lower than the control group. These results are in line with research conducted by Kondoh and Torii; the experiment group that was giving 1% MSG (1.1% MSG monohydrate, 60mM in water; 0.029 kcal / g solution; Ajinomoto, Tokyo, Japan) for six weeks had a mean value of body weight that was lower than the control group⁸. Meanwhile, Nakamura reported a higher mean body weight of mice in the control group (33.5 ± 2.0) than the

treatment group after being administered MSG 0.064% (32.9 ± 1.5)⁹. Dolnikoff found that subcutaneous injection of MSG 4g / kg BW for 30 days in neonatal rats showed a lower mean body weight (72.9 ± 1.5) than the control group (95.8 ± 1.6)¹⁰.

Several studies showed an increase in the body weight of mice. Sasaki proved that there was a significant increase in body weight (66.3 ± 1.2) with subcutaneous administration of 4mg/g BW MSG for 54 weeks ($p < 0.01$)⁴. A study of administering MSG orally for 32 weeks in neonatal mice showed no effect on

increasing body weight, abdominal fat weight (epididymis, mesenteric, perirenal), and leptin levels in the body. Consumption of MSG also does not cause fat accumulation⁹.

Reports on the effect of MSG consumption on body weight vary widely, with some studies showing an increase in body weight^{11,13}, while other studies have shown a decrease in body weight⁸ or no effect on body weight¹⁴. It is important to note that each study has a different administration route, MSG doses, and animal study age.

Direct exposure to high doses of glutamate or MSG causes cell death due to excitotoxicity, whereas direct injection of high doses of newborn mice causes neuron cell death in the hypothalamus, leading to obesity. Most oral glutamate will be metabolized through the first pass, for example, in the digestive organs (gut). Therefore the metabolism of MSG or glutamate depends on the route of administration⁹. This study used a low oral treatment dose which is the approximate average dose consumed by the human. This result is very different from the previous study by Olney et al. in mice given MSG injection of 4 g/kg body weight during pregnancy. This study reported that MSG administration led to obesity, neuroendocrine disorders, behavioural disorders, and brain damage to neonatal mice¹⁵.

L-glutamate receptors may also mediate the effect of MSG on body weight in the gastrointestinal (mouth or intestinal) associated with afferent fibres from the vagus nerve¹⁶. Glutamate receptors are associated with innervation in the mouth (associated with taste receptors and sensory nerves) and upper and lower gastrointestinal tract (associated with vagus afferents in the stomach)⁸. Monosodium glutamate stimulates oral glutamate receptors and produces an umami taste. MSG stimulation of umami taste increases the efferent activity of the pancreatic vagal nerve and stimulates insulin secretion. Furthermore, stimulation of the MSG solution on the mouth and intestinal receptors will increase the stomach's vagus nerve's efferent branch activity¹⁷.

According to Onaolapo, administering oral MSG will deliver the initial dose of MSG into the gastrointestinal

lumen, indirectly activating vagal afferents (from the gastric, celiac, and hepatic branches) by produce and release of NO and serotonin^{8,16}. Such activation affects adipocyte fat metabolism mediated by autonomic innervation and the function of the gastrointestinal tract itself (e.g. MSG is known to induce gastric emptying after consuming a high protein diet¹⁷. This hypothesis needs further investigation.

5. Conclusion

This research concluded that the Lee index did not increase in MSG-treated rats compared to the control group after oral monosodium glutamate intervention for 21 days.

6. References

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