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Effect of monosodium glutamate on hematological parameters in Wistar rats

Ashaolu J. O.^{1*}, Ukwenya V. O.¹, Okonoboh A. B.², Ghazal O. K.², Jimoh A. A. G.³

¹Department of Anatomy, College of Health Sciences, Bowen University, Iwo, Osun State, Nigeria.

²Department of Anatomy, College of Health Sciences, University of Ilorin, Ilorin, Kwara State, Nigeria.

³Department of Obstetrics and Gynaecology, College of Health Sciences, University of Ilorin, Ilorin, Kwara State, Nigeria.

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Monosodium glutamate (MSG) is a food additive commonly consumed as a flavor enhancer. However, both animal models and human clinical reports have established its harmful effects. The rats in two groups (A₁ and B₁) were administered with 5.5 g/kg body weight (b.wt) and 2.75 g/kg b.wt of MSG for 14 and 28 days respectively each, while Groups A₂ and B₂ were withdrawal groups for A₁ and B₁ which were sacrificed 14 days post-administration. At the end of the study periods, blood samples were analyzed for hematological parameters. Test results showed significant effect ($p < 0.05$ compared to control) on the neutrophil and lymphocyte count which are indicative of a compromised immune status and poisoning in the treated animals. Packed cell volume (PCV), hemoglobin (Hb), red blood cells (RBC), mean cell volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC) values analyzed were all indicative of an anemic condition in the treated animals. These findings support that MSG despite its flavoring functions, is detrimental to health.

Key words: Monosodium glutamate, hematological parameters, neutrophil and lymphocyte count, RBC count, PCV, hemoglobin concentration, MCV, MCH, MCHC, immunity, anemia, automatic hematological assay analyzer.

INTRODUCTION

Monosodium glutamate (MSG) is the naturally occurring L form of glutamic acid, used as a flavor enhancer. It is also used intravenously as an adjunct in the treatment of encephalopathies associated with hepatic disease (Schaumburg et al., 1969). Eweka (2007) reported the distortion of the cyto-architecture of the renal cortical structures and cellular necrosis associated with the kidney. MSG consumption may have some deleterious effects on the cerebellum of adult wistar rats at higher doses and by extension may affect the functions of the cerebellum and may lead to tremor, unstable and uncoordinated movement, and ataxia (Eweka and Om'Iniabohs, 2007). According to Samuels (1999), the evidence of toxicity is overwhelming. Exposed laboratory animals suffered brain lesions and neuroendocrine

disorders. Despite these, several international organizations and government institutions have declared MSG safe for consumption. Literature has shown that ingestion of drugs can alter normal range of hematological parameters (Ajagbonna et al., 2006). However, such studies dealing with the effects of MSG on hematological parameters are scarce. Therefore, this study examines the effect of monosodium glutamate on hematological parameters such as packed cell volume (PCV), hemoglobin (Hb), red blood cells (RBC), mean cell volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), neutrophil and lymphocyte count in Wistar rats, as well as the 14 days post-administration effects.

MATERIALS AND METHODS

Animal grouping and treatment schedule

Twenty five normal healthy adult Wistar rats of both sexes with

*Corresponding author. E-mail: olusco172003@yahoo.com Tel: +234-8137609462.

average weight of 182 g were obtained and maintained in the Animal Holdings of the Department of Anatomy, Faculty of Basic Medical Sciences, University of Ilorin, Ilorin, Nigeria in a very tidy environment with standard light, temperature and humidity. The rats gained maximum acclimatization before actual commencement of the experiment. The animals were randomly assigned into five groups A₁, A₂, B₁, B₂ and C of five animals each and were treated following the ethical guidelines of the laboratory animal committee of the College of Health Sciences, University of Ilorin. The rats in the treatment groups (A₁, A₂) were fed orally once daily MSG solution at the dose of 5.5 g/kg b.wt for 14 days. The rats in the treatment groups (B₁, B₂) were given 2.75 g/kg b.wt of MSG solution per day for 28 days. The control group received same amount of distilled water for the duration of the experiment. The rats in Group A₁ were sacrificed on the 15th day of the experiment. Those in Groups A₂, B₁ and C were sacrificed on the 29th day. However, the rats in Group B₂ were sacrificed on the 43rd day of the experiment. All animals were sacrificed by cervical dislocation, the thoracic cage was carefully cut open to access the heart, and blood sample was collected through cardiac puncture.

Hematological evaluation

Two milliliters of blood each were collected into heparinized sample bottles and were then analyzed for hematological parameters such as packed cell volume (PCV), hemoglobin concentration (Hb), total red blood cells (RBC) count, mean cell volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), total white blood cell (WBC) count and total platelets count using an automatic hematological assay analyzer, Advia 60[®] Hematology System (Bayer Diagnostics Europe Ltd., Ireland). Blood smears were stained with Giemsa for differential WBC count (Gulye et al., 1988), while neutrophil and lymphocyte counts were done.

Statistical analysis

The results were expressed as mean \pm S.E.M. The significance of the difference between means was determined by the student *t*-test using SPSS software and the results were regarded as significant at $P \leq 0.05$.

RESULTS AND DISCUSSION

The present study showed that both dose and concentration produce significant effect on hematological parameters. But causal relationship between MSG and diverse reactions is far from being established (Geha et al., 2000). The symptoms and regions of the body affected by Chinese restaurant syndrome (CRS) were noted to be similar to those of pain referred from the upper esophagus. Due to the fact that MSG was found not to be unique in producing CRS symptoms, it was proposed that CRS may be a manifestation of esophageal irritation (Kenney, 1980, 1986). The same doses of MSG taken in capsules is associated with increased level of blood sodium which was suggested to be a cause of CRS (Smith et al., 1982). Furthermore, the symptoms of CRS were noted to be similar to those observed after acetylcholine administration, indicating that MSG may also covert glutamate to acetylcholine via the tricarboxylic acid (TCA) cycle and these cholinergic mechanisms

could modulate CRS symptoms; thus it was proposed that CRS was a form of acetylcholinosis (Ghadimi et al., 1971).

Also, MSG mediated stimulation of peripheral receptors may be proposed as the mechanism for CRS (Schaumburg et al., 1969). The use of MSG was found to have no effect on blood glucose or cholesterol level, and that MSG consumption did not contribute to excessive weight gain (Go et al., 1973). Also, there was no correlation between the appearance of symptoms and blood glutamate concentrations (Kenney and Tidball, 1972; Hsu and Huang, 1985). The only biochemically demonstrable effects are reduction in serum cholesterol and b - lipoprotein levels. Supplements of glutamate as high as 100 g/day showed no toxic manifestations (Bazzano et al., 1970). But the present study indicates all doses of MSG administered showed significant decrease (A₁-19.76%, A₂-56.80%, B₁-38.89%, B₂- 66.67%) in neutrophil count and the decrease is higher in the groups that received treatment for longer days. The normal value of neutrophil count in humans is 3000 to 6000 / cu.mm of blood. This might be that MSG has a direct toxic effect on the neutrophils in the blood or it has a deleterious effect on blood production in the bone marrow, especially on the progenitor cells (aplasia) and that it is time-dependent. Neutrophils along with monocytes provide the first line of defense against invading micro organism, toxic substances, and foreign substances emphasizing the important role neutrophils play in the body defense (Hall, 2011). This might be indicative of the deterioration of immune status in the treated rat groups in response to the toxic effect of MSG. The observed increase (A₁-77.09%, A₂-140.00%, B₁-104.16%, B₂-154.12%) in lymphocyte count (normal value = 1500 to 2700 / cu.mm of blood) in all the treated animals might be due to the fact that MSG is perceived as a toxic agent in the treated animals or probably due to a considerable increase in granulocytes or could be a consequence of the interaction between MSG gastrointestinal macrophages. Macrophages serve as antigen presenting cell, and the antigenic products (polypeptides) to the helper T cells and the B lymphocytes bringing about their activation (Sembuligham, 2005). Macrophages also secrete substances called interleukin-1 /-cytokines, which brings about the activation, proliferation and increase in the lymphocyte count (Sembuligham, 2005; Barrett et al., 2010). The continual count increase (B₁-104.16%, B₂-154.12%) seen in Groups B₁ and B₂ that received treatment for longer days and in all the withdrawal groups indicate that MSG does not have a destructive effect on the lymphocytic cells. This also implies that MSG has a residual and prolonged effect within the body system.

Alao et al. (2010) reported that sudden withdrawal of MSG from experimental rats seems to have resulted in more degenerative changes on the frontal lobe. A gradual withdrawal might have produced a different result. Reduction effects were of MSG seen on the packed cell volume (A₁-103.78%, A₂-17.04%, B₁-21.49%, B₂-24.44%)

Table 1. Effect of monosodium glutamate on hematological parameters in adult Wistar rats.

Hematological parameter	Control group	Group A ₁ (%)	Group A ₂ (%)	Group B ₁ (%)	Group B ₂ (%)
Neutrophils (×100 / cu.mm)	54.00 ± 5.03	43.33 ± 0.67 (19.76)	23.33 ± 1.76* (56.80)	33.00 ± 4.04* (38.89)	18.00 ± 3.46* (66.67)
Lymphocytes (× 100 / cu.mm)	32.00 ± 6.43	56.67 ± 0.67(77.09)	76.67 ± 1.76* (140.00)	65.33 ± 4.67*(104.16)	81.33 ± 3.33* (154.12)
PCV (%)	45.00 ± 0.58	40.33 ± 1.20 (103.78)	37.33 ± 0.88* (17.04)	35.33 ± 0.88* (21.49)	34.00 ± 1.15* (24.44)
RBC (×10 ⁶ / cu.mm)	4.55 ± 0.64	4.13 ± 0.18 (9.23)	3.53 ± 0.18* (22.42)	3.17 ± 0.12* (30.33)	3.11 ± 0.09* (31.64)
Hb (g%)	15.00 ± 0.19	13.45 ± 0.40 (10.33)	12.44 ± 0.29* (17.06)	11.77 ± 0.29* (21.53)	11.33 ± 0.39* (24.47)
MCV (cu.microns)	99.00 ± 2.61	98.15 ± 6.97 (0.85)	106.03 ± 4.53 (7.10)	111.56 ± 2.38* (12.67)	112.93 ± 3.64 (14.07)
MCH (pg)	33.02 ± 0.87	32.53 ± 2.32 (1.48)	36.88 ± 2.43 (11.69)	34.22 ± 3.33 (3.63)	36.57 ± 2.21(10.75)
MCHC (%)	33.00 ± 0.00	33.33 ± 0.00* (0.00)	33.33 ± 0.01* (0.00)	33.31 ± 0.01 (0.93)	33.33 ± 0.01* (0.00)

Values are mean ± SD of five rats. *Significantly different from the control group at P= 0.05. Values in the parentheses are % change compared to control.

and hemoglobin concentration (A₁-10.33%, A₂-17.06%, B₁-21.53%, B₂-24.47%). The normal values of packed cell volume, hemoglobin concentration and RBC count in humans are 38 to 42%, 14 to 16 g% and 4 to 5.5 million / cu.mm respectively. RBC count suggests that it probably reduces the life span of red blood cells in the blood which might be as a result of direct toxicity. This might also have been mediated through a deleterious effect on the hemopoietic stem cells in the bone marrow. MSG might cause increased oxidative stress (a function of anaerobic respiration) in the tissues of the animals. MSG at a dose of 4 mg/g significantly (p < 0.01) induced the formation of micronucleated polychromatic erythrocytes (MNPCEs) (Farombi et al., 2006). Elphick et al. (2008) investigated the oxidative glutamate toxicity in HT22 murine hippocampal cells, a model for neuronal death by oxidative stress. These toxic effects were characterized by cell and nuclear condensation, yet occurred in the absence of either DNA fragmentation or mitochondrial cytochrome c release (Elphick et al., 2008). MCV and MCH values (normal values = 27 to 32 pg, 78 to 90 cu. micron respectively) were observed to be markedly increased (A₂-7.10%, B₂-

14.07%, A₂-11.69%, B₂-10.75%) in all the Withdrawal groups following the sudden withdrawal of MSG.

No ameliorating effect was observed, but the increased parameters observed are more indicative of anemia. Increased mean corpuscular volume (MCV) indicates the cells to be macrocytic (Sembulingham, 2005). Increase in MCV is seen in pernicious anemia (normochromic) and megaloblastic anemia (hypochromic) (Richards, 1993), while the increased MCH is indicative of macrocytic anemia (Sembulingham, 2005). However, the mean corpuscular hemoglobin concentration (MCHC) (normal value = 30 to 38% in humans) shows to be normal in both the treatment and control groups. Thus, macrocytic normochromic anemia (pernicious anemia) was more specifically indicated. This might be due to the atrophy of the gastric mucosa (gastritis) caused by the MSG which is acidic (L form of glutamic acid), resulting in reduced synthesis of the intrinsic factor, and thus poor absorption of vitamin B₁₂ which is the main cause of pernicious anaemia (Sembulingham, 2005).

The present study shows MSG administration has a significant effect on the neutrophil and

lymphocyte count, indicative of a compromised immune status and poisoning respectively in the treated animals. While alterations in counts of PCV, Hb, RBC, MCV and MCH were all indicative of anemic conditions in the treated animals. Hence, these findings support the fact that monosodium glutamate despite its flavoring functions is detrimental to health (Eweka, 2007).

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