ORIGINAL ARTICLE

Effect of Sub-chronic oral Experimental Exposure of Monosodium glutamate on Biomarkers of Hepatic and Renal function in Male Wistar Rats

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ABSTRACT

Background: Monosodium glutamate (MSG) is a food additive that acts as a preservative or as enhancer of palatability and is locally called Ajinomoto or white magi in Nigeria.

Objectives: This study assessed the effect of sub-chronic oral exposure to monosodium glutamate (MSG) on some plasma biomarkers of hepatic and renal function in adult male Wistar rats.

Methods: Sixty-four adult male Wistar rats of average weight 150 to 200 g were randomly assigned into two groups of MSG-treated and non-MSG-treated control rats (n=64). The control rats were orally given distilled water only while the MSG-treated rats were administered 5 g/kg body weight of MSG at concentration of 500 mg/ml daily throughout the period of the experiment that lasted 8 weeks; feed and water were provide to both groups *ad libitum*. A total of 8 rats, 4 per group were sacrificed weekly for blood sample collection and analysis of hepatic and renal biochemical indices.

Results: the result of biochemical analysis showed significant increase ($P \leq 0.05$) in mean of Alanine aminotransferase (ALT), Aspartate aminotransferase (AST), Alkaline phosphatase (ALP), Urea and Creatinine activities in the MSG-treated rats.

Conclusion: The increases in the levels of plasma biochemical parameters signal some level of alteration in the normal physiologic function of both liver and kidney.

Key words: Hepatic, Monosodium glutamate, plasma, Renal, Wistar rat.

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Access this article online

Quick Response Code

website: www.bornomedicaljournal.com

DOI: 10.31173/bomj.bomj_80_15

Introduction

Monosodium glutamate (MSG) is a food additive that acts as a preservative or as enhancer of palatability and is locally called Ajinomoto[1] or white magi in Nigeria. In early 1900s scientists isolated the ingredient (glutamate) in plants that is the essential taste component responsible for the greatly enhancing taste[2]. Glutamate is present in virtually all foods, including meat, fish, poultry, breast milk and vegetables, with vegetables tending to contain proportionally higher levels of free glutamate as MSG[3]. Various processed and prepared foods such as traditional seasoning sauce and certain restaurant foods contain significant amounts of free glutamate (as MSG), both from natural sources and from added monosodium glutamate. Although MSG has been reported to be safe when present in small amounts in any one food[4] the problem arises if small amounts are in different common foods that are consumed daily[5].

However, despite the numerous beneficial effects of MSG[6], its' safety usage has generated controversial argument locally and internationally[7]. The finding that MSG produces a bleaching effect to remove stains from clothes has led to a growing apprehension that the excellent bleaching property of MSG[8] could be injurious to the tissue and may, over time, induce terminal changes in consumers of MSG-seasoned foods[9].

With the Kidney as a major organ involved in the excretion of toxic metabolic waste products, particularly the nitrogenous compounds and the liver involved in many metabolic processes, they could be more prone to the harmful effect of a chemical or a drug meant for target organisms. Therefore, considering the discrepancies in the literature and growing safety concern for the use of MSG, there is therefore the need to evaluate this important food additive. This study therefore aimed at evaluating the effects of oral MSG exposure on some plasma biomarkers of hepatic and renal function in adult male Wistar rats.

Materials and Methods

Study Area

The experiment was conducted in Zaria, Northern Nigerian, which is located in the Northern Guinea Savannah zone (11^0 10 N, 07^0 38'E). Trees and grasses characterize the vegetation of this zone with average rainfall ranging between 1000 to 1250 mm and temperature of 17^0C to 33^0C[7].

Experimental Animals

Sixty-four adult male Wistar rats weighing between 150 to 200 g were purchased from Department of Human Anatomy, A.B.U Zaria, Kaduna state, Nigeria and used for the experiment. Rats were housed in aluminum cages covered with wire mesh and kept under natural thermal environmental conditions with ambient temperature of 24 ^{0}C - 27 ^{0}C, relative humidity of 70 - 80 % and approximately alternating 12-hour light/dark cycles. The animals were fed with pelletized commercial grower feed (Vital feed®, Jos, Nigeria) and water provided a*d libitum*. The rats were allowed to acclimatize for two weeks prior to the commencement of the experiment.

Design of the Experiment

Following two weeks of physiological adjustment, the rats were divided into 2 groups of MSG-treated and non-MSG-treated control rats (n=32). The non-MSG-treated control rats were provided administered feed and distilled water as placebo throughout the period of experiment while the MSG-treated rats were administered aqueous solution of MSG daily at a dose of 5 g/kg bodyweight for a period of 8 weeks.

Preparation and Administration Monosodium Glutamate

Food grade MSG (Ajinomoto containing 99+% of MSG manufactured by Ajinomoto co., inc. Tokyo, Japan, marketed by West African Seasoning Company Limited) was obtained in a dry form from the market. Aqueous solution of MSG was prepared daily by dissolving 16 g in 32 ml of distilled water to obtain a concentration of 500 mg/ml. The MSG-treated rats were orally administered MSG daily at a dose of 5 g/kg body weight per rats using a graduated syringe and a stainless steel intubation cannula. The dose used was based on LD_{50} before commencement of the study.

Sample Collection

From each of the two groups, blood samples were collected from four rats on weekly basis (i.e on day 7, 14, 21, 28, 35, 42, 49 and 56). Each rat was humanely sacrificed by jugular venesection; two milliliters of blood was obtained and dispensed into EDTA-impregnated sample bottle which were centrifuge immediately to obtain plasma for biochemical analysis.

Biochemical Analysis

Biochemical parameters; Alanine aminotransferase (ALT) (IU/L), Aspartate aminotransferase (AST) (IU/L), Alkaline phosphatase (ALP) (IU/L) Creatinine (mmol/l), Blood Urea Nitrogen (UN) (mmol/l) were analyzed using test kits obtained from Reckon Diagnostic Private Limited, (3/7 Gorwa, Vadodara 390016, Gujarat, India) with a fully automated analyzer (Rayto Chemray-120 fully automated clinical blood chemistry analyzer,

China, mainland) using standard methodology according to manufacturers' instruction.

Data Analysis

Data generated were summarized as mean ± standard error of mean and analyzed using Graph-pad prism version 5.0 (graph-pad software, San Diego, CA, USA). Differences between the two groups were tested using students' t-test and presented in figures. Values of $P \leq 0.05$ were considered significant.

Results

Clinical observations Following monitoring of rats at least twice daily for clinical sign of ill-health or behavioural changes, there were no visible clinical observations noticed from the beginning until termination of the experiment.

Mean of Alanine aminotransferase (ALT), Aspartate aminotransferase (AST), Alkaline phosphatase (AST)

Table 1 shows significant increase ($P < 0.05$) in plasma activities of both ALT and AST in the MSG-treated rats. The highest increase value for ALT and AST were 69 ± 3.7 IU/L and 80 ± 5.4 IU/L respectively which were observed at the week of termination of the experiment (week 8). Similarly, significant increase were observed in the mean values of ALP activity for the MSG-treated rats from week 1 postcommencement of MSG-exposure until week 8 of termination of the experiment as shown in table 1. Mean of urea and creatinine level Table 1 also shows significant increase in the mean values of plasma urea and creatinine level of the MSG-treated rats. The most significant ($P < 0.05$) values for urea and creatinine were 8.1 ± 0.63 mmol/L and 6.3 ± 2.7 mmol/L respectively, observed at the last week (8) post-commencement of treatment.

Discussion

The non visible clinical observation noticed from beginning to termination of the experiment was similar to that of Morselli and Garattini10 who concluded that there was no evidence that MSG could cause any clinical signs of abnormality.

Plasma levels of transaminases and phophatase (ALT, AST and ALP) were used as an indicator of impairment in liver structural integrity; they are released into the circulating blood only after structural damage[11]. The increase in plasma ALP activity could be attributed to increase synthesis in the presence of increasing biliary pressure[12]. Also, the metabolism of most amino acids and their derivatives occur to some extent in the liver[13] and essentially involves deamination to produce ammonium ion that could be toxic unless otherwise made less toxic via the reactions of the urea cycle. The sodium moiety in monosodium glutamate could easily dissociate to yield free glutamate. Thus, the possible ammonium ion overload that may occur with glutamate or monosodium glutamate intake could damage the liver, consequently releasing the transaminases; hence it's observed elevation in the plasma. The result is similar to Egbuonu et al.[14] and Mariyamma et al.[15] who reported the complicit role of oxidative stress in the pathogenesis of increase in plasma transaminases; it could induce alteration in membrane integrity, thus changing the membrane permeability resulting in leakage of intracellular enzymes.

Similarly, liver is the primary site for synthesis of plasma proteins. A disturbance of protein synthesis therefore occurs as a consequence of impaired hepatic function which will lead to a decrease in their plasma

concentration[16,17]. The reduction of the protein concentration in the monosodium glutamate treated rats could indicate a reduction in the synthetic function of the liver or increase rate of protein degradation.

Similarly, MSG-treatment in the present study resulted in alteration of some plasma renal biomarkers as reflected by the significant ($P < 0.05$) increase in mean plasma urea values. This corroborate with earlier findings of Inuwa et al.[18] who observed that blood urea increases as the ability of the kidney to filter fluid within the body declines. The increase in plasma urea concentration in the MSG-treated rats could be attributed to impairment of the urea cycle due to poorly performing kidneys or failure of renal excretion and subsequent leakage of the metabolite into circulation[19, 20]. The observed increase in the mean plasma creatinine level in the MSG-treated rats could be linked to a possible impairment and/or compromise of the renal functioning capacity as a result of MSG exposure. It could also be that MSG might have either interfered with creatinine metabolism leading to increased production or the kidney might have compromised all or part of its renal tubular excretion [21]. Our findings seemingly correlate with Manal and Nawal.[22] who also reported increase in creatinine level following MSG-exposure which was attributed to the role of oxidative stress in the pathogenesis of MSG induced increase in renal biomarkers earlier observed by Sandharbh et al.[23]. Conclusion In conclusion, alteration in the tested parameters suggests that Sub-chronic MSG exposure produce some level of toxicological effects on the hepatic and renal function when consumed at high doses. Our finding could be regarded as a preliminary or supportive research to earlier studies, this therefore necessitate further research to establish the pathophysiologic mechanism of subchronic MSG-induced toxicity on the studied organs.

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Table 1: Effect of Monosodium Glutamate on Plasma Markers of Hepatic and Renal Functions in Male Wistar Rat

PARAMETER	Group	Days of Experiment							
		7	14	21	28	35	42	49	56
ALT (IU/L)	Treated	43 ± 4.6	48 ± 1.9	53 ± 4.8	56 ± 2.3	57 ± 2.7	58 ± 2.7	62 ± 1.1*	69 ± 3.7*
	Control	40 ± 1.2	42 ± 1.1	40 ± 2.0	48 ± 4.0	47 ± 2.9	46 ± 1.3	45 ± 1.1	47 ± 2.9
AST (IU/L)	Treated	42 ± 3.1	47 ± 2.5	50 ± 3.4	51 ± 2.5	55 ± 3.4	59 ± 5.8	65 ± 5.5*	80 ± 5.4*
	Control	40 ± 1.8	43 ± 1.6	45 ± 1.9	42 ± 3.2	41 ± 3.2	43 ± 1.4	39 ± 2.4	43 ± 1.4
ALP (IU/L)	Treated	243±13*	260±7.4*	273±9.2*	287±5.2*	295±3.5*	298±3.2*	309±4.9*	322±3.4*
	Control	187±7.4	210±5.8	190±4.4	220±10	192±11	180±8.7	200±11	193±5.0

Blood Urea Nitrogen (UN) (mmol/l)	Treated	3.5 ± 0.19	4.1 ± 0.18	4.5 ± 0.31	4.8 ± 0.22	4.8 ± 0.15*	5.2±0.15*	6.2±0.59*	8.1±0.63*
	Control	3.0 ± 0.33	3.1 ± 0.09	3.3 ± 0.49	3.7 ± 0.34	2.7 ± 0.15	3.5 ± 0.28	3.0 ± 0.14	3.5 ± 0.35
Creatinine (mmol/l)	Treated	49 ± 1.4	50 ± 1.9	52 ± 4.5	54 ± 3.5	57 ± 4.1	57 ± 4.1	59 ± 1.1*	63 ± 2.7*
	Control	44 ± 1.9	46 ± 1.6	49 ± 1.3	45 ± 2.0	45 ± 2.1	47 ± 2.9	45 ± 1.8	41 ± 2.5

Mean (± SEM) of hepatic and renal function parameters in MSG-treated and control rats; Means with superscript * differs significantly from their corresponding control values.

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Cite this article as: Hassan Abdulsalam, Jamila A. Atata, Ali Waziri, Mohammed A. Chiroma, Joseph J. Gadzama, Modu B. Monguno, Sani N. Abdulazeez, Israel J. Barde. **Effect of Sub-chronic oral Experimental Exposure of Monosodium glutamate on Biomarkers of Hepatic and Renal function in Male Wistar Rats. Bo Med J 2018;15(1): 83-88. Source of Support:** Nil, **Conflict of Interest:** None declare