EFFECTS OF ORAL ADMINISTRATION OF MONOSODIUM GLUTAMATE (MSG) ON SERUM TESTOSTERONE LEVELS AND MUSCLE MASS DEVELOPMENT IN MALE RATS

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ABSTRACT

The effects of oral administration of monosodium glutamate (MSG), a food additive and flavour enhancer, on serum testosterone levels and muscle mass development was studied using 28 four-week-old male rats. Treatment with MSG was accomplished by oral administration of increasing doses (1mg/g body weight, 2mg/g body weight and 4mg/g body weight) of a 40% aqueous solution of monosodium glutamate to the male rats every 48 hours for 6 weeks, using a rat gavage needle. The results showed that MSG administration gave rise to significantly lowered serum testosterone levels (P<0.05), as well as significant reduction in the weight of skeletal muscles (P<0.05) when compared to controls. However, the muscle mass indices (milligram muscle weight per gram body weight) of the muscles studied did not differ significantly (P>0.05) between MSG-treated rats and control rats. These results indicate that MSG may have disrupted the hypothalamic-pituitary-testes regulatory axis that controls testosterone production, and so resulted in lowered serum testosterone levels and loss or considerable reduction in the stimulatory influence of testosterone on skeletal muscle growth.

Keywords: Monosodium glutamate, Testosterone, Muscle development, Male albino rats

INTRODUCTION

Monosodium glutamate (MSG), a white crystalline powder, is a sodium salt of the naturally occurring non-essential amino acid, glutamic acid (Furst and Stehle, 2004). MSG is commonly used as a food additive and is marketed as a flavour enhancer. Sensory enhancement of food with MSG can improve food palatability, increase salivation and local immunity, and allows for food acceptance (Schiffman, 2000). Through its stimulation of the orosensory receptors (Chaudhari *et al*., 2000) and improving palatability of meals, MSG influenced appetite positively and induced weight gain (Rogers *et al*., 1990). Generally, MSG is accepted as a safe food additive that needs no specified average daily intake or an upper limit intake (Samuels, 1999), and many reputable international organizations and nutritionists have continued to endorse its use in food. Such organizations as World Health Organization (WHO), Federation of American Societies for Experimental Biology (FASEB), as well as Food and Drug Administration (FDA) of the USA have maintained MSG in the list of "Generally Recognized As Safe" (GRAS) foods (Samuels, 1999). Similarly, Nigeria's National Agency for Drug Administration and Control

(NAFDAC) has endorsed MSG (Okwuraiwe, 1992).

However, some studies have indicated that monosodium glutamate was found to be toxic to humans and experimental animals (Kwok, 1968; Belluardo *et al*., 1990). It was associated with a 'MSG symptom complex' commonly referred to as 'Chinese restaurant syndrome' (Kwok, 1968). The 'Chinese restaurant syndrome' was characterized by numbness in the tongue and face, burning sensation in the neck, facial pressure or tightness, headache, fatigue, drowsiness, exacerbation of asthmatic symptoms, chest pain and nausea (Kenney and Tidball, 1972). Besides its association with the Chinese restaurant syndrome, MSG has also been reported to destroy neurons in the brain resulting in brain damage and endocrine disorders (Mozes and Sefcikova, 2004). Experimental studies (Burde *et al*., 1971; Bodnár *et al*., 2001) demonstrated that both subcutaneous injection and oral administration of MSG to immature animals resulted in neuronal losses in the hypothalamus.

Neuronal losses in the hypothalamus will invariably disrupt the hypothalamic-pituitary-testes regulatory axis that controls testosterone synthesis. Such disruption of the hypothalamic-pituitary-testes axis regulation may lead to loss of or reduction in the testosterone-synthesizing capacity of the Leydig cells of testes. Reduction in testosterone production may adversely affect the development of skeletal muscle mass through loss of the stimulatory influence of the androgen on the muscles (Ihemelandu and Ibebunjo, 1992; Igwebuike *et al*., 2001; Igwebuike, 2002; Igwebuike and Abdou, 2004). The purpose of this study was to verify whether consumption of monosodium glutamate will indeed lead to lowered serum testosterone levels and reduction in muscle mass of male rats.

MATERIALS AND METHODS

Experimental Animals: The 28 four-week-old male albino rats used for this study were obtained from the animal house unit of the Department of Veterinary Obstetrics and Reproductive Diseases, Faculty of Veterinary Medicine, University of Nigeria, Nsukka. The rats weighed between 40 and 60 grams at the commencement of the study. They were housed in fly-proof metal aluminum cages and fed commercially prepared feed *ad libitum*. Drinking water was provided. The rats were kept for a two-week acclimatization period before the commencement of the experiment. The young male rats were randomly assigned to 4 groups of 7 rats per group. The control group received no monosodium glutamate, while rats in the treatment groups were given oral doses of a 40% aqueous solution of monosodium glutamate every 48 hours for 6 weeks, using a rat gavage needle. On each treatment day, rats in the low dose group received 1mg/g body weight of MSG per rat, those in the medium dose group received 2mg/g body weight of MSG per rat, and rats in the high dose group received 4mg/g body weight of MSG per rat. At the end of 6 weeks of treatment with MSG, the rats were sacrificed by euthanasia using diethyl ether chamber.

Testosterone Assay: Prior to sacrificing each rat, 2 ml of blood was collected from the medial cantus of the eye into a test tube, and allowed to clot. The serum was collected and used for testosterone assay. The assay was carried out using ELISA technique.

Quantitative Measurement: The live body weight of each rat was determined before euthanasia was carried out. Following death, the biceps brachii, soleus and gastrocnemius muscles were carefully dissected from the right and left limbs of each rat and weighed. The mean weight of the right and left muscles was determined and used as weight for the particular muscle. The muscle mass index (milligram muscle weight per gram body weight) was determined for each muscle.

Statistical Analysis: Means and standard errors were calculated for each group of observations. The data obtained were statistically analyzed using ANOVA (SPSS 9.0 Statistical Package of SPSS Inc. USA).

RESULTS

Data on the live body weights and serum testosterone levels of the MSG-treated rats and controls are presented in Table 1. Treatment with MSG significantly reduced ($P<0.05$) the live body weights of the rats in the three treatment groups when compared to control rats. The mean serum testosterone levels of the rats that received the low dose, medium dose and high dose of monosodium glutamate in this study were significantly lower ($P<0.05$) than that of the control rats. Similarly, the weights of the muscles, including the biceps brachii, soleus and gastrocnemius muscles of the rats in the three MSG-treated groups were significantly reduced ($P<0.05$) compared to the weights of corresponding muscles of the control group (Table 2). The only exception was that the weight of biceps brachii muscle of the rats that received the high dose of MSG was not significantly different ($P>0.05$) from that of the control group (Table 2). The muscle mass indices of the biceps brachii, soleus and gastrocnemius muscles of the rats that received the three varied doses of MSG were not statistically different ($P>0.05$) from those of the corresponding muscles of the control rats (Table 2). Only the muscle mass index of the soleus muscle of the rats that received the medium dose of MSG differed significantly ($P<0.05$) from the control.

DISCUSSION

Testosterone is a male androgen produced by Leydig cells of the testes (95%) and by cells in the cortex of the adrenal gland (5%) (Urban, 1999). The lowered serum testosterone levels in MSG-treated rats in this study may have resulted from disruption of the hypothalamic-pituitary-testes regulatory axis that controls testosterone production by testicular Leydig cells. This proposition is supported by the reports of previous authors (Burde *et al*., 1971; Bodnár *et al*., 2001) who stated that administration of monosodium glutamate destroyed neurons of the hypothalamus in rats and mice. Such neuronal losses in the hypothalamus can result in disruption of the hypothalamic-pituitary-testes regulatory axis (Nemeroff *et al*., 1981). Further support for this suggestion is the report by Redding *et al*. (1971) that there was a marked decrease in growth hormone (GH) and luteinizing hormone (LH) content of the anterior pituitaries of male and female rats at 40 days of age following neonatal treatment with monosodium glutamate. It is known that luteinizing hormone, also known as interstitial cell stimulating hormone (ICSH) is responsible for the stimulation of testosterone production by Leydig cells (McLachlan *et al*., 1996). Decrease in pituitary content of this hormone will invariably have adverse effects on testosterone-synthesizing capacity of the Leydig cells. This may be the reason for the observed decrease in serum testosterone levels in the MSG-treated rats in the present study.

Reduction in the weights of the muscles of rats that received MSG was observed in this study. This suggests that consumption of monosodium glutamate may be detrimental to the growth of skeletal muscles. This reduction in muscle weight may be the end result of considerable decline or loss of the stimulatory influence of testosterone on the muscles following decrease in testosterone-synthesizing capacity of testicular Leydig cells. The stimulatory influence of testosterone on muscle growth has been demonstrated by several authors (Synder *et al*., 2000; Wang *et al*., 2000; Igwebuike and Abdou, 2004), and has been advanced as the reason for the greater muscle growth capacity in intact males when compared to intact females (Brandstetter *et al*., 2000). Several studies are in agreement that testosterone produces muscle hypertrophy by increasing fractional muscle protein synthesis (Urban *et al*., 1995; Brodsky *et al*., 1996).

The molecular basis for this anabolic effect is not very clear, but scientific evidence strongly suggest that testosterone may modulate these actions indirectly through stimulation of the insulin-like growth factor axis. It has been proposed that testosterone stimulates the expression of insulin-like growth factor-1 (IGF-1) and down-regulates insulin-like growth factor binding protein-4 (IGFBP-4) in the muscle (Urban *et al*., 1995).

Table 1: Live body weights and serum testosterone levels of male rats administered varying doses of MSG

Parameters	Control	Low dose (1mg/g b. wt.)	Medium dose (2mg/g b. wt.)	High dose (4mg/g b. wt.)	P level
Live body weight (g)	207.26 ±6.07[a]	182.01 ±5.39[b]	154.90 ±6.88[c]	178.13 ±4.00[b]	ab: P<0.05 ac: P<0.05
Serum testosterone (ng/ml)	4.45 ± 0.35[a]	1.11 ±0.28[b]	0.71 ±0.16[b]	1.38 ±0.63[b]	ab: P<0.05

Values are presented as mean ± SE. Different superscripts in a row indicate significant variation at the specified level of probability

Table 2: Absolute muscle weights and muscle mass indices of male rats administered varying doses of MSG

Parameters		Control	Low dose (1mg/g b. wt.)	Medium dose (2mg/g b. wt.)	High dose (4mg/g b. wt.)	P level
Muscle weights (mg)	**Biceps brachii muscle**	141.00 ±5.58[a]	117.00 ±7.80[b]	119.36 ±3.91[b]	126.21 ±3.25[ab]	ab: P<0.05
	Soleus muscle	92.86 ±1.76[a]	75.43 ±4.01[b]	75.50 ±2.11[b]	75.14 ±2.96[b]	ab: P<0.05
	Gastrocnemius muscle	1461.93 ±56.00[a]	1129.40 ±38.12[b]	1139.57 ±65.79[b]	1240.57 ±47.46[b]	ab: P<0.05
Muscle mass indices (mg/g)	**Biceps brachii muscle**	1.47 ±0.04[ab]	1.59 ±0.09[a]	1.30 ±0.07[b]	1.41 ±0.03[ab]	ab: P<0.05
	Soleus muscle	0.142 ±0.003[a]	0.162 ±0.004[b]	0.138 ±0.009[a]	0.144 ±0.004[a]	ab: P<0.05
	Gastrocnemius muscle	2.23 ±0.06[ab]	2.44 ± 0.09[b]	2.08 ± 0.08[a]	2.38 ± 0.05[b]	ab: P<0.05

Values are presented as mean ± SE. Different superscripts in a row indicate significant variation at the specified level of probability

These reciprocal changes in IGF-1 and IGFBP-4 are thought to provide a potential mechanism for amplifying the anabolic signal. This chain of stimulatory influences may be lost or considerably reduced in the muscles of the rats that were given MSG in this study, hence the smaller weights of the muscles of these rats relative to rats in the control group.

However, the muscle mass indices (milligram muscle weight per gram body weight), did not differ between the MSG-treated rats and controls. This observation is contrary to the reports of some previous authors who demonstrated that disruption of the hypothalamic-pituitary-testes axis regulation either by castration (Ihemelandu and Ibebunjo, 1992; Igwebuike, 2002) or by drug administration (Igwebuike *et al.*, 2001) gave rise to reduction in the muscle mass indices of skeletal muscles. The lack of significant differences between the muscle mass indices of the muscles of MSG-treated rats and controls in the present study suggests that consumption of monosodium glutamate did not adversely affect the contribution of individual skeletal muscles to the body weight of the rats. This may be related to the significant reduction in the live body weights of the MSG-treated rats relative to the control rats; since both the weights of the muscles and the body weight of the rats were

reduced following MSG administration. Skeletal muscles are known to contribute substantially to an animal's body weight. Therefore, it can be presumed that the reduction in weight of the skeletal muscles of the rats that received MSG in this study was responsible for the observed reduction in body weight. Remke *et al*. (1988) reported that treatment of neonatal rats with MSG induced reduction in body weight even when there was massive increase in fat tissue content.

In conclusion, our study has demonstrated that oral administration of monosodium glutamate to young male rats gave rise to lowered serum testosterone levels and reduction of skeletal muscle weights, but did not adversely affect the contribution of individual skeletal muscles to the body weight of the rats. These effects may have resulted from disruption of the hypothalamic-pituitary-testes axis regulation by monosodium glutamate.

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