RESEARCH ARTICLE

Sokoto Journal of Veterinary Sciences
(P-ISSN 1595-093X/ E-ISSN 2315-6201)
Okediran *et al*/*Sokoto Journal of Veterinary Sciences* (2014) 12(3): 42-46
http://dx.doi.org/10.4314/sokjvs.v12i3.8

Alterations in the lipid profile and liver enzymes of rats treated with monosodium glutamate

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Abstract
This study was carried out to evaluate the effects of monosodium glutamate on the liver and lipid profile of eighteen adult male Wistar rats as measured by biochemical parameters. The rats received monosodium glutamate at dose rate of 0, 0.5 and 1.0g per day for 28 days. There was significant increase (P<0.05) in aminotransferases i.e. alanine and aspartate aminotransferases as well as increase in total plasma cholesterol and low density lipoprotein cholesterol most obvious at higher dose of 1.0g of monosodium glutamate. Though there was decrease in plasma protein concentration, triglyceride and high density lipoprotein cholesterol which was not statistically significant, therefore monosodium glutamate has both hepatotoxic and dyslipidaemia effects due to its alterations in both aminotransferase activities and lipid profile, hence monosodium glutamate though a flavor enhancer food additive but it must be carefully used in food preparation due to it alterations in both the liver enzymes and the lipid profile.

Keywords: Adult rats, dyslipidaemia, flavor enhancer, hepatotoxic, monosodium glutamate
Received: 01-04-2014 Accepted: 12-11-2014

Introduction

Monosodium glutamate, a sodium salt of naturally occurring L-form of glutamic acid is one of the commonest food additives in the developed and developing world and can be found in various concentrations in numerous food products (Walker & Lupien 2000). Monosodium glutamate is a flavor enhancer and contains 78% glutamic acid, 22% sodium and water (Samuel, 1999). It is found in unlimited amounts in a wide variety of packaged foods such as processed meat and poultry, semi-preserved fish and fish products, food supplements, alcoholic beverages and seasoning (Erb, 2006). Monosodium glutamate is also found in a variety of vaccines and it is now being sprayed on crops and can become airborne, however the airborne effects of monosodium glutamate sprays have not been studied (Erb, 2000).

The wide distribution of monosodium glutamate distribution in food enables a continuous intake of this substance into organism which results in accumulation and rise of glutamic acid concentration in the blood (Garattini 2000). Monosodium glutamate has been shown to have a range of toxic effects. It has been shown to trigger diabetes mellitus (Nagata *et al*., 2006), cross placenta (Yu *et al*., 1997), cause ocular toxicity (Ohguro *et al*., 2002), cause genotoxicity (Farombi & Onyema 2006), associated with autism (Singh & Jensen 2003).

The safety of monosodium glutamate usage has generated much controversy, most communities and individuals often use monosodium as a bleaching agent for removal of stains from clothes. There is a growing apprehension that its excellent bleaching

properties could be harmful or injurious to the stomach mucosa (Eweka & Adjene 2007).

The liver plays a major role in metabolism and has a number of functions in the body, including glycogen storage, plasma protein synthesis and detoxification (Okediran *et al*. 2010). Since the liver is involved in the performance of these varied functions it may be susceptible to injury particularly in situation of toxicity. It would therefore be worthwhile to examine the effects of monosodium glutamate on the liver.

Materials and methods

Experimental Animals

Eighteen adult male Wistar albino rats having body weight of 120 ± 0.15g were normalized for a week before commencement of the experiment. They were maintained under standard laboratory conditions (temperature 28ºc, 14 hours light). They were equally fed dry ration (Fat/oil 6%, Crude fiber 5%, Calcium 1%, Available phosphorus 0.4%, Lysine 0.85%, Methionine 0.35%, Salt 0.3%, Crude protein 18%, Metabolisable Energy 2900 $Kcal.kg^{-1}$, Manufactured by TOPFEEDS®, Lagos, Nigeria) and water provided *ad libitum*. The Monosodium glutamate (3g/sachet containing 99+% of monosodium glutamate) was obtained from a popular market at Ibadan, Oyo state.

Treatment

After a week of normalization, they rars were randomly assigned to three groups A, B and C of six animals per group.

Group A: served as the control group and fed normal dry ration with 0g/day monosodium glutamate

Group B: was fed dry ration thoroughly mixed with 0.5g/day (0.69mg MSG/g of rat) of monosodium glutamate.

Group C: was fed dry ration thoroughly mixed with 1.0g/day (1.38mg MSG/g of rat) of monosodium glutamate.

The two doses of monosodium glutamate i.e. 0.5g/day and 1.0g/day were thoroughly mixed with fixed amount of feed (75g of dry ration) in each group daily, likewise the control was also given 75g of dry ration but without monosodium glutamate. After twenty eight days of feeding with varying doses of monosodium glutamate, blood samples were collected via the ocular median cantus using heparinized capillary tubes into heparinized tubes.

Plasma and biochemical analysis

The blood samples were collected and centrifuged at 4500 rpm for 15 minutes. The plasma was removed and assayed for alanine aminotransferase (ALT), aspartate aminotransferase (AST) activities, triglyceride, total cholesterol and it fractions such as high density lipoprotein (HDL) - cholesterol and proteins. All assays were performed using Randox® diagnostic kits supplied by Randox® Laboratories Limited, United Kingdom.

HDL fraction was extracted from the plasma as described by Gidez *et al*. 1982, after precipitating very low density (VLDL) and low density lipoprotein (LDL) with heparin-manganese chloride solution. HDL- cholesterol was then determined using Randox® cholesterol diagnostic kits. The concentration of LDL- cholesterol was calculated by a modification of the Friedelwald formular. The data obtained was analysed using analysis of variance (ANOVA) and level of significance compared by means of Duncan multiple range tests.

Results

Table 1 shows the effect of intake of monosodium glutamate on some transaminases and total plasma protein. There was significant increase (P<0.05) in the activities of the aminotransferases of the monosodium glutamate treated rats compared to the control group. The increase activity was more prominent in group C. While the ALT activity was about 1.3 times higher, the AST activity was about 1.1 times higher than the control group. There was reduction in the total plasma protein of the monosodium glutamate treated rats compared to the control group although this was not statistically significant.

Table 2 shows the effect of intake of monosodium glutamate on some lipid parameters. There was significant increase (P<0.05) in the plasma cholesterol of the monosodium glutamate treated rats compared to the control group. The increase was more prominent in group C which was about 1.3 times of the control group. Though there was reduction in both the triglyceride and HDL-cholesterol which was not statistically significant but there was significant increase in LDL-cholesterol of the monosodium glutamate treated rats compared to the control group.

Table 1- Effect of intake of monosodium glutamate on some transaminases and total plasma protein in male Wistar rats (mean ± SEM)

Groups	ALT ($IU.l^{-1}$)	AST ($IU.l^{-1}$)	Total protein ($g.l^{-1}$)
A	31.88±3.28[a]	125.26±3.37[a]	73.08±2.42[a]
B	34.64± 1.31[a]	125.62±10.69[a]	66.48±3.66[a]
C	40.74±3.04[b]	133.94±3.38[b]	65.34±1.88[a]

[a,b] values in the same column with different superscripts differ significantly (P<0.05)

Table 2- Effect of intake of monosodium glutamate on some lipid parameters in male Wistar rats (mean ± SEM)

Groups	Cholesterol ($mg.dl^{-1}$)	Triglyceride ($mg.dl^{-1}$)	HDL-Cholesterol ($mg.dl^{-1}$)	LDL-Cholesterol ($mg.\ dl^{-1}$)
A	93.26 ± 4.27[a]	108.34±7.88[a]	47.68±2.92[a]	32.29±2.26[a]
B	112.88± 7.58[b]	88.06±7.70[a]	46.23±2.11[a]	47.59±4.32[b]
C	119.24±2.38[b]	103.73±7.87[a]	42.67±2.92[a]	54.52±2.52[b]

[a,b] values in the same column with different superscripts differ significantly (P<0.05)

Discussion

The transaminases are abundant in the liver and are released into the blood stream following hepatocellular damage, making them sensitive marker of liver damage (Al-Mamary 2002). The marked increase in the plasma ALT and AST activities observed in the monosodium glutamate fed rats might be indicative of liver damage. Plasma levels of transaminases were used as an indicator of damage to the liver structural integrity because these enzymes are cytoplasmic in location and are released into the circulating blood only after structural damage (Janbaz and Gilani 2000; Hagar 2004). The metabolism of most amino acids and their derivatives occur to a significant extent in the liver (Mayes & Bender 2003) and essentially involves deamination to produce ammonium ion that could be toxic unless 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 observed elevation in the plasma. The result is similar to Onyema *et al*. (2006) and Egbuonu *et al*. (2009) who reported that monosodium glutamate increased the serum transaminases in male albino rats due to possible ammonium ion overload resulting from an increase level of glutamate. Also, Mariyamma *et al*. (2009) reported increase in plasma transaminases due to oxidative stress which induces alteration in the membrane integrity, thus changing the membrane permeability resulting in leakage of intracellular enzymes.

Liver is the primary site of the 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 (Keith *et al*. 1999). 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.

Lipids and lipoprotein abnormalities play a major role in the pathogenesis and progression of atherosclerosis and cardiovascular diseases (Ginsberg, 1994; Gotto, 1994; Chrysohoou *et al*., 2004). Dyslipidaemia as a risk factor for cardiovascular disease in both urbanized and underdeveloped rural countries have been reported (Van der Sande 2001). We observed significant increase in total plasma cholesterol accompanied with increase LDL-cholesterol while HDL-cholesterol and triglyceride was not significantly altered. It is possible that monosodium glutamate was able to increase the activities of 3-hydroxyl-3-methylglutaryl coenzyme A (HMG CoA) reductase, the rate limiting enzyme in cholesterol biosynthesis resulting in increase synthesis of cholesterol in the MSG treated rats. Mariyamma *et al*. (2009) reported hyperlipidaemia with significantly elevated levels of serum Triacylglycerol and cholesterol in monosodium glutamate treated rats and proposed that a shift in glucose metabolism towards lipogenesis might account for the hyperlipidaemia.

HDL and LDL are two of the four main groups of plasma lipoproteins that are involved in lipid metabolism and the exchange of cholesterol, cholesterol ester and triglycerides between tissue (Gordon & Rifkind 1989; McNamara 1999). Epidemiological studies have shown that elevated concentrations of total or LDL-cholesterol in the blood are powerful risk factors for coronary disease (Law 1999). Most extrahepatic tissues, although having a requirement for cholesterol, have low activity of the cholesterol biosynthetic pathway. Their cholesterol requirements are supplied by LDL which is internalized by receptor mediated endocytosis. The major function of HDL-cholesterol is to scavenge cholesterol from extrahepatic tissue and get transported to the liver where they are utilized in synthesis of steroid hormone or bile acid. This role of HDL has been shown to be responsible for its atheroprotective properties (Das 2003). The observation of increased total plasma cholesterol and LDL-cholesterol levels and normal HDL-cholesterol levels suggests that reverse cholesterol transport is not affected; rather cholesterol synthesis and transport to the peripheral tissue might be affected. It is possible that in addition to increase activity of HMGCoA reductase there is also reduction of LDL receptors for cholesterol.

In conclusion monosodium glutamate can induce both hepatocellular damage as well as dyslipidaemia as manifested in rats treated with monosodium glutamate in the diet.

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