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Effects of α-tocopherol against monosodium glutamate induced hepatotoxicity

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ABSTRACT

To investigate the protective effect of α-Tocopherol (α-TP) in monosodium glutamate (MSG) induced liver injury in albino rat model. Experimental/Analytical study Place and Duration: Animal House, Isra University Hyderabad from February to September 2013.Subjects and Methods: Sixty albino rats were divided into three groups; Group 1. Controls received 0.9% isotonic saline, Group 2. received MSG orally (3mg/kg), and Group 3. received the MSG orally (3mg/kg) + α-TP (0.2 mg/kg). Blood samples were collected for liver biochemical assays. The animals were sacrificed, liver tissue, after fixation in 4% formaldehyde, was embedded in paraffin. Tissue sections of 5µ thickness were subjected to haematoxylin and eosin staining and were assessed by light microscopy. The data was analyzed on SPSS 21.0 using appropriate statistical tests. A p-value of ≤ 0.05 was taken statistically significant.Results: The liver biochemical and histological findings reveal statistically significant differences among the controls, MSG and MSG+ α-TP groups (p=0.0001). Liver enzymes and histology was deranged significantly in MSG group compared to controls and MSG+α-TP group (p=0.0001). The MSG+α-TP group shows less elevation of liver enzymes and derangement in liver histology when compared to MSG group (p=0.001). The histological findings of congestion, inflammatory cell infiltrate, vacuolar degeneration and necrosis were found prominently in MSG group animal. The monosodium glutamate has deleterious effects on liver. It is important to reconsider the monosodium glutamate as a food flavor additive. α-tocopherol protects against monosodium glutamate induced liver injury.

Introduction

Monosodium glutamate (MSG) is commonly known as AJINOMOTO.[1] MSG is the sodium salt of a naturally occurring amino acid; the glutamic acid. Biochemically MSG contains 78% glutamic acid and remaining 22% sodium.[2] Glutamate is produced in body and plays role in human metabolism.[3,4]

MSG is commonly marketed as a flavour enhancer and is used as a food additive particularly in West African and Asian dishes.[5,6] Generally, monosodium glutamate is accepted as a safe food additive that needs no specificied average daily intake or an upper limit intake.[2] However, inadvertent abuse of this food additive may occur because of its abundance, mostly without labeling, in many food ingredients.[7] An experimental study[8] demonstrated that both subcutaneous injection and oral administration of MSG to immature rats and mice resulted in neuronal losses in the hypothalamus. The ability of monosodium glutamate to damage nerve cells of the hypothalamus is a pointer to the fact that it may alter the neural control of reproductive hormone secretion via the hypothalamic-pituitary-gonadal regulatory axis. The effects of such toxicants on male reproduction may be anatomical or only functional, depending on whether they produce structural changes in the reproductive system, or merely affect the functions of the reproductive organs.[9]

The ingestion of MSG has been alleged to cause or exacerbate numerous conditions, including asthma, urticaria, atopic dermatitis, ventricular arrhythmia, neuropathy and abdominal discomfort.[10]

The α-tocopherol (α-TP) administration has been reported to be beneficial in preventing formaldehyde-induced tissue damage in rats.[11] The preventive effect of α-tocopherol on cypermethrin or endotoxin-induced oxidative stress in rat tissues is suggestive of its antioxidant activity.[12,13]

The present study was designed to observe effects of MSG on liver and possible protective role of α-tocopherol in albino rat model at animal house of Isra University.

Materials and Methods

The present experimental study included sixty albino rats at animal house of Isra University from March to July 2013. Albino rats of 250-300 grams were included while female rats, and rats weighing <250 grams or >300 grams were excluded from the study. The Animals were housed in animal house at an optimal room temperature with 55-60% humidity and exposed to 12 hour light-dark cycles. The chaw like fresh alfalfa and clean water are provided freely.

The chemical used was monosodium glutamate (C5H9NO4-Na+). The MSG was purchased from the open market of Hyderabad under the license of Ajinomoto co.INC. Tokyo, Japan. A stock solution was prepared by dissolving 30 and 60 g of MSG crystals in 100 ml of distilled water. The dose schedule was so adjusted that the amount of MSG administration per animal was as per their respective weight.

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The MSG doses were given for six weeks. The applied doses were selected according to as referenced.[14] The rats were divided into four groups;

Group 1. Control Group (n=20) Rats received 0.9% isotonic saline orally on alternate day for three successive weeks and served as control group,

Group 2. (n=20) Rats were given 3 mg/kg of monosodium glutamate orally.

Group 3. (n=20) Rats were given 3 mg/kg of monosodium glutamate mixed with 0.2 mg/kg α-tocopherol (α-TP) orally.

The blood samples were collected from peripheral veins at twenty four hours of experimental period. Sera were separated by centrifugation at 300xs for ten minutes. Serum samples were used to determine liver enzymes. Liver enzyme assays were determined for alanine transaminase (ALT), aspartate transaminase (AST), alkaline phophatase (ALP) and lactate dehyderogenase (LDH) using commercially available diagnostic kits.

After fixation in 4% formaldehyde, samples were embedded in paraffin. Sections of 5µ thickness were subjected to haematoxylin and eosin. Hepatic morphology was assessed by light microscopy. A total of five sections for each liver tissue sample were observed under light microscope. In H & E staining, damaged hepatocytes graded as 0= normal, += mild damage (swollen and pale cytoplasm), ++= moderate damage (vacuolated cytoplasm), +++= severe damage and ++++= very severe damage (pyknotic nucleus and eosinophil cytoplasm).[15]

The data was analyzed on SPSS version 21.0 (IBM corporation). The continous variables were presented as mean±SD using one-way ANOVA and Tukey-Cramer test for multiple comparisons. Chi-square test was used for categorical variables. A p-value of ≤ 0.5 was taken statistically significant.

Result

The present study observes major differences in liver injury between and among groups as indicated by blood enzyme levels in different animal groups. The ALT, AST, LDH and ALP in serum of Rats treated with MSG were found elevated compared with control group after three weeks, with a highly significant p-value (p=0.001).

The MSG+α-TP group showed a significant reduction in the liver enzymes compared with the MSG (p=0.001) and controls (p=0.001). The animals in MSG+α-TP group showed significant reduction in the liver enzyme elevation compared to MSG group alone (p=0.001). The finding showed significant hepato protection by the α-TP in MSG induced injury. The liver enzyme assays among different groups are shown in table.1.

Different parameters of histological score of liver injury are shown in Table. 2. The liver sections of controls showed intact central venules and hepatocytes arranged in compact cords. Normal looking hepatocytes with prominent nucleus, nucleolus and well preserved cytoplasm were seen in controls (Figure.1). On the contrary, MSG group showed derangement of hepatocytes cords, hydropic changes with congestion of central venules and sinusoids, and abundant inflammatory cell infiltration (Figure.2). The centrilobular hepatocytes showed hydropic changes and necrosis, while midzonal and peripheral hepatocytes show vacuolar degeneration and fatty changes in MSG group (Figure 2). In MSG+α-TP animals, liver tissue sections reveal less significant derangement of hepatocytes cords, hepatocytes damage and necrosis was limited compared with MSG group (Figure.3).

Table. 1. Liver enzyme levels in controls, MSG and MSG+α-TP* groups

Groups	ALT (IU)	AST (IU)	LDH (IU)	ALP (IU)
Group. 1 (Controls)	48.9±3.19	91.2±16.81	711.5±51.7	93.6±8.91
Group. 2 (MSG)	189.6±11.91	499.7 ±21.9	2778.8±139.6	167.1±8.02
Group. 3 (MSG+α-TP)	87.7±17.92	171.3±19.3	2138.6±153.3	136.7±18.14

Table 2. Histology of liver injury of controls, MSG and MSG+α-TP* groups

Groups	Inflammatory cell infiltrate	Congestion	Vacuolar degeneration	Necrosis
Group. 1 (Controls)	0	0	0	0
Group. 2 (MSG)	++++	++++	+++	++++
Group. 3 (MSG+α-TP)	+++	++	++	++

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