ORIGINAL ARTICLE

EFFECT OF MONOSODIUM GLUTAMATE ON THE SERUM ESTROGEN AND PROGESTERONE LEVELS IN FEMALE RAT AND PREVENTION OF THIS EFFECT WITH DILTIAZEM

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Background: Glutamate is found in a wide variety of foods. It induces the uterine fibroid in the rats by increasing the levels of estradiol. Diltiazem is an effective preventive medication. This study was conducted to analyse the effect of monosodium glutamate on the serum estrogen and progesterone levels in adult Sprague Dawley rat and its prevention with diltiazem. **Methods:** This Laboratory based randomized controlled trial was conducted in the department of Anatomy, Army Medical College, Rawalpindi in collaboration with National Institute of Health (NIH), Islamabad from 9th April to 23rd April 2012. In this experimental study, 30 adult female Sprague Dawley rats of average weight of 500 g were randomly assigned into three groups. The experimental group B was given 0.08 mg/kg of monosodium glutamate (MSG) orally and experimental group C was given 0.08 mg/kg of MSG and 10 mg/kg of diltiazem in distilled water orally for 14 days. The control group (A) received only laboratory diet. Using intracardiac route 5 ml blood was taken from each animal for hormonal assay. **Results:** Hormone assay of the serum in the experimental group B showed increase in serum estrogen and progesterone levels as compared to the group A and there was minor increase in the hormonal levels in group C. **Conclusion:** MSG causes increase in the serum estrogen and progesterone levels in adult female rats and diltiazem prevents this effect.

Keywords: Diltiazem, Estrogen, Monosodium Glutamate, Progesterone

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INTRODUCTION

Monosodium glutamate (MSG) is the sodium salt of the non-essential amino acid glutamic acid, which is one of the most abundant amino acids found in nature and exists both as free glutamate and bound with other amino acids in protein. Animal proteins contain 11–22% by weight of glutamic acid and the plant proteins have as much as 40% glutamate. Glutamate is found in a wide variety of foods where it has a flavour enhancing effect. It is also found in relatively high concentration in foods such as tomatoes, mushrooms, peas and cheese. As a result of its flavour enhancing effects, glutamate is often deliberately added to foods usually as a purified monosodium salt. MSG is sold in open market in Pakistan. MSG increases the appetite by stimulating the appetite centre in the hypothalamus.[1–3] There are certain reports indicating the toxicity of MSG to experimental animals and human beings.[4] In testicular tissues ascorbic acid content is reduced by MSG.[5] The degenerative and atrophic changes in the fallopian tubes are induced by MSG when administred in higher dosage and for prolonged period.[6] It induces the uterine fibroid in rats by increasing the levels of total protein, cholesterol and estradiol.[7]

Diltiazem is a member of the class of drugs known as calcium channel blockers, used in the treatment and prevention of hypertension, various types of angina and superaventricular tachycardia.[8,9] It is also an effective preventive medication for migraine.[10] Diltiazem prevents the effects of MSG by reducing the intracellular calcium overload. Diltiazem blocks the calcium channels in the cell membrane, so reducing permeability of cell membrane for calcium ions. Previous studies have shown that pretreatment with diltiazem prevents the effects of MSG on hypothalamus of rats.[11]

The effect of MSG on the serum estrogen and progesterone levels has been studied however the role of diltiazem in prevention of this effect has not been investigated. This study was conducted to analyse the effect of monosodium glutamate on the serum estrogen and progesterone levels in adult Sprague Dawley rat and prevention with diltiazem.

MATERIAL AND METHODS

This laboratory based randomized controlled trial was carried out at the Anatomy Department, Army Medical College, Rawalpindi in collaboration with National Institute of Health (NIH), Islamabad from 9th April to 23rd April 2012. Ethical considerations were fulfilled and ethical approval was sought from the Ethical Committee of Army Medical College, Rawalpindi prior to the commencement of the study. Thirty adult female Sprague Dawley rats weighing 490–510 grams were obtained from the animal house of NIH, Islamabad. The rats were kept in cages at standard room temperature maintained on 12 hour light/dark cycle. Rats were randomly divided into three groups A (control group), B

and C (experimental groups) with 10 rats in each group using lottery method.

Group A was fed on laboratory diet for 14 days. Group B was fed on normal lab diet and was given 0.5 ml of distilled water by oral gavage tube containing Monosodium Glutamate 0.08 mg/kg body weight/day at 10 am daily for 14 days. Rats in group C were fed on laboratory diet and was given 1 ml of distilled water containing diltiazem 10 mg/kg body weight/day and 0.5 ml distilled water containing Monosodium glutamate 0.08 mg/kg body weight/day by oral gavage tube at 10 AM daily for 14 days. The animals were euthanized by ether anesthesia after 5 cc blood was drawn through cardiac puncture. This blood was collected in labelled non-heparinized test tubes and centrifuged at 5000 rpm for 5 minutes to separate serum. Serum was then placed in freezer at -20°C for hormone assay.

Data was analysed using SPSS-18. Mean and standard deviation (SD) were calculated for serum estrogen and progesterone levels of control and experimental groups. Comparison of the variables were made using the ANOVA followed by post-hoc Tukey test. *p-value* of ≤0.05 was considered as statistically significant.

RESULTS

The mean serum estrogen level of control group-A was 83.53±9.87 pmol/l, for group-B it was 136.97±12.50 pmol/l, and for group C it was 64.79±17.85 pmol/L. The difference in the mean of serum estrogen levels between three groups were found statistically significant. (Tabel-1). The mean serum progesterone level of control group A was 24.47±2.11 ng/ml, for group B it was 30.29±1.15 ng/ml, and for group C it was 26.86±1.31 ng/ml. The difference in the mean serum progesterone levels between three groups was found statistically significant. (Tabel-2).

Table-1: Comparison of estrogen levels between the groups

Parameter	Groups			F	*p*
	A Mean±SD	B Mean±SD	C Mean±SD		
Estrogen level (pmol/l)	83.53±9.88	136.97±12.51		112.4	0.000
		136.97±12.51	64.79±17.85	109.6	0.000
	83.53±9.88		64.79±17.85	8.4	0.014

p-value ≤0.05 is statistically significant.

Table-2: Comparison of progesterone levels between the groups

Parameter	Group			F	*p*
	A Mean±SD	B Mean±SD	C Mean±SD		
Progestrone level (ng/ml)	24.47±2.11	30.29±1.15		58.7	0.000
		30.29±1.15	26.86±1.31	38.8	0.000
	24.47±2.11		26.86±1.31	9.2	0.006

DISCUSSION

MSG is the sodium salt of the non-essential amino acid glutamic acid and has long been used due to its flavour enhancing properties as it increases the appetite by stimulating the appetite centre as well as debated for its safety and harmful effects.

The mean serum estrogen levels were significantly higher in MSG treated group B (136.97±12.5 pmol/l) compared to control group A (83.53±9.8 pmol/l) ($p<0.05$) and the group C (64.79±17.8 pmol/l) ($p<0.05$). This implies that MSG increases serum estrogen levels and diltiazem protects the body from MSG induced increase in estrogen level.

The increase in the levels of estrogen found by Obochi was 119.2% but in our study it was 63.9%. The MSG causes activation of enzyme aromatase which catalyzes the conversion of testosterone to estradiol, therefore resulting in increased estradiol synthesis.[6] However, this study was different in two aspects; dosage of MSG in this study was 100 mg per kg of body weight and duration of this study was 60 days but in our study dosage was 0.08 mg MSG per kg of body weight and duration was 14 days. This difference explains the differing results of the investigation.

Similar to findings regarding estrogen levels, the mean serum progesterone levels were also significantly higher in MSG treated group compared to control group ($p<0.05$) and the group treated with MSG and diltiazem ($p<0.05$). These findings are similar to the findings of Lamperti and Blaha,[12] who found increased levels of progesterone in the plasma and interstitial tissue in MSG treated animals, which were significantly higher than those found in control animals. The reason for increase in progesterone levels in group B was the increased levels of luteinising hormone due to MSG treatment.

CONCLUSION

Administration of MSG results in an increase in serum levels of estrogen and progesterone in rats while co-administration of diltiazem has preventive effect against the rise in levels of estrogens and progesterone.

RECOMMENDATIONS

It is a well-recognized fact that MSG is widely used throughout the world by almost all populations. Based upon the findings of this study, MSG has potential threats that lead to gynaecological problems. This study recommends exploring the role of diltiazem further in prevention of MSG induced changes in the human beings which could

help in managing a major cause of hormonal disturbances and fibroids.

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