Available online at www.elixirpublishers.com (Elixir International Journal)

Human Anatomy

Elixir Human Anatomy 68 (2014) 22054-22057

ISSN: 2229-712X

The effects of oral administration of monosodium glutamate on testicular histology- An experimental study in a rat model

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ARTICLE INFO

Article history:

Received: 13 January 2014;

Received in revised form:

2 February 2014;

Accepted: 28 February 2014;

Keywords

Monosodium,
Glutamate,
Testicular,
Histology,
Rat.

ABSTRACT

The monosodium glutamate is commonly used food flavoring agent used worldwide. The present experimental study investigated the effects of orally administered monosodium glutamate (MSG) on the histology of testes of adult male Wistar rat model. Forty rats were divided into three groups; Group A served as controls, Group B. received MSG orally (1 mg/kg), Group C. received MSG orally (2mg/kg) and Group D. received MSG orally (4 mg/kg). Tissue sections of testis from rats in the control (Group A), showed the normal histological features for the seminiferous tubules and interstices. Group B rats revealed normal spermatogenic cells, many spermatids, and edematous interstitial spaces with mild hyperemia. The Group C rats showed inflammatory exudates in interstitial spaces, spermatids were fewer and changes of degeneration of Leydig cells. Group D rats showed severely reduced spermatogonia, very few to totally absent spermatids in the tubules. Sertoli cells were reduced in the tissue sections. The Leydig cells were also diminished in count with severe vacuolar degeneration. Overall, the MSG treated rats showed altered histology of testicular tissue. The present study concluded that the glutamate has deleterious effects on the testicular histology in adult male Wistar rats particularly in high dose therefore caution must be taken for its frequent use in large quantities as a food flavor additive.

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] MSG has a toxic effect on the testis by causing a significant oligozoospermia and increases abnormal sperm morphology in a dose-dependent fashion in male Wistar rats.[11] It has been implicated in male infertility by causing testicular hemorrhage, degeneration and alteration of sperm cell population and morphology.[12] Previous scientific investigations aimed at determining the effect of MSG on testes.[4,5] MSG caused a reduction in the sperm count.[13] In the last few years, fear had increased due to the adverse reactions and toxicity of MSG, with few and limited literature regarding the histological studies of the damage in testis of animals treated with MSG. So the present study aimed to investigate the effects of MSG on the testicular histology in adult male Wistar rats.

Materials And Methods

The present experimental study included forty young adult male Wistar rats at animal house of Isra University from November 2012 to July 2013. Adult male Wistar rats of 250-300 grams were included in the study. Female rats, weight <250 grams or >300 grams were excluded from the study.

Animals: 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.

Chemical: 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

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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. The MSG doses were given for six weeks. The applied doses were selected according to as referenced.[14]

Experimental details: The rats were divided into three groups;

Group A. Control Group (n=10) Rats received 0.9% isotonic saline orally on alternate day for three successive weeks and served as control group,

Group B. Experimental Group-Low dose (n=10) Rats were given 1 mg/kg of monosodium glutamate orally.

Group C. Experimental Group- Medium dose (n=10) Rats were given 2mg/kg of monosodium glutamate orally.

Group D. Experimental Group- High dose (n=10) Rats were given 4mg/kg of monosodium glutamate orally.

Procedure of performing testicular histology: At the end of the experimental period, the animals were sacrificed by cervical dislocation and the abdominal cavity was opened up to expose the testis which were quickly dissected out, and fixed in 10% formal saline for routine histological techniques. The tissues were dehydrated in an ascending grade of alcohol (ethanol), cleared in xylene and embedded in paraffin wax. Serial sections of 3–4 lm thick were obtained using a rotator microtome. The deparaffinized sections were stained routinely with hematoxylin and eosin. Sections of testes were examined by light microscope. Photomicrographs of the desired sections were obtained for further observations.

Result

The present study was conducted to evaluate the effects of monosodium glutamate (MSG) on the histology of testis in rat model. The MSG was given in different doses in the experimental group animals as mentioned in methodology. The control group revealed normal histology. Tissue sections of testis from rats in the control (Group A), showed the normal histological features for the seminiferous tubules and interstices of rats. The tubules showed normal cells of the different stages of spermatogenesis (from spermatogonia to spermatids), Sertoli cells and interstitial (Leydig) cells (Figure 1).

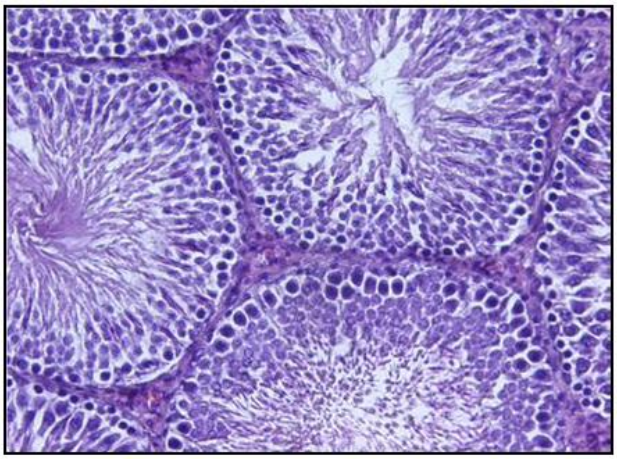

Figure. 1. Section of testis from rats of control group (Group A) rat showing semniferous tubules (T) and interstitial spaces (N) showing normal Leydig cells (H & E stains, × 400)

The experimental groups were studied separately for the microscopic structure of rat testes. The major derangements were observed in the testes of high dose MSG treated rats. The histological details of experimental rats are shown in figure 2-4. The Group B rats (1 mg/kg body weight of MSG) revealed seminiferous tubule with normal looking spermatogenic cells and there were many spermatids present but the interstitial spaces were found edematous with mild hyperemia. (Figure 2). The Group C rats (2 mg/kg body weight of MSG) showed similar, but more severe histological changes when compared with controls. The interstitial spaces revealed exudative edema fluid with lot of inflammatory cells. The spermatids were fewer and Leydig cells showed moderate degree of degeneration (Figure 3). More severe changes were observed in the Group D rats (4 mg/kg body weight of MSG). The spermatogonia were reduced severely. Spermatids were very few to totally absent in the tubules. Sertoli cells were reduced in the tissue sections. The Leydig cells were also diminished in count with severe vacuolar degeneration (Figure 4). Overall, the MSG treated rats showed altered histology of testicular tissue.

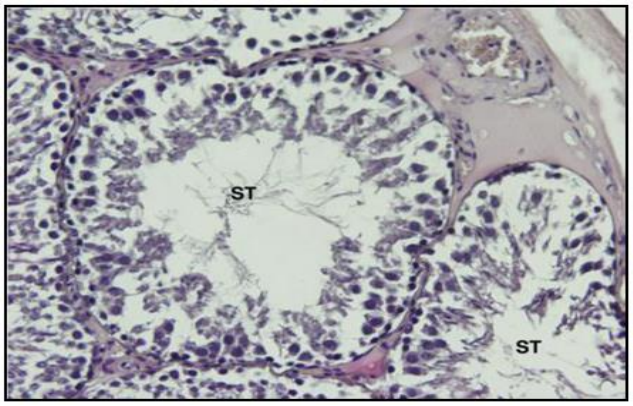

Figure 2. Section of testis from rats (experimental group B) treated with monosodium glutamate (1mg/kg body weight) showing seminiferous tubule (T) with lots of spermatids, and oedematous interstitial space (N). (H & E stains, × 400)

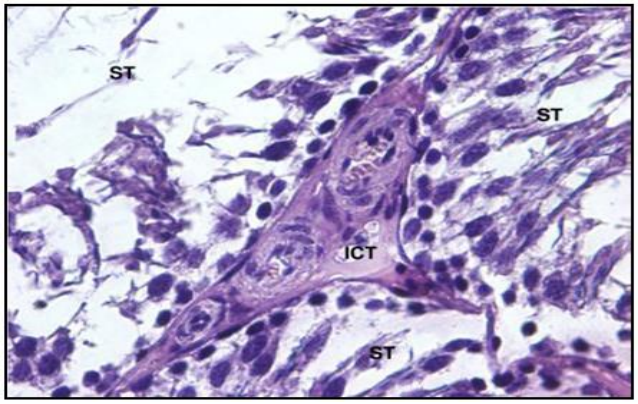

Figure 3. Section of testis from rats (experimental group C) treated with monosodium glutamate (2mg/kg body weight) showing seminiferous tubule (T) with only few spermatids and interstitial space (N) with inflammatory exudates. H&E stains, ×400

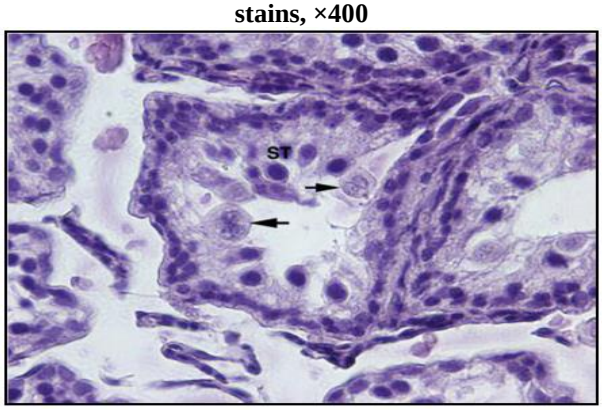

Figure 4. Section of testis from rats (experimental group D) treated with monosodium glutamate (4mg/kg body weight) showing seminiferous tubule (T) with only few spermatogonia and spermatids abset. H & E stains, ×400

Discussion

Great deals of changes recorded in the present study are comparable to the previously conducted studies on the histology of testes of different animals treated with MSG.[4, 5, 15] The studies of Das, et al[16] and Mohamed[17] have reported that both the germinal epithelium and Leydig cells are affected in the testes of mice model. Another previous study[18] has concluded that these histological changes might have been caused by direct local effect of MSG on the testicular cells or indirectly through an imbalance of hypothalamo-pituitary hormones. Balasubramanian et al.[19] explained the congestion of blood vessels as being due to the inhibition of prostaglandins synthesis, since these compounds are known to be involved in the regulation of testicular blood flow. Focusing on sloughing cells of seminiferous tubules; spermatids and spermatogonia with vacuolar degeneration proved the presence of signs of deterioration of testicular histology. The cells of seminiferous tubules showed that vacuolation and exfoliation might be a sign of testicular toxicity and cell degeneration.[20] Present study showed pyknotic of cell nuclei which indicates the loss of functional efficiency of the seminiferous tubule and Leydig cells.

Our results are highly consistent with previous study which demonstrated similar results of MSG on the testes of male rats.[21] The maturation arrest observed in the present study is supported by previous studies[22, 23] who concluded that this arrest might be due to the testosterone inhibition which caused stopping of spermatogenesis. Previous researches have explained the mechanisms by which MSG inhibits the spermatogenesis. The glutamate receptors are present in different tissues: the hypothalamus, spleen, thymus, liver, kidneys, endocrine system, ovaries, etc.[24]Earlier studies proved the presence of functional glutamate transporters and receptors in testes of rats [25,26] and in mice.[27] Therefore, testes are considered as a target organ for MSG. So, one of the mechanisms may be a direct effect of MSG via glutamate receptors and transporters on the epithelial cells of the seminiferous tubules. The second mechanism was proved by other researchers who stipulate that there are neurotoxin effects of MSG on the function of hypothalamus–pituitary–gonadal system.[28,29] 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.[30] In mammals, spermatogenesis is totally dependent upon testosterone.[31,32] Glutamate is a predominant excitatory neurotransmitter in the mammalian central nervous system.[33] Such excessive activation of glutamate receptors and overloading with intracellular calcium can induce neural death.[34] Therefore, the present study suggested that spermatogenesis was affected indirectly via the hypothalamic lesions. The ability of MSG to damage nerve cells of the hypothalamus is a pointing fact that it may alter the neural control of reproductive hormone secretion via the hypothalamic–pituitary–gonadal regulatory axis. Such alterations in reproductive hormone secretion may adversely affect the reproductive capacity of the affected animals. The third mechanism reported that exposure to MSG resulted in a decrease in the testicular ascorbic acid level that could lead to oxidative damage in rat testes,[35] and oxidative damage in different organs.[36] Overall, the findings of present study are in consistency with previous mentioned studies. However further studies are recommended.

Conclusion

The present study concludes that monosodium glutamate have deleterious effects on the histology of testicular tissue of adult male Wistar rats. Thus, it is important to consider the common use of monosodium glutamate as a flavor additive for food dishes. Further studies are recommended with high doses of monosodium glutamate.

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