Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/xwbz9296

EFFECT OF MONOSODIUM GLUTAMATE ON THE MICROSCOPIC ANATOMY OF THYROID GLAND IN MALE RABBITS

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ABSTRACT:
BACKGROUND: Monosodium Glutamate is a commonly used food additive owing to its "meaty" taste. However prolonged intake of MSG adversely affects all organs of the body.
AIMS AND OBJECTIVES: This study aims to study the histological effect of monosodium glutamate on thyroid gland of adult male rabbits.
METHODOLOGY: The animals were divided into three groups of 5 rabbits each; Group A (control), Group B (low dose) fed 4g/kg of MSG, and Group C (high dose) fed 6g/kg of MSG. One animal from each group was sacrificed at the end of 6th, 12th, 18th and 24th week. Thyroid glands were dissected and sections were stained with haematoxylin and eosin stain. These were examined under a compound microscope and images taken.
RESULTS: Histologically significant changes were observed in Group B and Group C. Follicular hyperplasia and hypertrophy was seen. The lining epithelium of the follicular cells became of the squamous type and follicles were filled with abundant colloid.
CONCLUSION: Oral administration of MSG has a profound impact on thyroid tissue integrity and function. Therefore, its use should be restricted as much as possible given its widespread cytotoxic effects on various organs of the body.

KEYWORDS: Monosodium glutamate, food additive, hypothyroidism, colloid, rabbits

INTRODUCTION

The food industry is highly dependent on flavouring agents. These make industrially prepared food attractive to potential customers. Monosodium glutamate is a commonly used flavouring agent. Also known as aji-no-moto, it is a sodium salt of glutamic acid. MSG was discovered in the early 20th century in Tokyo by a chemistry professor, Kikunae Ikeda [1]. He extracted it from edible seaweed and discovered its flavour-enhancing properties [2]. Monosodium glutamate is available in two isomeric forms: L-glutamate and D-glutamate. Flavouring properties are seen only in the L form. It imparts a "meaty taste" also known as "umami" to the food we eat.
Uses of MSG can be enumerated as below:

1. It is added to processed food such as sauces, noodles, and soups as a taste enhancer.
2. It can be used in patients who have lost their appetite as in cases of cancer, radiation therapy and organ transplantation [3].
3. It is used for weight gain.
4. MSG is also used as an adjunct in the treatment of hepatic coma [4].

MSG has been labelled safe by the Food and Drug Administration (FDA). Its use is however limited in baby food [5]. MSG has been found to have serious side effects in humans and experimental animals. These include metabolic syndrome, asthma, headaches and nausea. Continuous intake of MSG has been found to have cytotoxic effects on the kidneys, heart, liver and reproductive organs [6]. In kidneys, it is responsible for altering the renal architecture and causes degeneration of renal tubules [7]. MSG may cause exacerbation of asthma along with migraines [8]. In high doses it acts as an excitotoxin on the central nervous system and may cause Alzheimer's, Parkinson's disease, multiple sclerosis and seizures. In pregnancy, it may cause insulin resistance leading to type 2 diabetes and obesity. It has even been found to cross the placenta and reach the foetus [9].

In some individuals, it may cause a symptom complex called "Chinese Restaurant Syndrome". Symptoms include headache, dizziness and palpitations. Individuals may also present with muscle tightness, numbing, flushing, sweating and blistering of arms. The symptoms appear 20 minutes after ingestion of MSG [10].

The oral median lethal dose (LD50) in mice and rats is 10-20g/kg body weight and in humans, it is about 60mg/kg body weight [11].

This study aims to study the histological effects of monosodium glutamate on the thyroid gland in adult male rabbits.

MATERIAL AND METHODS: The present experimental study was conducted in the Postgraduate Department of Anatomy, Government Medical College, Srinagar, after obtaining ethical clearance from the Institutional Ethical Committee as per letter no. IAEC/Pharma/MC/17 dated 12-01-2021. Fifteen male rabbits belonging to the Chinchilla breed weighing an average of 2-2.5kgs were obtained from the Animal House of Government Medical College, Srinagar for the study. The study was conducted on healthy male rabbits (weight 2 to 2.5 kg) and rabbits having less physical activity or not feeding well were excluded from the study. Female rabbits were also excluded. The animals were randomly divided into three groups, with each group consisting of five rabbits:

GROUP A: served as the *control group*, these were fed normal drinking water.

GROUP B: *low dose group*, these were given MSG mixed with drinking water in the dose of 4g/kg.

GROUP C: *high dose group*, these were fed MSG mixed with drinking water in the dose of 6g/kg.

One rabbit from each group was sacrificed in four different sittings at 6^{th}, 12^{th}, 18^{th} and 24^{th} week. Thus, a total of 12 animals were sacrificed in the study. The rabbits were sacrificed after anaesthetizing them with chloroform as per guidelines laid down by the "Committee for Purpose of Control and Supervision of Experiment on Animals" (CPCSEA). Thyroid glands were dissected out using standard dissection techniques. The tissues were processed manually using standard histological techniques. Sections measuring 5-6 μm were cut and fixed on glass slides. These sections were stained with Haematoxylin and Eosin. Appropriate photographs were taken using a photographic microscope.

OBSERVATIONS AND RESULTS:

Gross appearance: The macroscopic structure of the thyroid gland in all the specimens appeared normal. The colour, texture and size appeared within the normal range.

Microscopic features:

Group A (control): Microscopically the gland appeared normal with follicles lined by cuboidal epithelium. The lumen of the follicles was filled with colloid. Parafollicular cells were also present between the follicular cells and the basement membrane.

Group B (low dose): The normal thyroid architecture was maintained at 6 weeks. However inter-parenchymal haemorrhages were seen along with vascular congestion. Histological study at 12 weeks revealed other changes as well. Follicular hyperplasia was observed (Figure 1a). At 18 weeks, the lining epithelium of the follicular cells became of the squamous type. The follicles were filled with abundant colloid as in Fig 1b. All these changes gave a hypothyroid picture, indicating that intake of MSG causes hypothyroid changes. Follicular haemorrhages were also observed as seen in Fig 1c. In addition to these changes, the shape of the follicles was also distorted. There was a disruption of the basement membrane of the cells. These changes can be seen in Fig 1d. The cytoplasm appeared vacuolated, with pyknotic nuclei. Parenchymal haemorrhages were more prominent. Also, there was a reduction in the amount of colloid in the follicles. These changes were exaggerated at 24 weeks.

***Group C (high dose)*:** A histological study of the high dose group done at 6 weeks revealed some changes. There was an enlargement in the size of the thyroid follicles. In addition to follicular hypertrophy, follicular hyperplasia was also observed. The follicles were filled with darkly stained abundant colloid. There was an increase in the glandular and stromal vascularity as well. Inter parenchymal haemorrhagic areas were also seen. The high-dose group at 12 weeks showed a squamous type of lining epithelium of the follicles. The amount of colloid was also increased within the follicles. There was disruption of the basement membranes of the cells along with increased vascularity. Stromal hyperplasia was also seen. At 18 and 24 weeks, these changes were more prominent with an increased number of parenchymal haemorrhages as seen in Fig 1e. Haemorrhages within the acini of the gland were also observed. Vascular congestion was also seen. Exfoliated cells were observed within the colloid as in Fig 1f. However, at 24 weeks the follicles showed absent colloid.

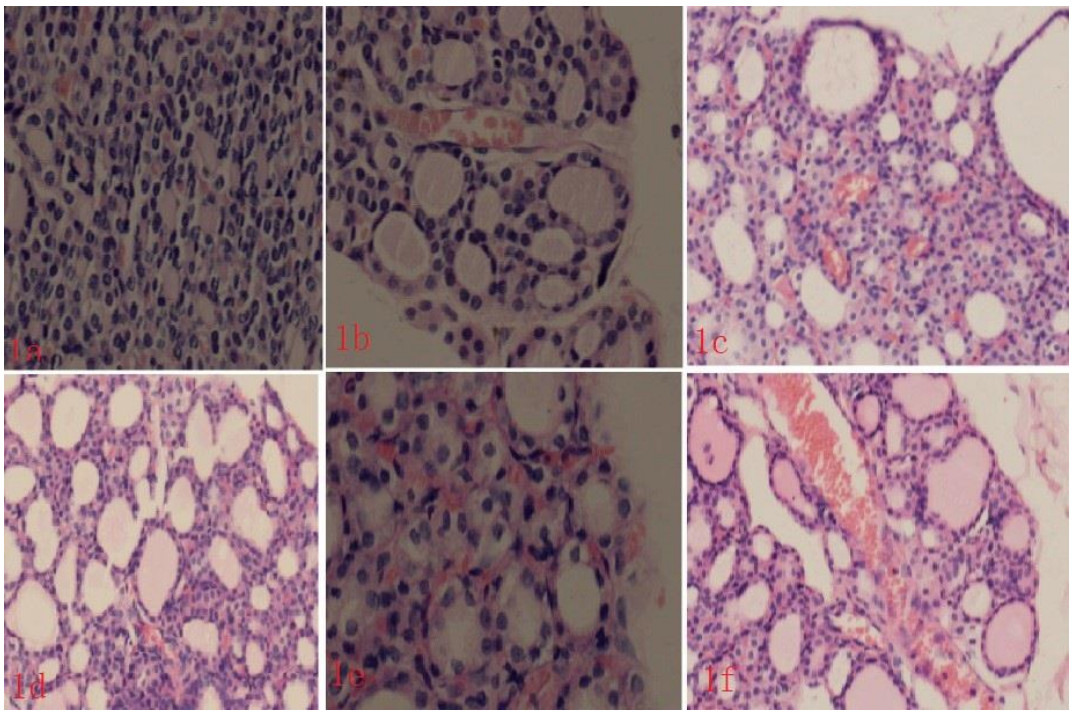

Figure 1: Microphotograph of the thyroid gland of a rabbit treated with Monosodium Glutamate showing changes at different times and doses of the MSG

1a: Group B at 12th week showing follicular hyperplasia with parenchymal haemorrhages
1b: Group B at 12th week showing darkly stained and abundant colloid with cuboidal epithelium.
1c: Group B at 18th week showing parenchymal haemorrhages, vacuolated cytoplasm
1d: Group B at 24th week showing disruption of basement membrane and distortion of thyroid follicles.
1e: Group C at 24th week showing Parenchymal haemorrhages.
1f: Group C at 24th week showing vascular congestion and exfoliated cells in the colloid.

DISCUSSION: Monosodium glutamate which has an "umami" taste is one of the most commonly used food additives in today's time. Its use began in Japan in 1908 and very soon was used globally as a taste enhancer. Processed, packaged food items and sauces are the most common sources of MSG which are used routinely. Although the FDA has labelled it as safe for use, there has been a debate about its safety and harmful effects as it affects almost all the organs in the body. Therefore, MSG is one of the most researched food additives. Experimental studies done on humans as well as animals have confirmed its cytotoxic effect on many organs of the body. The present study was done to perform a detailed investigation into the effects of Monosodium Glutamate on the thyroid gland.
This study was conducted on 15 male Chinchilla rabbits which were divided into three groups; control group, low dose group and high dose group, to evaluate the effects of different doses of Monosodium Glutamate at different intervals of time. The time frames started from 6 weeks up to 24 weeks with a 6-week gap in between the sittings i.e., 6 weeks, 12 weeks, 18 weeks and 24 weeks. The present study showed that the histological changes induced by MSG on the thyroid gland were dose and duration-dependent. Histological changes were observed at 6 weeks in the form of parenchymal haemorrhages and vascular congestion. Tissue observed in the later weeks in both the low dose, as well as high dose groups, showed follicular hyperplasia as well as follicular hypertrophy. The lining epithelium was of squamous type, with an increase in the amount of colloid. These changes pointed towards a hypothyroid picture. The results were in concordance with a study done by Dhindsa K.S et al (1980) [12]. Other changes that could be seen include disruption of the basement membrane along with vacuolated cytoplasm and pyknotic nuclei. The study conducted by Khalaf HA et al (2015) [13] showed similar changes. However, a study conducted by Cekic S et al (2004) [14] showed absent colloid within the follicles when observed at 6 months. A similar picture was observed in the low-dose group in this study at 18 weeks. A study at 24 weeks showed absent colloid in many follicles. Rani P et al (2013) [15] conducted a similar study and at the end of 30 days observed reduced colloid in some follicles. Also, follicles showed a columnar type of epithelium. These changes indicate a hyperthyroid condition. Hence the study was contradictory to the changes observed in my study. Noya DA et al (2021) [16] conducted a study on 40 adult male albino rats to observe the protective effect of pomegranate peel extract on the pituitary-thyroid axis exposed to monosodium glutamate. It was observed that the administration of pomegranate peel extract induced improvement in the changes caused by MSG intake.

CONCLUSION: The present study was conducted to evaluate the effects of Monosodium Glutamate on the thyroid gland. The rabbits received 4g/kg body weight and 6gm/kg body weight of MSG respectively. Microscopic changes which were reported in the experimental groups were dose and duration-dependent. The thyroid gland showed follicular hyperplasia and hypertrophy. The lining epithelium of the follicles was of the squamous type and the follicles were filled with darkly stained abundant colloid giving a hypothyroid picture. In addition, parenchymal haemorrhages were observed. There was an increased glandular and stromal vascularity. In the subsequent weeks, the shape of the follicles was distorted. The basement membrane of follicles was disrupted and the cytoplasm appeared vacuolated with a pyknotic nuclei.
It can be concluded that MSG-administered to male rabbits has a profound impact on the thyroid tissue integrity. This is of particular importance, given the prevalence of MSG in commercially packaged food for human consumption. Therefore, its use should be restricted as much as possible.

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