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The influence of long-term treatment with monosodium glutamate on gastric mucosa *in rats*

Wpływ długotrwałego podawania glutaminianu sodowego na śluzówkę żołądka szczurów

INTRODUCTION

Well known flavor enhancer monosodium glutamate (MG), E 621 is widely used in food industries. In 1968, a report appeared in the New England Journal of Medicine describing a constellation of symptoms in patients who dined in one of the growing number of Chinese restaurants. The symptoms of the so-called «Chinese restaurant syndrome» included numbness, radiating to the back, arms, and neck; weakness; and palpitations [6]. Later reports included other symptoms, such as tightness, flushing, tearing, dizziness, syncope, and facial pressure [3]. But the mechanism of the genesis the «Chinese restaurant syndrome» is still unclear [4]. Today also there are not data about the influence of prolonged consumption of MG on gastric mucosa (GM). Therefore, the aim of this work was to study the effects of long-term injection of MG on GM and the stability of GM to the stress action in rats.

MATERIAL AND METHODS

The study was carried out on 42 rats maintained in accordance with the guidelines of Animal Ethical Research Committee of Taras Shevchenko National University of Kyiv. Animals were divided into 4 groups. The animals were deprived of food for 24 hr prior to the experiments with an easy access to water. To the rats of I group during 30 days we injected 0.5 ml water (per os, one a day). The animals of II group in 30 days of water injection (0.5 ml per os, one a day) were subjected to the water immersion restraint stress (WRS) [7] (stress-control). The rats of III and IV group during 30 days received 15 and 30 mg/kg of MG (0.5 ml per os, one a day), consequently and after that they were subjected to the WRS. For 30 days in rats of all groups we investigated the state of GM. We chose doses 15 and 30 mg/kg (corresponding to 1 and 2 g for human) because according to the literature 1 g MG has no inauspicious action on the human [3], but 3 g is hazardous to health [1]. We used a lethal dose of urethane (3 g/kg, intraperitoneally) for rats [2]. We cut up their stomachs along the small curvature and carefully washed out. Then on gastroscope at transillumination by means of

a magnifier (x4) we conducted a careful examination. We counted up the area of ulcers and length of erosions. Our data by test Shapiro-Wilks' W test were normally distributed. All results are expressed as the M±m of n values. Statistical comparisons between groups were conducted using the Student's t-test for unpaired data. Statistical significance was set at $p<0.05$.

RESULTS

It was established that GM in rats of I group was healthy. In GM of rats in 30 days of MG injection in daily dose 15 mg/kg ulcers and erosions were developed. The area of ulcers was 4.0±0.22 mm² (Fig. 1) and the length of erosions was 2.57±0.2 mm (Fig. 2). GM had red color, which was caused by a large number of dot hemorrhages and increased fragility of vessels, there were blood clots on the surface of GM. Increase of the daily dose of MG to 30 mg/kg enhanced the damages of GM. The area of ulcers was 4.86±0.26 mm² and the length of erosions was 3.43±0.2 mm. In GM massive hemorrhages were recorded. GM had saturated red color.

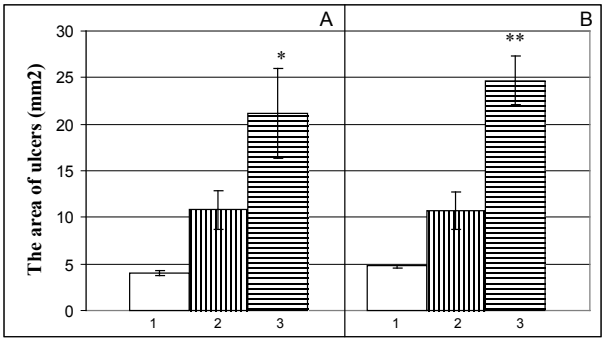

Fig. 1. The influence of monosodium glutamate (15 (A) and 30 (B) mg/kg, per os during 30 days) on area of ulcers in rats (M±m): 1 – glutamate; 2 – stress-control; 3 – glutamate+stress; * $p<0.05$, ** $p<0.01$ compared with a group of stress-control

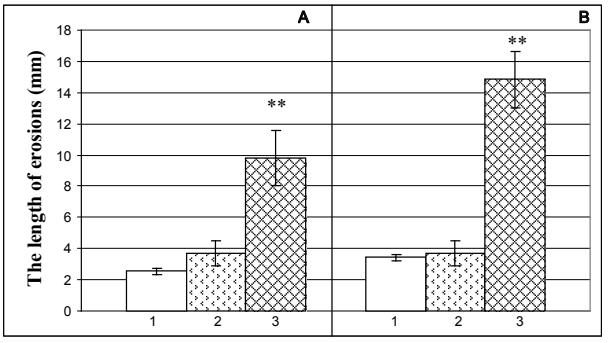

Fig. 2. The influence of monosodium glutamate (15 (A) and 30 (B) mg/kg, per os during 30 days) on length of erosions in rats (M±m): 1 – glutamate; 2 – stress-control; 3 – glutamate+stress; ** $p<0,01$ compared with a group of stress-control

WRS in rats of II group (stress-control) evoked the development of ulcers (10.79±2.02 mm^2) and erosions (3.7±0.8 mm). MG injection in a dose 15 and 30 mg/kg WRS evoked more profound destructive processes in GM. The area of ulcers was 21.21±4.83 and 24.7±2.6 mm^2 and the length of erosions was 9.8±1.8 and 14.8±1.8, mm accordingly. Thus, the area of ulcers and length of erosions in GM of rats which received 15 mg/kg MG were increased respectively by 97% ($p<0.05$) and by 168% ($p<0.01$) compared with the group of stress-control. A double daily dose of MG showed a much stronger effect on GM in rats which were exposed to stress. The area of ulcers and length of erosions in GM were increased by 129%, ($p<0.01$) and by 304% ($p<0.01$), respectively, compared with the group of stress-control.

DISCUSSION

We showed that the injection of monosodium glutamate during 30 days to rats in doses 15 and 30 mg/kg (1 and 2 gram of MG on average statistical person) evoked GM lesions and strengthened the stress action on GM. Taking into account the data of literature about pharmacological blockade of central glutamate receptors results in an attenuation of stress-induced responses of several hormones and mediators, such as adrenocorticotropic hormone, prolactin, and catecholamines [5,8] we concluded that excitement of glutamate receptors against the background of long-term injection of MG increases the stress action on GM via enhancement of stress-induced responses of adrenocorticotropic hormone and catecholamines. Therefore the long-term excessive consumption of MG can lead to gastritis and ulcer disease of stomach. Secondly, the maximum daily dose of MG, as well as other food additives must be reviewed with regard to their effect on GM.

CONCLUSIONS

1. Long-term consumption of MG even in safety dose leads to the appearance of ulcers, erosions and hemorrhages in GM.
2. MG decreases stability of GM to stress action.
3. The maximum daily dose of MG as well as other food additives must be reviewed with regard to their effect on GM.

REFERENCES

1. Allen D.H. et al.: Monosodium L-glutamate-induced asthma. J. Allergy Clin. Immunol., 80, 530, 1987.
2. Cao Y. et al.: Purinergic modulation of respiration via medullary raphe nuclei in rats. Respir. Physiol. Neurobiol., 155, 114, 2007.
3. Geha R. et al.: Review of alleged reactions to monosodium glutamate and outcome of a multicenter double-blind placebo-controlled study. J. Nutr., 130, 1058, 2000.
4. Freeman M.: Reconsidering the effects of monosodium glutamate: a literature review. J. Am. Acad. Nurse Pract., 18, 482, 2006.
5. Jezova D. et al.: Endogenous excitatory amino acids are involved in stress-induced adrenocorticotropin and catecholamine release. Neuroendocrinol., 62, 326, 1995.

6. Kwok R.H.M: Chinese-restaurant syndrome. N. Engl. J. Med., 278, 796, 1968.
7. Takagi K. et al.: The effects of drugs on the production and recovery process of the stress ulcer. Japan. J. Pharmacol., 18, 9, 1968.
8. Zelena D. et al.: Simultaneous blockade of two glutamate receptor subtypes (NMDA and AMPA) results in stressor-specific inhibition of prolactin and corticotropin release. Neuroendocrinol., 69, 316, 1999.

SUMMARY

In acute experiments on 42 white rats we showed that the injection of monosodium glutamate (MG) during 30 days to rats in doses 15 and 30 mg/kg (1 and 2 gram of MG on average statistical person) evoked gastric mucosa (GM) lesions (ulcers, erosions and hemorrhages) and strengthened the stress action on GM. We concluded that the long-term excessive consumption of MG can lead to gastritis and ulcer disease of stomach. Secondly, the maximum daily dose of MG, as well as other food additives must be reviewed with regard to their effect on GM.
Keywords: monosodium glutamate, gastric mucosa, water immersion restraint stress

STRESZCZENIE

W doświadczeniu przeprowadzonym na 42 białych szczurach wykazano, że podawanie glutaminianu sodu przez okres 30 dni w dawkach 15 i 30 mg/kg (średnio 1 i 2 g MG) wywoływało uszkodzenia śluzówki żołądka (GM) (wrzody, nadżerki i krwawienia) i nasilało oddziaływanie stresu na GM. Stwierdzono, że długotrwała nadmierna konsumpcja MG może prowadzić do zapalenia błony śluzowej i choroby wrzodowej żołądka. Ponadto niezbędna jest rewizja maksymalnej dobowej dawki MG oraz innych dodatków do żywności z uwzględnieniem ich oddziaływania na śluzówkę żołądka.
Słowa kluczowe: glutaminian sodu, śluzówka żołądka, wodny zanurzeniowy stres immobilizacyjny