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The influence of long-term treatment with monosodium glutamate on pancreas in rats

Wpływ długotrwałego oddziaływania glutaminianu sodu na trzustkę szczurów

INTRODUCTION

Monosodium glutamate (MG) is a food additive used as a flavoring agent to enhance taste. Although the evaluations conducted by the U.S. Food and Drug Administration and some other organizations concluded that MG was a safe food ingredient for the general population, none of them answered the question: is MG consumption healthy [3]? However, its excessive consumption causes a number of diseases as well as "Chinese Restaurant Syndrome" [8]. Understanding the influence of MG on the pancreas may lead to a new understanding of the physiology of this tissue and the pathophysiology of diseases like diabetes, pancreatitis. In our work we chose doses of MG – 15 and 30 mg/kg which correspond to 1 and 2 g for human because due to the literature 1 g MG has no inauspicious action on the human [4], but 3 g is hazardous to health [1].

Therefore, the aim of this work was to study the effects of long-term injection of MG on pancreatic tissue in rats.

MATERIAL AND METHODS

The study was carried out on 30 white rats maintained in accordance with the guidelines of Animal Ethical Research Committee of Taras Shevchenko National University of Kyiv. The animals were deprived of food for 24 hr prior to the experiments with an easy access to water. The rats were divided into 3 groups. To the rats of I group during 30 days we injected 0.5 ml water (per os, once a day). The animals of II and III group during 30 days received 15 and 30 mg/kg of MG (0.5 ml per os, once a day), consequently. During 30 days in all rats we performed histological and morphometric studies of pancreatic tissue. We used a lethal dose of urethane (3 g/kg, intraperitoneally) for rats [2]. Tissue sections of the pancreas was fixed in 10% formalin, embedded in paraffin, stained with hematoxylin and eosin. On micrographs obtained with increasing x 150–900 we delineated the cross section of nuclei of endocrine and exocrine pancreatic cells, cross section of exocrine pancreatic

cells and the distance between lobules of the pancreas. Then we calculated their area using the free software UTHSCSA ImageTool developed in Texas state university, San Antonio, Texas in 1995–2002 years and accessible in the Internet at ftp://maxrad6.uthscsa.edu.

Our data were normally distributed by test Shapiro-Wilks' W test. All results are expressed as the M±SD 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 shown that pancreatic tissue in rats of I group was of normal structure. The histological evaluation of pancreatic tissue of rats in 30 days of MG injection in the doses 15 and 30 mg/kg there showed massive edema and inflammation which are characteristic of acute pancreatitis. There was also marked leukocyte infiltration in the pancreatitis groups. The morphometric analysis confirmed pathological changes in pancreatic tissue. The cross-sectional area of nuclei of endocrine cells was increased by 14.6% ($p<0.001$) and 15.6% ($p<0.001$). The cross-sectional area of nuclei of exocrine pancreatic cells was increased by 10.2% ($p<0.001$) and 13.8% ($p<0.001$). The distance between lobules of the pancreas was increased by 90.5% ($p<0.001$) and 89.2% ($p<0.001$) but the cross-sectional area of the exocrine pancreatic cells was decreased by 5.9% ($p<0.001$) and 5.9% ($p<0.001$) (Table 1).

Table 1. The influence of long-term injection with monosodium glutamate on pancreas in rats

	Control (0.5 ml H_2O), M±SD	Glutamate (15 mg/kg), M±SD	Glutamate (30 mg/kg), M±SD
Cross-sectional area of nuclei of endocrine cells (μm^2)	20.5±1.6 n=10	23.5±1.4*** n=10	23.7±1.5*** n=10
Cross-sectional area of nuclei of exocrine pancreatic cells (μm^2)	19.6±1.4 n=10	21.6±1.6*** n=10	22.3±1.5***/### n=10
Cross-sectional area of the exocrine pancreatic cells (μm^2)	1243.1±17.7 n=10	1170.2±27.3*** n=10	1169.9±25.0*** n=10
The distance between lobules of the pancreas (μm)	17.6±1.7 n=10	33.6±1.6*** n=10	33.3±1.6*** n=10

SD – standard deviation *** $p<0.001$ compared with control ### $p<0.001$ compared with group of glutamate (15 mg/kg), n – number of animals

DISCUSSION

MG has a long history of use in foods as a flavor enhancer. In the United States, the Food and Drug Administration has classified MG to be generally recognized as safe. Nevertheless, there is an ongoing debate concerning whether MG causes any of the alleged reactions [1, 4]. A complex of symptoms after ingestion of a Chinese meal was first described in 1968 [7]. MG was suggested to

trigger these symptoms, which were referred to collectively as Chinese Restaurant Syndrome. Since then, clinical studies have been performed by many groups, with varying degrees of rigor in the experimental design ranging from uncontrolled open challenges to double-blind, placebo controlled studies. Challenges in subjects who reported adverse reactions to MG have included relatively few subjects and have failed to show significant reactions to MG. Results of surveys and of clinical tests with MG in the general population reveal no evidence of effects [3]. But our findings cast doubt on the traditional claim that the use of food additive MG within reasonable limits (1 gram per day) is safe [4]. We showed that the daily injection of MG to rats in the dose 15 mg/kg and 30 mg/kg during 30 days leads to the inflammation of pancreas. Today, it is found that consumption of MG in the amount of 3 grams per day is dangerous to human health [1]. In our experiments it was shown that the lower dose of sodium glutamate (1 and 2 grams per day on average statistical person) is also dangerous. It was established that the injection of MG to rats in the doses of 15 and 30 mg/kg (1 and 2 grams of MG per average statistical person) during 30 days leads to an increase of the cross-sectional area of nuclei of endocrine and exocrine pancreatic cells. It points to intensification of synthetic processes in pancreatic cells. And a simultaneous decrease of the cross-sectional area of the exocrine pancreatic cells is evidence of stimulation of secretory processes in exocrine cells.

With respect to the mechanism of MG action on pancreas, the presence of high affinity glutamate/aspartate uptake system, similar to that described in the central nervous system, has been demonstrated in pancreatic tissue [6]. Also, numerous studies have shown the presence of glutamate receptors in endocrine pancreatic cells [5]. We concluded that the development of pancreatitis in rats after long-term injection of MG is a result of the increase of synthetic and secretory processes in pancreatic cells. Thus, we can include glutamate in the group of substances stimulating pancreatic secretion.

CONCLUSIONS

Long-term consumption of MG even in safety doses leads to the development of pancreatitis. The maximum daily dose of MG as well as other food additives must be reviewed with regard to their effect on pancreas.

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SUMMARY

The effects of long-term injection of food additive monosodium glutamate (MG) on pancreatic tissue in 30 white rats was investigated. It was established that during 30 days of daily MG injection in the doses 15 and 30 mg/kg the cross-sectional area of nuclei of endocrine cells, the cross-sectional area of nuclei of exocrine pancreatic cells, the distance between lobules of the pancreas were increased but the cross-sectional area of the exocrine pancreatic cells was decreased. Thus histological evaluation of pancreatic tissue of rats in 30 days of MG injection indicates that pancreatitis is developed.

Key words: monosodium glutamate, pancreas, pancreatitis

STRESZCZENIE

Zbadano wpływ długotrwałych injekcji glutaminianu sodu (MG) na komórki trzustki szczurów. Stwierdzono, że w 30 dniu eksperymentu w efekcie codziennych injekcji MG w dawkach 15 i 30 mg/ kg masy ciała powierzchnie przekroju jąder komórek endokrynnych i komórek egzokrynnych oraz odległości pomiędzy płacikami trzustki uległy zwiększeniu, natomiast powierzchnie przekroju komórek egzokrynnych trzustki istotnemu obniżeniu. W ten sposób ocena histologiczna tkanek w 30 dniu injekcji MG wskazuje na rozwój zapalenia trzustki u szczurów.

Słowa kluczowe: glutaminian sodu, trzustka, zapalenie trzustki