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Effect of environmental hyperthermia on gastrin, somatostatin and motilin in rat ulcerated antral mucosa

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Supported by Guangdong Provincial Natural Science Foundation, No.010578, Key Technological Program of Guangzhou, No.2002Z3-E0131 and Key Program in Social Development of Guangdong Province, No.2002C31210

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Received: 2003-05-12 **Accepted:** 2003-06-07

Abstract

AIM: To study the effect of environmental hyperthermia on gastrin, somatostatin and motilin in rat ulcerated antral mucosa.

METHODS: Forty-two Wistar rats were equally divided into six groups, according to the room temperature (high and normal) and the treatment (acetic acid, normal saline and no treatment). Levels of gastrin, somatostatin and motilin in rat ulcerated antral mucosa were measured with a radioimmunoassay method.

RESULTS: The average temperature and humidity were 32.5 °C and 66.7% for the high temperature group, and 21.1 °C and 49.3% for the normal temperature group, respectively. Gastric ulcer model was successfully induced in rat injected with 0.05 mL acetic acid into the antrum. In rats with gastric ulcers, the levels of gastrin and motilin increased, whereas the somatostatin level declined in antral mucosa, compared with those in rats treated with normal saline and the controls. However, the change extent in the levels of gastrin, motilin and somatostatin in antral mucosa was less in the high temperature group than in the normal temperature group.

CONCLUSION: The levels of gastrin, somatostatin and motilin in rat ulcerated antral mucosal tissue remain relatively stable in a high temperature environment, which may relate to the equilibration of the dynamic system.

Sun FP, Song YG. Effect of environmental hyperthermia on gastrin, somatostatin and motilin in rat ulcerated antral mucosa. *World J Gastroenterol* 2004; 10(23): 3528-3530
<http://www.wjgnet.com/1007-9327/10/3528.asp>

INTRODUCTION

The abnormal secretion of gastrointestinal hormones such as gastrin, somatostatin, motilin may affect the function of alimentary tract^[1,2]. In a high temperature living environment, body could develop adaptation reaction to hyperthermia, meanwhile induces a series of compensatory regulations in the central nervous system and endocrine system^[3-8], the content

of gastrointestinal hormones could be changed accordingly. Our experiment investigated the influence of ambient temperature on gastrin, somatostatin, motilin in rat ulcerated antral mucosa and their biological significance.

MATERIALS AND METHODS

Animals and preparation

We used healthy adult male Wistar rats weighing 200-260 g (purchased from Experimental Animal Center, Sun Yat-Sen University of Medical Sciences). The rats were raised in our Experimental Animal Center and fed with standard rat chow. The rats were randomly divided into six groups of seven rats each, respectively. They were high temperature ulcer group, normal temperature ulcer group, high temperature saline group, normal temperature saline group, high temperature control group, normal temperature control group. The room temperature of the hyperthermia group was not interfered, but that of the normal group was controlled by airconditioning.

Radioimmunoassay kits of gastrin and motilin were purchased from Tianjin Qianye Biotech Co. Ltd, and the kits of somatostatin from Department of Neurobiology of Second Military Medical University.

The temperature of the animal houses was measured by catathermometer (produced by Shanghai Medical Instrument Factory) at 8:00 and 20:00 everyday, the relative humidity was converted through the scale at the base of the catathermometer, and average values of dry bulb temperature and relative humidity were recorded. The dry bulb temperature (°C) in houses on the d 0, 1, 2, 3 after model-making and the day of rat sacrifice was 31.7, 32.5, 33.0, 32.8, 32.4 (average 32.5±0.5) for the high temperature group, and 21.2, 21.1, 21.0, 21.3, 21.1 (average 21.1±0.1) for the normal temperature group, respectively. The relative humidity (%) was 58.0, 65.5, 69.0, 76.0, 65.0 (average 66.7±6.6) for the high temperature group and 46.5, 48.0, 51.5, 53.0, 47.5 (average 49.3±2.8) for normal temperature group, respectively.

Establishment of rat model and measurement of gastrin, somatostatin and motilin

The rats of high temperature ulcer group and normal temperature ulcer group were anesthetized with 30 g/L sodium pentobarbital intraperitoneally. The abdomen was opened and 0.05 mL acetic acid was injected into the antral tissues. Omentum majus and antral tissue of the injection site were stitched. The peritoneum, parietal abdomen and ventral muscle, and skin were stitched continually. The rats of high temperature saline group and normal temperature saline group were injected with 0.05 mL saline instead of acetic acid at the same site. The rats of control group did not receive any treatment. After operation, the model-making rats were raised separately, and fasted overnight with free access to water one day before sacrifice. No treatment was given to normal control group. The rat stomach was separated and split from the greater curvature, and mucosa of gastric antrum was scraped about 0.1 g to be boiled after weighed on electronic analytical balance. The boiled tissue was homogenized into homogenates in a homogenizer with 1 mL of 1 mol/L acetic acid and neutralized

with 1 mL of 1 mol/L NaOH, the liquid of homogenates was centrifuged at 3 500 r/min for 15 min to obtain supernatant, and the samples were then stored at -70 °C until assay. Gastrin, somatostatin and motilin were measured by using radioimmunoassay (RIA) method, measurement procedures were performed according to the instructions attached to the kits. The unit of result was transformed to ng/g.

Statistical analysis

Data among the groups were analyzed with factorial analysis of variance by SPSS 10.0 software. The comparison between the two means of different groups was analyzed by Student-Newman-Keuls. $P < 0.05$ was considered statistically significant.

RESULTS

Observation of gross specimens

Gastric contents of the rats in high temperature and normal temperature ulcer groups obviously increased, the diameter of round shape ulcers on the frontal wall of gastric antrum was about 0.5-0.7 cm, the center of the ulcer was pale covered with offwhite membrane, the base was flat with clear verge, and the mucosa around the ulcer had hyperemia and edema. Gastric contents of the rats in the other groups were suitable, mucosa plica of gastric antrum was obvious, and its color was pale red without hyperemia and edema. There was no ulcer on the surface.

Level of gastrin in rat antral mucosa of each group

The difference of gastrin level in antral mucosa between ulcer group and nonulcer group was significant ($F = 9.500$, $P = 0.000$), gastrin levels in ulcer group (average 5.99 ng/g) were higher than those in control group (3.68 ng/g) and saline group (3.98 ng/g). But the differences in gastrin levels among the groups were insignificant in high and normal temperature groups ($F = 1.465$, $P = 0.234$). There was no mutual effect between the two treatment factors of ulcer and temperature ($F = 0.980$, $P = 0.385$). The gastrin level in ulcerated antral mucosa increased significantly ($P < 0.01$). But the level of gastrin in antral mucosa in the high temperature ulcer group increased less than that in the normal temperature ulcer group ($P < 0.05$) (Table1).

Table 1 Gastrin in rat antral mucosa ($n=7$, ng/g, mean \pm SD)

Group	Ulcer	Normal saline	Control
HT	5.24 \pm 1.65	3.91 \pm 1.31	3.64 \pm 1.15 ^b
NT	6.73 \pm 2.29 ^a	4.04 \pm 1.28	3.71 \pm 1.13

^a $P < 0.05$, vs high temperature ulcer group ^b $P < 0.01$ vs ulcer group.

Level of somatostatin in rat antral mucosa of each group

The difference of somatostatin level in antral mucosa between ulcer group and nonulcer group was significant ($F=15.087$, $P = 0.000$), somatostatin levels in ulcer group (average 0.62 ng/g) were less than those in control group (1.37 ng/g) and saline group (1.24 ng/g). But the differences of somatostatin levels were insignificant in high and normal temperature groups ($F = 2.789$, $P = 0.104$). There was no mutual effect between the two treatment factors of ulcer and temperature ($F = 1.416$, $P = 0.256$). The level of somatostatin in gastric ulcerated antral mucosa declined significantly ($P < 0.01$). But the level of somatostatin in antral mucosa in the high temperature ulcer group declined less than that in the normal temperature ulcer group ($P < 0.05$) (Table2).

Level of motilin in rat antral mucosa of each group

The difference of motilin level in antral mucosa between ulcer group and nonulcer group was significant ($F = 18.178$, $P = 0.000$), motilin levels in ulcer group (average 8.04 ng/g) were higher than

those in control group (4.27 ng/g) and saline group (4.58 ng/g). But the differences of motilin levels were insignificant in high and normal temperature groups ($F = 3.632$, $P = 0.065$). There was no mutual effect between the two treatment factors of ulcer and temperature ($F = 2.611$, $P = 0.087$). The level of motilin in gastric ulcerated antral mucosa increased significantly ($P < 0.01$). But the level of motilin in antral mucosa in the high temperature ulcer group increased less than that in the normal temperature ulcer group ($P < 0.05$) (Table3).

Table 2 Somatostatin in rat antral mucosa ($n = 7$, ng/g, mean \pm SD)

Group	Ulcer	Normal saline	Control
HT	0.86 \pm 0.30	1.28 \pm 0.46	1.39 \pm 0.50 ^b
NT	0.37 \pm 0.15 ^a	1.19 \pm 0.41	1.36 \pm 0.41

^a $P < 0.05$, vs high temperature ulcer group ^b $P < 0.01$ vs ulcer group.

Table 3 Motilin in rat antral mucosa ($n = 7$, ng/g, mean \pm SD)

Group	Ulcer	Salt	Cont
HT	6.58 \pm 2.04	4.46 \pm 1.30	4.22 \pm 1.24 ^b
NT	9.50 \pm 2.98 ^a	4.70 \pm 1.43	4.31 \pm 1.40

^a $P < 0.05$, vs high temperature ulcer group ^b $P < 0.01$ vs ulcer group.

DISCUSSION

Our experiment established the model of rat gastric ulcer. Gastrin, somatostatin and motilin were measured with the RIA method. The result revealed that gastrin and motilin in antral mucosa tissue increased, and somatostatin declined when the rats had gastric ulcer. Compensative changes of gastrointestinal tract and other organs took place to accommodate hyperthermia. Our experiment detected the level of gastrin, somatostatin and motilin in antral mucosa tissue of gastric ulcer rats in high and normal temperature environments. We discovered that the level of gastrin and motilin in antral mucosa in the high temperature ulcer group increased less than that in the normal temperature ulcer group, the level of somatostatin in the high temperature ulcer group declined less than that in the normal temperature ulcer group.

Complex changes of many cytokines in body occurred in heat stress environment^[9-15]. Hyperthermia could change heat stress proteins (HSP), atrial natriuretic factor (ANF), angiotensin, nerve growth factor (NGF), cortisol and plasma protein, blood sugar, serum lipoprotein, microelement as well as body immune system correspondingly^[16-20]. The system of neuroendocrine, cytokine and heat stress constituted an organic network, in which a chain in dynamic action could make internal milieu stable^[21,22]. The result of this experiment indicates that the levels of gastrin, somatostatin and motilin in antral mucosa tissue remain relatively stable in a high temperature environment. This may relate to the equilibration of the dynamic system.

REFERENCES

- 1 Kaminska B, Kozielska E, Korzon M, Czaja M, Banach P. Bleeding from alimentary tract in pseudo Zollinger-Ellison syndrome. *Med Sci Monit* 2000; **6**: 596-601
- 2 Ku SK, Lee HS, Lee JH. An immunohistochemical study of endocrine cells in the alimentary tract of the red-bellied frog, *Bombina orientalis*. *J Vet Med Sci* 2000; **62**: 589-594
- 3 de Freitas MS, Spohr TC, Benedito AB, Caetano MS, Margulis B, Lopes UG, Moura-Neto V. Neurite outgrowth is impaired on HSP70-positive astrocytes through a mechanism that requires NF-kappaB activation. *Brain Res* 2002; **958**: 359-370
- 4 Pacheco-Lopez G, Espinosa E, Zamorano-Rojas HM, Ramirez-Amaya V, Bermudez-Rattoni F. Peripheral protein immuniza-

- tion induces rapid activation of the CNS, as measured by c-Fos expression. *J Neuroimmunol* 2002; **131**: 50-59
- 5 **Deng X**, Jayanthi S, Ladenheim B, Krasnova IN, Cadet JL. Mice with partial deficiency of c-Jun show attenuation of methamphetamine-induced neuronal apoptosis. *Mol Pharmacol* 2002; **62**: 993-1000
- 6 **Fernandez F**, Aguerre S, Mormede P, Chaouloff F. Influences of the corticotropic axis and sympathetic activity on neurochemical consequences of 3,4-methylenedioxymethamphetamine (MDMA) administration in Fischer 344 rats. *Eur J Neurosci* 2002; **16**: 607-618
- 7 **Watanabe YG**. Immunohistochemical study on the fetal rat pituitary in hyperthermia-induced exencephaly. *Zoolog Sci* 2002; **19**: 689-694
- 8 **Khan VR**, Brown IR. The effect of hyperthermia on the induction of cell death in brain, testis, and thymus of the adult and developing rat. *Cell Stress Chaperones* 2002; **7**: 73-90
- 9 **Nelson EA**, Wong Y, Yu LM, Fok TF, Li K. Effects of hyperthermia and muramyl dipeptide on IL-1beta, IL-6, and mortality in a neonatal rat model. *Pediatr Res* 2002; **52**: 886-891
- 10 **Mearow KM**, Dodge ME, Rahimtula M, Yegappan C. Stress-mediated signaling in PC12 cells-the role of the small heat shock protein, Hsp27, and Akt in protecting cells from heat stress and nerve growth factor withdrawal. *J Neurochem* 2002; **83**: 452-462
- 11 **Henderson RF**, Barr EB, Blackwell WB, Clark CR, Conn CA, Kalra R, March TH, Sopori ML, Tesfaigzi Y, Menache MG, Mash DC. Response of rats to low levels of sarin. *Toxicol Appl Pharmacol* 2002; **184**: 67-76
- 12 **Suganuma T**, Irie K, Fujii E, Yoshioka T, Muraki T. Effect of heat stress on lipopolysaccharide-induced vascular permeability change in mice. *J Pharmacol Exp Ther* 2002; **303**: 656-663
- 13 **Nambiar MP**, Fisher CU, Enyedy EJ, Warke VG, Kumar A, Tsokos GC. Oxidative stress is involved in the heat stress-induced downregulation of TCR zeta chain expression and TCR/CD3-mediated [Ca(2+)](i) response in human T-lymphocytes. *Cell Immunol* 2002; **215**: 151-161
- 14 **Wang Y**, Li C, Wang X, Zhang J, Chang Z. Heat shock response inhibits IL-18 expression through the JNK pathway in murine peritoneal macrophages. *Biochem Biophys Res Commun* 2002; **296**: 742-748
- 15 **DuBose DA**, Balcius J, Morehouse D. Heat stress and/or endotoxin effects on cytokine expression by human whole blood. *Shock* 2002; **17**: 217-221
- 16 **Hildebrandt B**, Wust P, Ahlers O, Dieing A, Sreenivasa G, Kerner T, Felix R, Riess H. The cellular and molecular basis of hyperthermia. *Crit Rev Oncol Hematol* 2002; **43**: 33-56
- 17 **Roigas J**, Wallen ES, Loening SA, Moseley PL. Estramustine phosphate enhances the effects of hyperthermia and induces the small heat shock protein HSP27 in the human prostate carcinoma cell line PC-3. *Urol Res* 2002; **30**: 130-135
- 18 **van den Berg AP**, van den Berg-Blok AE, Kal HB, Reinhold HS. A moderate elevation of blood glucose level increases the effectiveness of thermoradiotherapy in a rat tumor model II. Improved tumor control at clinically achievable temperatures. *Int J Radiat Oncol Biol Phys* 2001; **50**: 793-801
- 19 **Afek A**, Keren G, Harats D, George J. Whole body hyperthermia accelerates atherogenesis in low-density lipoprotein receptor deficient mice. *Exp Mol Pathol* 2001; **71**: 63-72
- 20 **Ben-Hur T**, Cialic R, Itzik A, Barak O, Yirmiyya R, Weidenfeld J. A novel permissive role for glucocorticoids in induction of febrile and behavioral signs of experimental herpes simplex virus encephalitis. *Neuroscience* 2001; **108**: 119-127
- 21 **Michael GJ**, Priestley JV. Differential expression of the mRNA for the vanilloid receptor subtype 1 in cells of the adult rat dorsal root and nodose ganglia and its downregulation by axotomy. *J Neurosci* 1999; **19**: 1844-1854
- 22 **Dux M**, Sann H, Schemann M, Jancso G. Changes in fibre populations of the rat hairy skin following selective chemodenervation by capsaicin. *Cell Tissue Res* 1999; **296**: 471-477

Edited by Ma JY and Wang XL Proofread by Xu FM