

Serum inflammatory markers in obese mice: Effect of ghrelin

Majid Khazaei, Zoya Tahergorabi¹Department of Physiology, Isfahan University of Medical Sciences, Isfahan, ¹Birjand University of Medical Sciences, Birjand, Iran

Abstract

Background: Ghrelin is involved in modulation of food intake and energy homeostasis; however, it may play a role in cardiovascular system and atherosclerosis process. This study aimed to investigate the effect of ghrelin on serum inflammatory markers in control and obese mice.

Materials and Methods: Ghrelin (100 mg/kg/day, twice daily) was administered interaperitoneally to control and diet-induced obese mice. After 10 days, blood samples were taken.

Results: Results showed that administration of ghrelin did not change serum hsCRP level; however, it reduced serum IL-6 concentration in obese mice ($P < 0.05$).

Conclusion: It seems that the exact role and mechanism of ghrelin in prevention or treatment of atherosclerosis needs more studies.

Key Words: C-reactive protein, ghrelin, inflammation, interleukin-6, obesity

Address for correspondence:

Dr. Majid Khazaei, Associate Professor of Physiology, Faculty of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran.

E-mail: khazaei@med.mui.ac.ir

Received: 27.05.2013, Accepted: 21.07.2013

INTRODUCTION

Ghrelin is a 28 amino acid peptide, which is produced and secreted by the stomach. Although it involves in modulation of food intake and energy homeostasis,^[1] recently, it was shown that ghrelin and its receptor (GHSr) are present in cardiovascular system.^[2] Thus, it seems that it plays a role in cardiovascular disease.^[2,3] Ghrelin inhibits endothelial apoptosis and inflammation,^[4,5] enhances left ventricular function, vasodilation, and decreases peripheral vascular disease.^[6,7]

Studies indicated that plasma ghrelin concentration reduced in obese subjects,^[8] and it seems that reduced plasma ghrelin is associated with chronic low-grade inflammation and possibly atherosclerosis during obesity.^[9] On the hand, an *in vitro* study indicated that ghrelin inhibited monocyte binding, NF κ B activation, and production of inflammatory cytokines in human endothelial cells.^[5]

In this study, we investigated the effect of ghrelin on serum high-sensitive C-reactive protein (hsCRP) and interleukine-6 (IL-6) concentrations in obese and control mice.

MATERIALS AND METHODS

Twenty-four male mice (5 weeks old, weight: 15-16 g), purchased from Pasteur Institute of Iran, were divided into obese and control groups. The animals were housed in animal room on 12:12 h light-dark cycle at 20-25°C. The obese group was placed on high-fat

| Access this article online | |
|---|----------------------------------|
| Quick Response Code: | Website: www.advbiores.net |
|  | DOI: 10.4103/2277-9175.161556 |

Copyright: © 2015 Khazaei. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

How to cite this article: Khazaei M, Tahergorabi Z. Serum inflammatory markers in obese mice: Effect of ghrelin. Adv Biomed Res 2015;4:145.

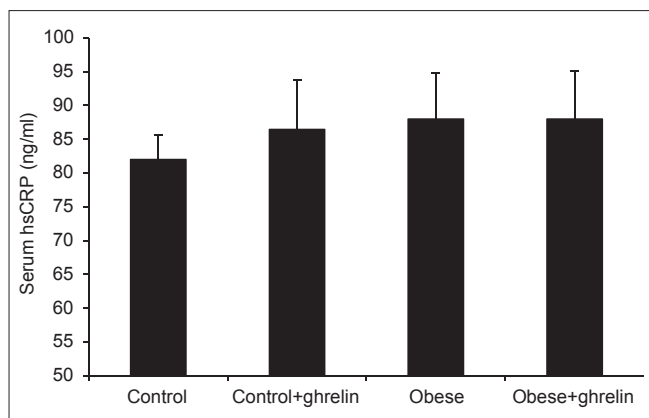


Figure 1: Serum hsCRP concentrations in experimental groups

diet obtained from BioServ Company (laboratories BioServ, Cat #F3282, USA), and control group received standard diet with free access to food and water. The ethical committee of the Isfahan University of Medical Sciences approved the study protocol. After 15 weeks, in the half of each group, the ghrelin (Tocris Co. Bristol, UK.) was administered 100 mg/kg/day twice daily for 10 days. Then, serum samples were taken. The serum hsCRP and IL-6 concentrations were measured by ELISA kits (Biovendor, and BD Biosciences, USA; respectively). The data was analyzed by One-Way ANOVA test using Tukey's post-hoc test. P less than 0.05 was considered statistically significant.

RESULTS

Obese animals had significantly higher body weight than control (44.6 ± 3.5 vs. 24.1 ± 2.7 gr; respectively). Serum hsCRP and IL-6 concentrations were slightly higher in obese mice compared to control, although they were not statistically significant ($P > 0.05$). Administration of ghrelin did not change serum hsCRP level in control and obese animals ($P > 0.05$), however, reduced serum IL-6 concentration in obese mice ($P < 0.05$) [Figures 1 and 2].

DISCUSSION

Atherosclerosis is a chronic low-grade inflammation status, which is associated with many cardiovascular risk factors such as hypertension and diabetes mellitus. Recently, it is suggested that ghrelin may be involved during atherosclerosis process.^[2,5] Endothelial cells have receptor for ghrelin, suggesting that ghrelin could play a role in cardiovascular disease.^[10] Zhang *et al.* demonstrated that ghrelin has a protective role against atherosclerosis.^[11] However, recently, Habegger *et al.* showed that in LDL receptor-null mice, absence or presence of ghrelin receptor does not alter atherosclerosis in diet-induced obese mice.^[12]

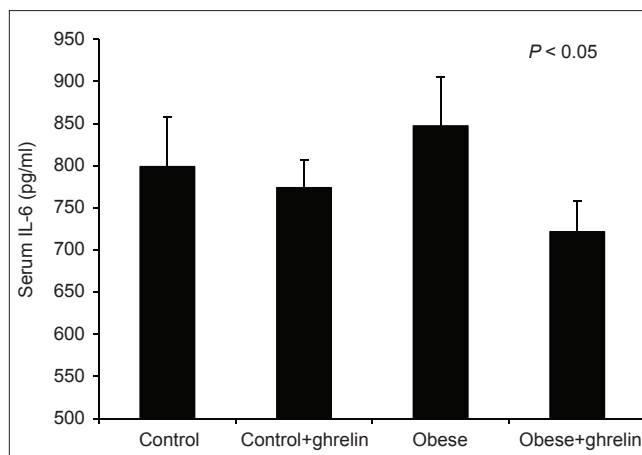


Figure 2: Effect of ghrelin on serum IL-6 concentration in control and diet-induced obese mice

In an *in vitro* study in human umbilical vein endothelial cells (HUVECs), ghrelin inhibited basal and TNF- α and endotoxin-induced cytokine production, and it is suggested that these anti-inflammatory actions of ghrelin play a role in atherosclerosis in obese subjects.^[5] In addition, administration of ghrelin agonist decreased plasma IL-6 concentration in a model of arthritis.^[13] Ghrelin may play a role in atherosclerosis by altering the other factors, which affect this process such as stimulation of NO production,^[14] and it seems that the exact role and mechanism of ghrelin in prevention or treatment of atherosclerosis needs more studies.

ACKNOWLEDGMENT

The authors thank Vice chancellor of the Isfahan University of Medical Sciences for their support.

REFERENCES

1. Kojima M, Kangawa K. Structure and function of ghrelin. *Results Probl Cell Differ* 2008;46:89-115.
2. Tesouro M. Metabolic and cardiovascular effects of ghrelin. *Curr Diabetes Rev* 2010;6:228-35.
3. Leite-Moreira AF, Soares JB. Physiological, pathological and potential therapeutic roles of ghrelin. *Drug Discov Today* 2007;12:276-88.
4. Iglesias MJ, Pineiro R, Blanco M, Gallego R, Dieguez C, Gualillo O, *et al.* Growth hormone releasing peptide (ghrelin) is synthesized and secreted by cardiomyocytes. *Cardiovasc Res* 2004;62:481-8.
5. Li WG, Gavrilu D, Liu X, Wang L, Gunnlaugsson S, Stoll LL, *et al.* Ghrelin inhibits proinflammatory responses and nuclear factor-kappaB activation in human endothelial cells. *Circulation* 2004;109:2221-6.
6. Granata R, Settanni F, Biancone L, Trovato L, Nano R, Bertuzzi F, *et al.* Acylated and unacylated ghrelin promote proliferation and inhibit apoptosis of pancreatic beta-cells and human islets: Involvement of 3',5'-cyclic adenosine monophosphate/protein kinase A, extracellular signal-regulated kinase 1/2, and phosphatidylinositol 3-Kinase/Akt signaling. *Endocrinology* 2007;148:512-29.
7. Granata R, Isgaard J, Alloati G, Ghigo E. Cardiovascular actions of the ghrelin gene-derived peptides and growth hormone-releasing hormone. *Exp Biol Med (Maywood)* 2011;236:505-14.

8. Tolle V, Kadem M, Bluet-Pajot MT, Frere D, Foulon C, Bossu C, *et al.* Balance in ghrelin and leptin plasma levels in anorexia nervosa patients and constitutionally thin women. *J Clin Endocrinol Metab* 2003;88:109-16.
9. Poykko SM, Kellokoski E, Ukkola O, Kauma H, Paivansalo M, Kesaniemi YA, *et al.* Plasma ghrelin concentrations are positively associated with carotid artery atherosclerosis in males. *J Intern Med* 2006;260:43-52.
10. Gnanapavan S, Kola B, Bustin SA, Morris DG, McGee P, Fairclough P, *et al.* The tissue distribution of the mRNA of ghrelin and subtypes of its receptor, GHS-R, in humans. *J Clin Endocrinol Metab* 2002;87:2988.
11. Kishimoto I, Tokudome T, Hosoda H, Miyazato M, Kangawa K. Ghrelin and cardiovascular diseases. *J Cardiol* 2012;59:8-13.
12. Habegger KM, Grant E, Pfluger PT, Perez-Tilve D, Daugherty A, Bruemmer D, *et al.* Ghrelin Receptor Deficiency does not Affect Diet-Induced Atherosclerosis in Low-Density Lipoprotein Receptor-Null Mice. *Front Endocrinol (Lausanne)* 2011;2:67.
13. Granado M, Priego T, Martin AI, Villanua MA, Lopez-Calderon A. Anti-inflammatory effect of the ghrelin agonist growth hormone-releasing peptide-2 (GHRP-2) in arthritic rats. *Am J Physiol Endocrinol Metab* 2005;288:E486-92.
14. Tesouro M, Schinzari F, Iantorno M, Rizza S, Melina D, Lauro D, *et al.* Ghrelin improves endothelial function in patients with metabolic syndrome. *Circulation* 2005;112:2986-92.

Source of Support: Nil, **Conflict of Interest:** None declared.