Brief Report

Serum inflammatory markers in obese mice: Effect of ghrelin

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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

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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]

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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, NFκB 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

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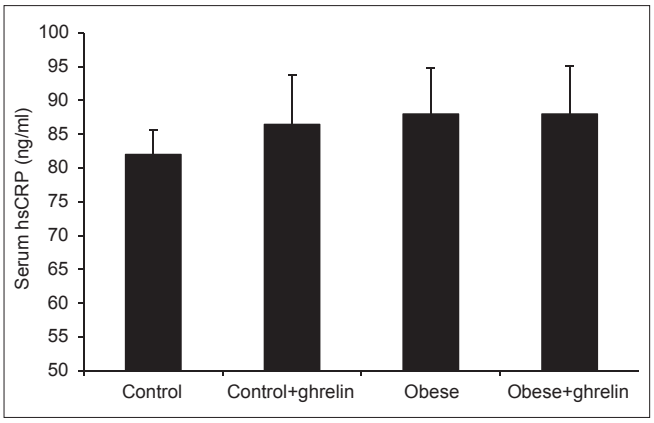

Figure 1: Serum hsCRP concentrations in experimental groups

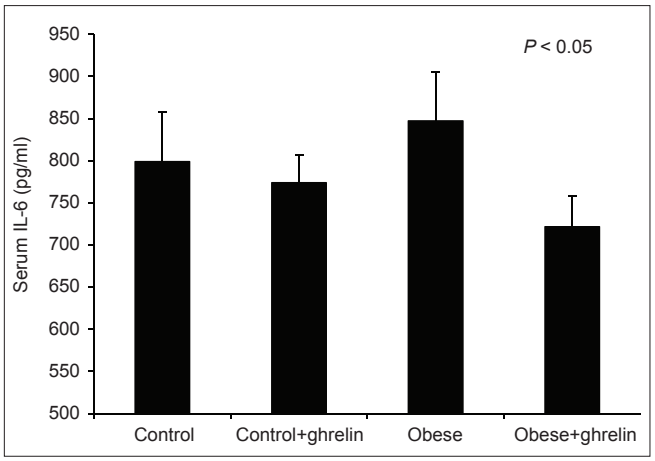

Figure 2: Effect of ghrelin on serum IL-6 concentration in control and diet-induced obese mice

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]

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.

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