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ORIGINAL ARTICLE

Effect of Peripheral Obestatin Infusion on Serum Glucose and some Enzymatic Parameters in rats

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ABSTRACT
The present study investigates possible effect of peripherally-administrated obestatin on serum glucose and some of serum enzymatic parameters include alanine transaminase (ALT) and aspartate aminotransferase (AST) in rats. Twenty-seven male wistar rats weighing 100± 5g were divided to 3 experimental groups; Group 1: control group (C) that normally reared for 2 weeks and no treated with injections, Group 2: placebo that treated with basal solution (50 ml distilled water), and Group 3: Group Obestatin that subjected to twice injection during the test with obestatin (50 ml solution contained 10 µg obestatin/rat). Blood samples were taken and centrifuged for obtaining serum. Data analysis had shown obestatin infusion had moderate (not-significant) effect on glucose level of serum (increase glucose). The ALT concentration was significantly decreased in group obestatin in compared with control (102.3 U/L in compared with 150.7 U/L, respectively for obestatin and control). There is no significant difference between groups for AST level. It is concluded that peripheral administration of obestatin can decrease serum ALT, and has moderate (not significant) effect on glucose concentration in rat model.
Key words: *enzymatic parameters, glycemic status, obestatin.*

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INTRODUCTION

Obestatin is a regulatory peptide [1] that is potentially produced in the endocrine cells the gastrointestinal tract, and testis of mammals including humans and rodent. Obestatin is encoded by the "ghrelin gene" which codes both of ghrelin and obestatin. . It has 23 amino acids in biochemical structure (figure 1).

These peptides involved and regulate appetite and energy status. A study [2] showed that treatment with ghrelin increased body weight, whereas the same dose of obestatin suppressed food intake and reduced weight gain. Acute administration of obestatin inhibited feeding in rodent (fatty rats). Interestingly, the dose-response relationship was U-shaped to the extent that both low and high doses [3].Obestatin inhibited insulin secretion from rat islets in a dose-dependent manner. Therefore, hyper-glycemic condition, exogenous obestatin acts as a potent inhibitor of insulin secretion in anaesthetized rats *in vivo* [4].

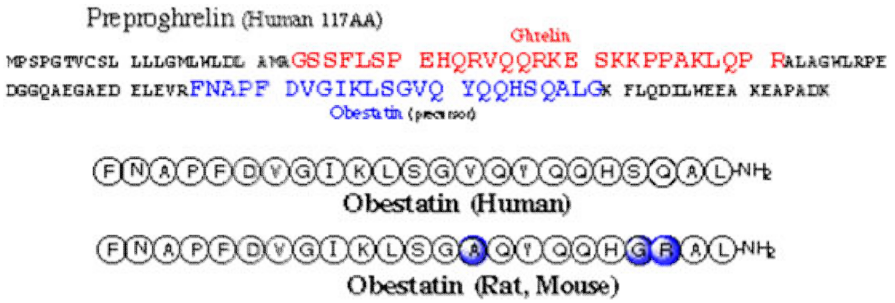


Figure1. Peptidic structure of human and rodent obestatin [1]

Obestatin may contribute in weight gain regulations and appetite [5, 1]. Ghrelin and obestatin has same bio-molecular origin but they have different concentration and peripherial level in blood circulation (ghrelin is 10 to 20 times more than obestatin) [1, 6]. In a comparative term, two functional differences are reported for obestatin and ghrelin [7]: "antagonism of GH-releasing" and "suppression of ghrelin-induced appetite stimulation". In the published studies, there is limited information on possible effect of exogenous obestatin on glucose and enzymatic parameters [8,9].So, propose of present study was to investigation on possible effect of peripherally-infused exogenous obestatin on serum ghrelin and two enzymatic parameters in rats.

MATERIALS AND METHODS

General condition:

Twenty-seven male wistar rats weighing 100± 5g confirmation of routine veterinary examinations were selected for experiment. Animals kept for 1 wk to 12 hours of light and 12 hours dark lighting conditions and temperatures of 22ºc to get used to the conditions of the experiment. During the trial, animals were fed with standard diets formulated for laboratory rodents, enterprise Niroo-SahandCo©,Tabriz.

Grouping

Animals divided into three groups/treatments (each group or treatments of 9 animals) in arranging to completely randomized design (CRD).

- Group 1: control group (C) that normally reared for 2 weeks and no treated with injections.
- Group 2: placebo (P) that treated with twice injection during the test with hormone-free (50 ml distilled water) solution.
- Group 3: Group Obestatin (O) that subjected to twice injection during the test with obestatin (50 ml solution contained 10µgobestatin/rat).

Obestatin infusion

Lyophilized powder of obestatin (product no.: O0266, Rat obestatin, Sigma-Aldrich Co., USA) was dissolved in basal solution (distilled water). Solution was injected intra-peripherally in 50 ml volume contained 10 µg obestatin, per rat. Two time injection process done at day-1 and day-7 of experimental period (during 3-week experimental period).

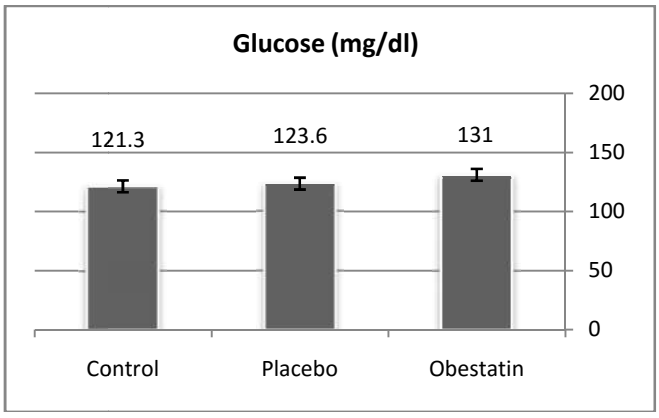
Data analysis

The blood was taken from heart after anesthesia, in according to animal ethics and animal welfare regulations. Centrifuged blood (serum) was analyzed for glucose, ALT, and AST level by Elisa kit (Pars Azmoon Co., Tehran). Obtained data were analyzed with one-way ANOVA method, and Tukey-test was applied for comparison of group means ($P<0.05$).SAS v.19 software was used for all of statistical analysis.

RESULTS AND DISCUSSION

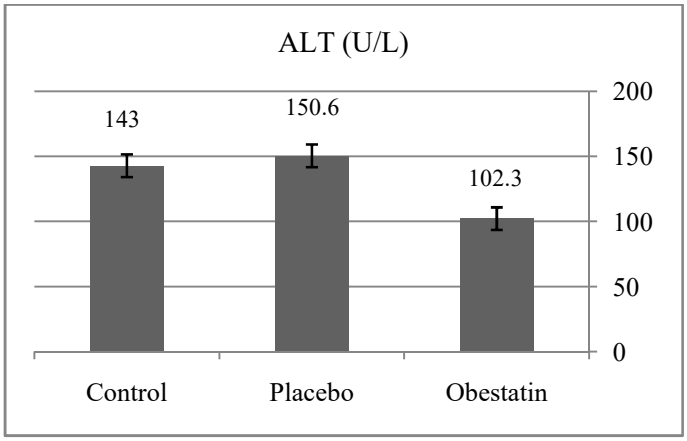
Data obtained from statistical analysis of glucose and enzymatic measures(ALT, AST) are presented in figures1, 2 and 3, respectively.

In according to figure 2, there is no significant difference for glucose level between obestatin-administrated groups and control. There is a minor increase in glucose rate, due to obestatin administration (figure 2). In figure 3, obestatin infusion cause smaller level of ALT in serum (294 U/L in compared with 367 U/L) ($P<0.05$), and in figure 4, there is no significant difference for AST between groups.



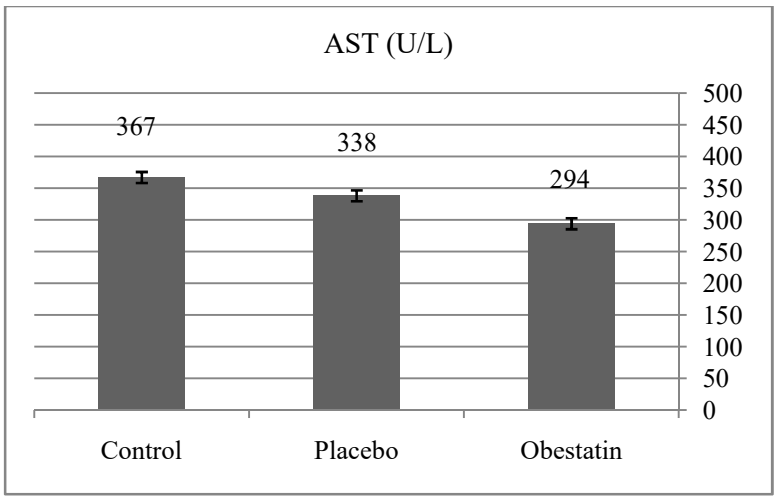
– *P: 0.7311, SEM: 8.775.*

Figure 2. Serum glucose concentration in obestatin-injected rats



– *P: 0.0013, SEM: 5.213.*

Figure3. Serum ALT level in obestatin-injected rats



– *P: 0.0997, SEM: 19.71.*

Figure 4. Serum AST level in obestatin-injected rats.

Information on effect of obestatin on glycemic status is limited. Whereas, it is identified that ghrelin can increase blood glucose due to stimulating insulin releasing from beta cells. A report stated that there is negative and inverse correlation between serum obestatin and insulin level [10]. In newborn rats treated with streptozotocin (STZ), obestatin reduced diabetes at adult age, by preventing β-cell loss, reducing glucose levels and secretion in pancreatic islets [11]. In not-diabetic condition, it is no effect on glucose and insulin levels, in both basal and fasting, in rats and mice [12]. Obestatin-induced insulin release in response to glucose has been also observed, *in vitro* [11]. Qi *et al.*, [13] had reported that fasting plasma obestatinis correlate negatively with blood glucose concentration.

In present study (figure 2), in according to Green *et al*., [12], the obestatin didn't have significant effect on glucose concentration. It is suggested that obestatin is not efficient peptide in glycemic regulation of body in healthy condition.

In published and available literature, there is not direct experimental focus on ALT and AST following obestatin administration. Prodam *et al*., [14] had a study on possible correlation of obestatin with enzymatic parameters include AST, which the results were not significant for possible correlation of obestatin and AST.Similiarly, Zou *et al.,* [15] reported that serum ALT level is an independent factor from obestatin. In present study, ALT level is declined in obstatin-infused groups (figure 3). It seems that obestatin may have possible effect on alanine metabolism in body. Whereas, this issue should be evaluated in future studies.

CONCLUSION

It is concluded that peripheral administration of obestatin can decrease serum ALT, and has moderate (not significant) effect on glucose concentration in rat model. It seems that obestatin may have possible effect on alanine metabolism in body.

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