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Assessment of Obestatin, Ghrelin Hormones Levels and Ghrelin to Obestatin Ratio in Hypertensive Patients

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Abstract: The present study aims to assess ghrelin, obestatin hormones levels and ghrelin to obestatin ratio in patients with hypertension disease and to find out a possible relationship between obestatin, ghrelin level with different criteria including, systolic blood pressure, diastolic blood pressure and Body Mass Index (BMI) in patients with hypertension disease and compared with healthy controls. The 69 patients are diagnosed with hypertension disease (33 males and 36 females) and 20 control healthy subjects (10 males and 10 females) having no history of diabetes mellitus, renal failure and other disease enrolled in this study. The patients are selected from both sexes (males and females) their ages ranged between 40-70 years old. Patients with hypertension disease are recruited from Al-Sader teaching city in Al-Najaf Al-Ashraf Governorate/Iraq. Results of the present study in general revealed a significant increase ($p<0.05$) in obestatin level in patients with hypertension diseases in a comparison with control group and significant decrease ($p<0.05$) in ghrelin level in patients with hypertension disease comparing with control group and ratio of ghrelin to obestatin ratio was decreased in patients undergo from hypertension when compared with control group. The result showed a positive correlation among obestatin, systolic pressure, diastolic pressure and Body Mass Index (BMI) with negative correlation between gherlin, systolic pressure, diastolic pressure and negative correlation between ghrelin to obestatin ratio with blood pressure. The present study concluded that ghrelin, obestatin and ghrelin/obestatin ratio might play role in blood pressure regulation.

Key words: Hypertension, obestatin, ghrelin, BMI, patients

INTRODUCTION

Hypertension is a serious public health problem in many societies due to its high prevalence and the associated with increase in the risk of cardiovascular and renal disease (WHO, 1999). Hypertension is the leading risk factor for the mortality and it is in the third rank as a cause of disability adjust life years (CDC, 2006). Most hypertensive patients are facing problem to control their blood pressure though the extensive use of anti-hypertensive drugs is being used. It is assumed that improving diagnosis, treatment and control of hypertension, overall mortality and stroke incidence can be reduced (Bosworth *et al*., 2003).

Obestatin, a 23-amino acid peptide derived from the ghrelin precursor protein is a risk factor for cardiovascular disease (Klonoff *et al*., 2008). In previous studies, obestatin was found correlated with Intima-Media Thickness (IMT) which is regarded as a biomarker of early arteriosclerosis, suggesting that obestatin plays a positive role in inhibiting carotid atherosclerosis at the early stage (Cui *et al*., 2012). Obestatin has been identified to be associated with insulin resistance metabolic dysfunctions, suppressing food intake, jejunal contraction and body weight gain (Zhang *et al*., 2005).

Ghrelin is a 28-amino acid peptide with an n-octanoylated serine 3 residue (Kojima *et al*., 1999). It is produced primarily (80%) by specialized epithelial cells lining the fundus of the stomach (De La Cour *et al*., 2001) but is also produced in smaller amounts by the placenta, kidney, pituitary and hypothalamus (Kojima *et al*., 1999). It is released into circulation and is involved in various functions including control of food intake, fat mass, thermoregulation, sleep and memory (Tschop *et al*., 2000; Tsubone *et al*., 2005; Korhonen *et al*., 2008).

MATERIALS AND METHODS

Samples of the study: Sixty nine patients were diagnosed with hypertension disease and twenty control healthy

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subjects (10 males and 10 females) having no history of diabetic mellitus and heart failure and other disease participated in this study.

The patients of this study were both sexes (33 males and 36 females) their ages ranged 40-70 years old. Hypertensive patients recruited from Al Sader Teaching city in Al-Najaf Province.

Blood sample: The 5mL of venous blood samples were drown by using a disposable needle and plastic syringes from each patients and controls subject. Blood was left at room temperature for 10 min for clotting, centrifuged 3000 rpm for 10 min and then serum was separated and transported into new disposable tubes.

Measurement of blood pressure: Blood pressure was measured by sphygmomanometer (SK-MINIATUR300B Germany). Both systolic and diastolic blood pressure was recorded in mm Hg, the value of the last reading of the blood pressure was taken for each subject.

Measurement of ghrelin and obestatin serum: Obestatin and ghrelin ELISA kits were used for the quantitative determination of obestatin and ghrelin in human serum were supplied by CUSA Biological/USA.

Statistical analysis: The results were expressed as (mean±SE). t-test and ANOVA test was used for the comparison between the patients and control groups. Correlation coefficients were calculated to estimate the correlation between parameters.

The difference between groups is considered as statistically different when ($p<0.05$). All statistical analysis was performed using SPSS Statistics Version 17.0, IBM-USA. While the figures constructed using graph pad program Version 5.01 USA.

RESULTS

Effect of hypertension on levels of obestatin and ghrelin: The serum concentration of obestatin and ghrelin in patients with hypertension disease and control groups are presented in Fig. 1 and 2. The results of patients with hypertension disease in Fig. 1 indicated a significant increase ($p<0.05$) in obestatin 183.64±8.73 comparing with control groups 24.42±0.67 also, the results of patients with hypertension disease in Fig. 2 indicated a significant decrease ($p<0.05$) in ghrelin 279.81±3.34 when compared with control groups 534.2±8.46.

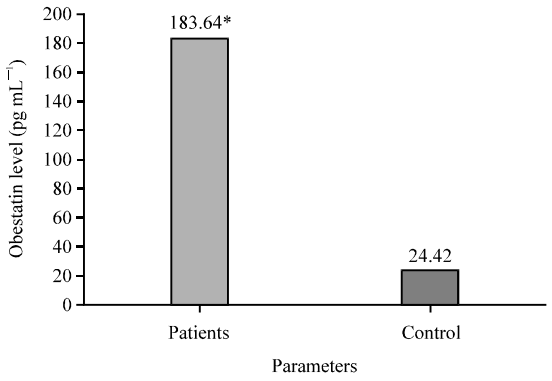

Fig. 1: Obestatin level in patients with hypertension disease and control groups; values are means±SE; *mean significant difference at ($p<0.05$)

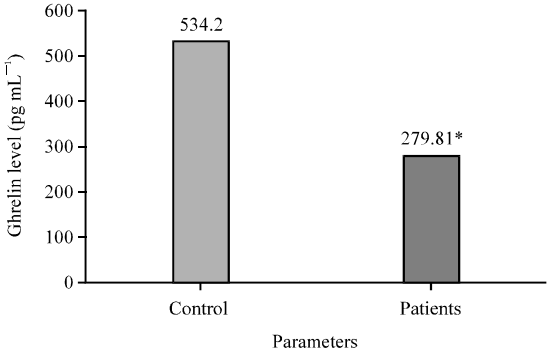

Fig. 2: Ghrelin level in patients with hypertension disease and control groups; values are means±SE; *mean significant difference at ($p<0.05$)

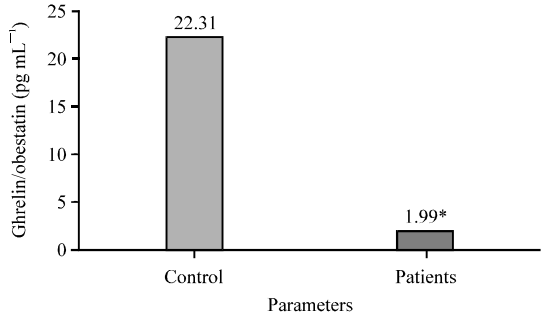

Fig. 3: Ghrelin/obestatin ratio in patients with hypertension disease and control groups; values are means±SE; *mean significant difference at ($p<0.05$)

Effect of hypertension on ghrelin/obestatin ratio: The results presented in Fig. 3 indicated significant decrease ($p<0.05$) in ghrelin/obestatin ratio of hypertensive patients 1.99±0.23 comparing with control groups 22.31±0.8.

The correlation between obestatin level and systolic pressure: The results of correlation and linear regression between obestatin level and systolic pressure in patients are indicated:

The presence of a significant positive correlation ($p<0.05$) between obestatin level and systolic pressure of hypertension disease patients (males and females) ($r = 0.111$, obestatin = 115.935+5.697 systolic pressure) (Fig. 4).

The presence of a significant positive correlation ($p<0.05$) between obestatin level and systolic pressure in females of hypertension disease patients ($r = 0.498$, obestatin = 93.565+12.839 systolic pressure) (Fig. 5).

The presence of a significant positive correlation ($p<0.05$) between obestatin level and systolic pressure in males of hypertension disease patients ($r = 0.473$, obestatin = -34.087+14.705 systolic pressure) (Fig. 6).

The correlation between ghrelin level and diastolic pressure: The results of correlation and linear regression between ghrelin level and diastolic pressure in patients are indicated:

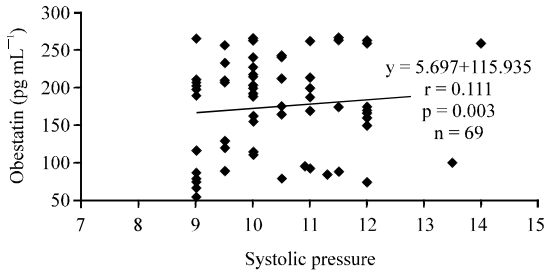

Fig. 4: The correlation between obestatin level and systolic pressure in patients with hypertension disease

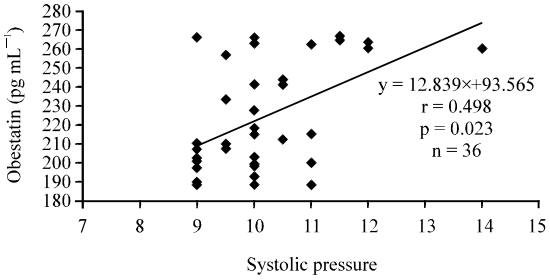

Fig. 5: The correlation between obestatin level and systolic pressure in females of hypertension disease patients

The presence of a significant negative correlation ($p<0.05$) between ghrelin level and diastolic pressure in patients with hypertension disease (males and females) ($r = 0.589$, ghrelin = 411.801±9.656 diastolic pressure) (Fig. 7).

The presence of a significant negative correlation ($p<0.05$) between ghrelin level and diastolic pressure in females of hypertension disease patients ($r = 0.509$, ghrelin = 406.163±9.019 diastolic pressure) (Fig. 8).

The presence of a significant negative correlation ($p<0.05$) between ghrelin level and diastolic pressure in males of hypertension disease patients ($r = 0.694$, ghrelin = 416.88±10.281 diastolic pressure) (Fig. 9).

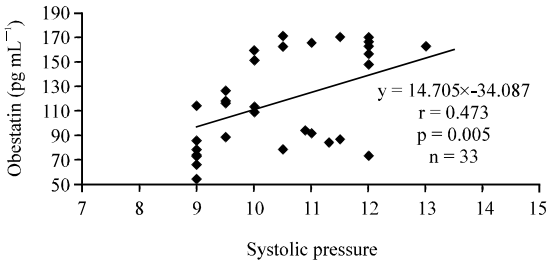

Fig. 6: The correlation between obestatin level and systolic pressure in males of hypertension disease patients

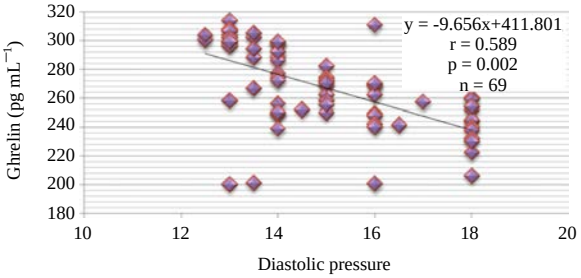

Fig. 7: The correlation between ghrelin level and diastolic pressure in patients with hypertension disease

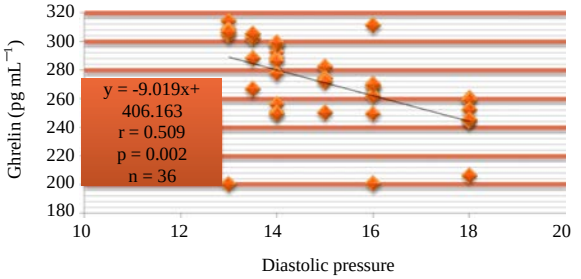

Fig. 8: The correlation between ghrelin level and diastolic pressure in females of hypertension disease patients

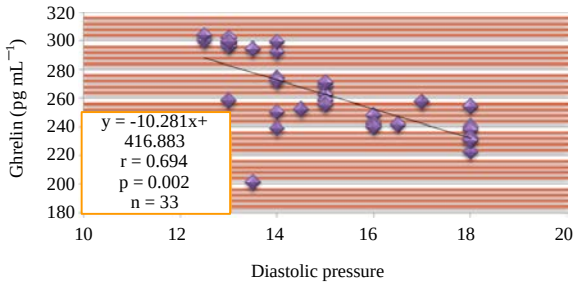

Fig. 9: The correlation between ghrelin level and diastolic pressure in males of hypertension disease patients

DISCUSSION

Obestatin and ghrelin/obestatin level: The present study showed a significant increase ($p<0.05$) in obestatin level in hypertensive patients in comparing with control group. One study proved that a positive correlation between obestatin level and systolic blood pressure (Li *et al*., 2010). Previous study was found that plasma obestatin level was posstively correlated with mean of arterial blood pressure in pregnant women with pregnancy induced hypertension (Ren *et al*., 2009). Another study had proved that intravenous injection of obestatin does not change blood pressure level in spontaneously hypertensive rats (Li *et al*., 2009). Many researchers reported that obestatin opposing ghrelin action in many diseases including hypertension, prostat cancer and gastric cancer (Gourcerol *et al*., 2006; Tremblay *et al*., 2007; Kobelt *et al*., 2008; Mondal *et al*., 2008). Obestatin was initially reported to be endogenous ligand for orphan G-protein coupled receptor GPR39 (Zhang *et al*., 2005). Previous studies have been showed a specific binding of obestatin to various types of GPR39 increasing blood pressure (Ren *et al*., 2009).

The opposite effect of obestatin to ghrelin have been reported by many researchers (Zhang *et al*., 2005; Lagaud *et al*., 2007). Previous study was thought to be close to that of ghrelin and obestatin due to the common origin of both peptides and describing a putative opposite effect of obestatin when compared to ghrelin (Zhang *et al*., 2005). Study by Zhang *et al*. (2005) have shown that obestatin could modulate ghrelin action also have anorectic properties related to peripheral mechanism involving afferent vagal signal. The differences between women and men have been shown in many studies reported higher plasma ghrelin and obestatin in women (Greenman *et al*., 2004; Akamizu *et al*., 2005; Makovey *et al*., 2007; Lippl *et al*., 2008). The differences between females and males may be associated with hormonal status, especially estrogen in women may be play a roles in this state (Najm, 2013). The results of present study indicated significant decrease ($p<0.05$) in ghrelin/obestatin in hypertension patients in comparing with control patients in comparing with control group. Obestatin and ghrelin were encoded by the same gene and derived from the same peptide precursor, the ratio of ghrelin to obestatin was significantly lower in hypertension group which may suggest there was more of profound disturbance of ghrelin and compared with obestatin in hypertension and might be play a role in the regulation of blood pressure (Li *et al*., 2010).

The results of patients with hypertension disease indicated a significant decrease ($p<0.05$) in ghrelin level comparing with control group. Study by Poykko *et al*. (2003) proved that decrease in ghrelin level in hypertensive patients. Previous studies have been shown that ghrelin has important role to decrease blood pressure probably by acting at the nucleus of the solitary tract, one of the most important regions regulating blood pressure and the sympathetic nervous system (Pilowsky and Goodchild, 2002; Matsumura *et al*., 2002; Lin *et al*., 2004). The present study pointed out that ghrelin was decreased and had a negatively associated with hypertension. Ghrelin may be associated with hypertension by Met72 alleles and high total ghrelin level with Met72 alleles carries status leading to decrease hypertension (Ukkola *et al*., 2002; Poykko *et al*., 2003). Ghrelin adminstration also has a direct effect as a vasodilatory effects through GH or nitric oxide independent mechanisms and attenuated monocrota-line-induced pulmonary hypertension (Makino *et al*., 2002).

The results of Fig. 5 indicate no significant differences ($p>0.05$) in serum ghrelin level at all ages in females and males also no significant differences was shown between males and females. The results of present study are consistent with other studies that demonstrated lower ghrelin level in older than those in healthy younger (Rigamonti *et al*., 2002; Makovey *et al*., 2007). Some studies have indicated that both acylated ghrelin and total level are reduced with increasing aging (Kozakowski *et al*., 2008; Prodam *et al*., 2009).

CONCLUSION

The present results revealed a significant positive correlation ($p<0.05$) between obestatin level and systolic in both males and females hypertension patients. Study by Ren *et al*. (2009) found that a significant positive correlation with mean of arterial pressure in normal and pregnant women. Another study has shown that fasting obestatin level was negatively correlated with systolic pressure in humans. One study have explored the association between obestatin and cardiovascular disease

and associated with endothelial and cardiomyocytes and resulting increment in hypertension (Iglesias *et al*., 2007).

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