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The effect of Ramadan fasting on serum leptin, neuropeptide Y and insulin in pregnant women

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Abstract

Background: Many pregnant Muslim women choose to fast during Ramadan every year worldwide. This study aimed to examine the effect of Ramadan fasting on serum leptin, neuropeptide Y and insulin in pregnant women and find whether fasting during pregnancy could have a negative effect on the health of mothers and fetuses.

Methods: This cross-sectional study was conducted on 39 healthy volunteer fasting pregnant women. Serum leptin, neuropeptide Y, insulin levels, body mass index and weight were measured five times on 0, 7th, 14th and 28th days of Ramadan and on the 14th day post-Ramadan. The data were analyzed by SPSS software (version 11.5) using repeated measures ANOVA to find whether any changes occurred in the variables of interest during the study, and Pearson correlation coefficient was used to examine the relations among the variables.

Results: A significant change in fasting blood sugar, neuropeptide Y and leptin was observed during the study ($p< 0.05$). Fasting blood sugar decreased significantly during Ramadan and increased after Ramadan, with the lowest value at the end of Ramadan. Neuropeptide Y increased both during Ramadan and two weeks after Ramadan. Also, leptin decreased significantly two weeks after Ramadan compared to the end of Ramadan. No significant change was observed in insulin level during the study ($p>0.05$).

Conclusion: The result of this study revealed the important role of leptin and neuropeptide Y in the long term regulation of energy balance in pregnant women with chronic diurnal fasting, and it further revealed that Ramadan fasting did not significantly change the serum insulin level.

Keywords: Leptin, Insulin, Neuropeptide Y, Pregnancy, Fasting.

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Introduction

Leptin, a circulating 16-kDa polypeptide, is synthesized predominantly in adipocytes. Leptin plays an important role in the regulation of body weight due to reducing food intake and increasing energy expenditure (1). Leptin can signal the body fat level to the brain to control energy homeostasis by regulating the activity of neurons in the hypothalamus. In a study, leptin in maternal plasma increased from 15.5 ± 9.0µg/L in the 18th week of pregnancy to 17.7±10.7 µg/L in the 35th week (2). Circulating leptin concentrations increase during human pregnancy. Also, leptin contributes greatly to the growth and development of the embryo, fetus and infant (3), because it is synthesized by placental tissue and changes with adipocity and glucose metabolism in pregnancy (4).

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Neuropeptide Y, a polypeptide containing 36 amino acids, is a potent orexigenic agent that regulates eating behaviour. Neuropeptide Y is synthesized in the hypothalamic arcuate nuclei and secreted by nerve terminals in the paraventricular nucleus. The major stimuli for neuropeptide Y synthesis and secretion are food deprivation, reduced circulating insulin levels and elevated serum glucocorticoid levels. Therefore, neuropeptide Y initiates the outflow of efferent stimuli in the brain, resulting in increased appetite and food intake (5). Previous studies have suggested that neuropeptide Y is involved in hyperphagia during pregnancy and lactation (6). In a study, the mean plasma neuropeptide Y concentration was higher in pregnant women during the first trimester of gestation compared to non-pregnant women. In another study, the mean plasma neuropeptide Y was 129 ± 12 pmol/L during the first trimester compared to 40 ± 8pmol/L in non-pregnant women; this value was 144 ± 13 and 156 ± 24 pmol/L in the second and third trimesters of pregnancy, respectively (7). It seems that the leptin-neuropeptide Y mechanism counteracts the vasoconstriction attributable to the preeclamptic changes in the placenta and may cause trophic changes in placental tissue through its receptors. Placental neuropeptide Y production could not affect the neuropeptide Y concentrations in the maternal or fetal circulation (8, 9).

Insulin is a hormone which plays a key role in the metabolism of blood glucose, causing the glucose level to decrease in the blood and increase in the liver. In addition, an increase in fat is usually accompanied with an increase in insulin (10). Insulin also inhibits food intake in animals through modulating neuropeptide Y expression (11). On the other hand, the up-regulation of maternal islet function has a vital role in accommodating the heightened demand for insulin during pregnancy. In 0, 45, 90, 135 and 180 minutes after glucose loading in pregnant women, the mean plasma insulin level was 25.2, 77.2, 57.0, 57.8 and 44.7 µU/ml, respectively.

Ramadan is the ninth month in the Muslim lunar calendar. Ramadan fasting is one of the five pillars of Islam. The majority of Muslims fast from dawn to dusk during the whole month of Ramadan. The daily fast (neither food nor drink) in Ramadan lasts nearly 12-19 hours every day depending on the geographic location and the season (12). The fasting Muslims usually have 2 meals per day, Iftar at sunset and Sahari before dawn (13). Many pregnant Muslim women fast during Ramadan every year worldwide. Fasting during pregnancy in the form of skipping breakfast and other meals may have a negative effect on the health of mothers and their fetuses. Pregnancy is a state characterized by physiological hyperphagia (14) and modifications in maternal adiposity which causes an increase in adipose tissue mass during the early phase, followed by a decrease in the fat mass during the late phase. In a study conducted on animals, lipogenic pathway was predominant during the earlier phase, but it grew more active in the final phase (15). Increased insulin secretion stimulates triglycerides synthesis (16), and increased fat stores stimulate the release of leptin by the adipocytes (17, 18). Consequently, leptin inhibits neuropeptide Y secretion, while energy loss is accompanied by reduced leptin secretion and stimulated neuropeptide Y synthesis (19).

Very little research exists on those pregnant women who fast during Ramadan, and no research has yet examined the effect of fasting on leptin, neuropeptide Y and insulin level during pregnancy. Because leptin, neuropeptide Y and insulin are involved in the modulation of energy balance, we attempted to evaluate these parameters during Ramadan and after Ramadan in fasting pregnant women.

Methods

This cross-sectional study was conducted in the Ramadan of 2012 (from July 21st to August 18th) in Shahrekord University of Medical Sciences, Iran. This study was conducted on 39 healthy volunteer fasting

Table 1. Blood factors measured during Ramadan and two weeks after Ramadan

	First week	Second week	Fourth week	Two weeks after Ramadan	p
FBS (mg/dL)	75.3 (± 19.5)	74.3 (± 9.7)	65.7 (± 15.4)	75.8 (± 14.4)	0.027
Insulin (µU/mL)	16.37(± 8.19)	13.23 (± 4.23)	16.19 (± 8.4)	17.94 (± 9.92)	0.076
Leptin (µg/mL)	27 (± 13.1)	24.3 (± 12.5)	30.3 (± 14.9)	25.7 (± 14)	0.011
Neuropeptide Y (pmol/L)	528 (± 101)	534 (± 106)	553 (± 137)	628 (± 180)	0.001

pregnant women aged 18-45 years, with a gestational age of 7 to 39 weeks and a mean (± SD) of 22.4 (± 7.9) weeks. All the participants signed an informed written consent in which the experimental procedures was described in detail, and they were excluded from the study if they had diabetic mellitus, hypertension or if they were smokers. All the participants abstained from food and drink during the day from dawn to sunset and ate only during the night and completed fasting till the end of Ramadan. This research was approved by the scientific advisory and Ethics Committee of Shahrekord University of Medical Sciences. The participants were weighed barefoot with light clothes, standing on a standard pro-calibrated balance. To determine body mass index (BMI), body mass was measured to the nearest one kg and height to the nearest one cm. At the end of Ramadan, fasting venous samples were taken at 1:00 - 2:00 a.m. to measure the serum level of leptin, neuropeptide Y and insulin. All the samples of collected sera were kept at -20°C until analysis. Serum leptin levels were measured by radioimmunoassay according to the instructions of the manufacturer (Linco, St. Charles, Mo). Neuropeptide Y was assayed through competitive radioimmunoassay by direct assay without extraction using reagents (Euro-Diagnostica AB, Sweden). The human insulin specific radioimmunoassay detects insulin with a sensitivity of 2 µ u/ml. Blood glucose was measured by the hexokinase kit (Pars Azmoon Co., Iran). All measurements were done five times on 0, 7th, 14th and 28th day of Ramadan and on the14th day post-Ramadan.

The mean (± SD) was used for descriptive statistics. The parametric repeated measures ANOVA was applied to determine whether any changes occurred among the variables of interest during the study. The multivariate F-tests of Greenhouse-Geisser were used for within the subject analysis due to the violation of sphericity assumptions. The tests of within-subject contrast were used to compare the mean of measurements. Pearson correlation coefficient was utilized to evaluate the relations among the variables. Statistical significance was defined as $p< 0.05$ and analysis was performed by SPSS.

Results

Thirty nine healthy fasting pregnant women voluntarily participated in this cross-sectional study with the following conditions: an age range of 17 to 42 years and a mean of 26.9 (± 6.4), gestational age of 7 to 35 weeks with a mean of 21.9 (±7.5) and a BMI of 18.3 to 35.9 kg/m^2 with a mean of 25 (±4.2) at the beginning of the study.

The results relevant to the concerned variables including serum fasting blood sugar (FBS), insulin, neuropeptide Y and leptin are demonstrated in Table 1, and the trends are shown in Figs. 1 to 4.

During the study, the weight and BMI of women did not change significantly. FBS decreased significantly during Ramadan

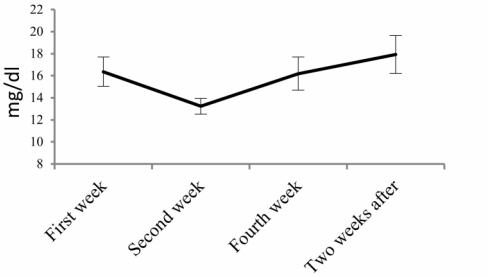

Fig.1. Two weeks after compared with the fourth week (p= 0.009)

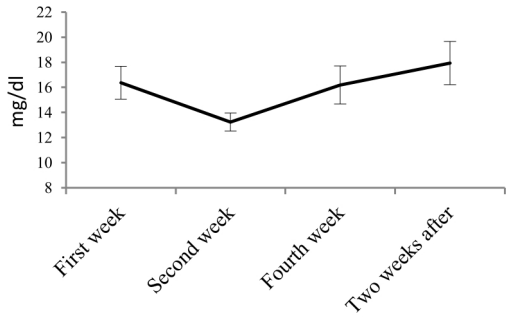

Fig. 2. Two weeks after compared with the second week (p=0.018)

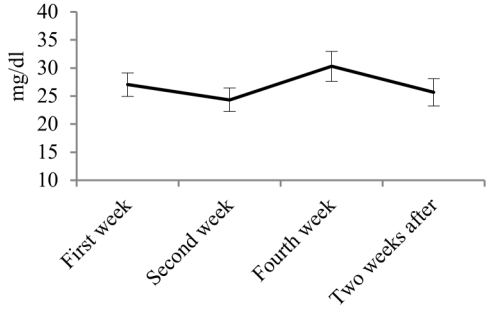

Fig. 3. Two weeks after compared with the fourth week (p=0.002)

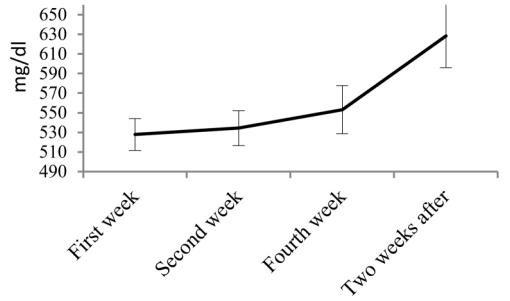

Fig. 4. Two week after compare to the fourth week (p=0.001)

and increased significantly after Ramadan in such a way that the level of estrogen at the end of Ramadan was the lowest of all. Therefore, FBS was significantly higher two weeks after Ramadan compared to the end of Ramadan (p= 0.009) (Fig. 1).

No significant change was found in the insulin level during the study.

An unusual trend was observed in leptin level during the study (Fig. 3): Leptin level decreased until the second week, and then it increased at the end of Ramadan and it decreased again significantly two weeks after Ramadan compared to the fourth week of Ramadan (p= 0.02).

A monotonous increasing trend was found in neuropeptide Y during Ramadan and two weeks after Ramadan on such a way that neuropeptide Y was significantly higher two weeks after Ramadan than its value at the end of Ramadan (p= 0.001) (Fig. 4).

Serum leptin was correlated with BMI corresponding measurement at the second and fourth weeks of Ramadan and at two weeks after Ramadan. However, no significant correlation was found between neuropeptide Y and BMI.

Discussion

The mean of leptin during the first, second and third trimesters and in the postnatal stage was higher in pregnant women compared to the non-pregnant because of the increase in food intake with the advancement of pregnancy (20). Leptin concentration gradually elevated during the first to third trimesters with a peak at 28th week, and its levels were significantly correlated with maternal weight and BMI (21). On the other hand, the increase of leptin levels during pregnancy may be due to a decrease in the rate of leptin clearance from maternal blood circulation (22, 23). The elevation of the serum leptin during pregnancy has also been reported by other investigators (24). Also, previous studies indicated that short-term total fasting or a chronic reduction in caloric intake resulted in the reduction of leptin by 30% to 66% of basal level (25, 26). Leptin secretion decreases in response to fasting (27) and increases in response to positive energy balance induced by overfeeding (25). Because energy intake increases during Ramadan, it is possible that the elevated levels of leptin in this study may have been due to the compensatory increase in food intake during the night (28).

Our findings support those of previous studies. In our study, serum leptin level in the fourth week of Ramadan significantly increased and was correlated with BMI in the second and fourth weeks of Ramadan. A study showed that plasma leptin is secreted in a pulsatile fashion with peak levels at night and a nadir at noon (29). Also,

there is evidence that the diurnal rhythm of leptin secretion is related to the meal pattern and that shifting meal time causes a comparable shift in plasma leptin rhythm (30). Because Ramadan fasting was associated with a forward shifting of lunchtime by approximately 8 hours per day in our study, this shifting caused an increased level of leptin in the circadian pattern of leptin with progressive proximity toward the peak nocturnal level. Therefore, the elevation of serum leptin level in our study may be due to the changes in shifting meal time because serum leptin is considered to reflect the state of nutrition and energy reserve (31). Furthermore, serum leptin and its potential role in pregnancy BMI have been reported (32).

In the present study, during Ramadan and two weeks after Ramadan the serum level of neuropeptide Y increased significantly compared to the level measured prior to Ramadan. This finding is in accordance with that of previous studies indicating that the level of neuropeptide Y mRNA content in the arcuate nucleus significantly increased during pregnancy (33). On the other hand, it has been demonstrated that diet restriction and starvation rapidly induce an accumulation of neuropeptide Y in the paraventricular nucleus by increasing neuropeptide Y mRNA level in the arcuate nucleus (34). A study on rats also showed a very high concentration of prepro-neuropeptide Y mRNA following 96 hours of food deprivation (35). Therefore, the elevation of neuropeptide Y in our study may be due to the progression of pregnancy and fasting from dawn to dusk during the whole month of Ramadan. Nevertheless, in another study, the neuropeptide Y decreased during Ramadan in non-pregnant women (36).

In our study, however, insulin did not significantly increase during Ramadan. Insulin increases in pregnant and non-pregnant women in Ramadan because fasting insulin and leptin are closely correlated with weight loss in obese women.

In the present study, leptin, neuropeptide Y and insulin were considerably higher in fasting pregnant women compared to the baseline levels obtained in the previous studies conducted on non-fasting pregnant women; and this could be due to the need for more energy in fasting pregnant women who experience increased decomposition of lipid tissue. Then, they consume more food and as a result their blood glucose and insulin increase, and the additional glucose causes the blood to turn into fat.

Having no control group was one of the limitations of this study. However, we measured the normal levels of serum leptin, neuropeptide Y and insulin in non- fasting pregnant women as well.

Conclusion

The results of this study revealed that circulating insulin and leptin relatively increased in pregnant women during Ramadan fasting. In addition, it was found that serum neuropeptide Y level progressively increased during Ramadan and two weeks after Ramadan. However, the increase in serum neuropeptide Y was similar to that of leptin in fasting pregnant women. These data provide an insight into the important role of leptin and neuropeptide Y in the long term regulation of energy balance in pregnant women, with chronic diurnal fasting. Also, these results show that the level of factors considered in this study were higher in fasting pregnant women compared to non-fasting pregnant women. The present work described the relationship between leptin and BMI. Leptin levels were correlated significantly with BMI during and after fasting, but neuropeptide Y had no relationship with BMI. The most important finding which was derived from this study was the lack of negative feedback between leptin and serum neuropeptide Y concentrations in fasting pregnant women during Ramadan.

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Conflict of interest

The authors of this work declare no conflict of interest.

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