Original Article

Effect of intended fasting on Serum Leptin, Adiponectin and Ghrelin levels

Banu Mesci[1], Aytekin Oguz[2], Berrin Erok[3], Damla Coksert Kilic[4], Arzu Akalin[5]

ABSTRACT

Objective: Physiology of gastrointestinal system including its hormones is in strong interaction with the brain. During Ramadan, "intention" to fast may act on this physiology. We aimed to find out if there was a difference between the effects of Ramadan fasting and non-Ramadan fasting on serum levels of some gastrointestinal hormones i.e.; leptin, adiponectin and ghrelin.

Methodology: Forty two healthy subjects were included in the study. Blood samples were obtained in the morning in two different days. The first day was during the last week of the Ramadan when they were fasting, and the second day was during the first week after the Ramadan with the same duration of fasting.

Results: The comparison of the leptin, adiponectin and ghrelin levels in this two measurements did not reveal any statistically significant differences (12.25 vs.11.56 ng/ml, 485.19 vs. 286.52 pg/ml, and 15.18 vs. 24.07 ng/ml; p=0.317, p=0.282, p=0.604 respectively)

Conclusion: Although it was not statistically significant, approximately fifty percent higher adiponectin and fifty percent lower ghrelin levels with Ramadan fasting suggests that there could be a different fasting physiology with intended fasting during Ramadan, which needs to be further investigated.

KEY WORDS: Ramadan, Leptin, Adiponectin, Ghrelin.

Pak J Med Sci October - December 2012 Vol. 28 No. 5 909-912

How to cite this article:

Mesci B, Oguz A, Erok B, Kilic DC, Akalin A. Effect of intended fasting on Serum Leptin, Adiponectin and Ghrelin levels. Pak J Med Sci 2012;28(5):909-912

1. Banu Mesci, MD,
Assistant Professor,
2. Aytekin Oguz, MD,
Professor,
3. Berrin Erok, MD,
Medical Faculty,
4. Damla Coksert Kilic, MD,
5. Arzu Akalin, MD,
Assistant Professor, Department of Family Medicine,
1,2,4: Department of Internal Medicine,
Goztepe Training and Research Hospital,
Istanbul Medeniyet University,
Istanbul, Turkey.
3, 5: Istanbul Yeditepe University,
Istanbul, Turkey.

Correspondence:

Dr. Banu Mesci, MD,
Oncu sk, Seher apt,
5/10 Suadiye Kadikoy,
Istanbul, Turkey.
E-mail: banualpaslan@gmail.com

* Received for Publication: May 27, 2012
* Accepted for Publication: July 15, 2012

INTRODUCTION

Food intake is mainly controlled by the gut and the brain.[1,2] Peptides released from the gut convey information about energy needs to the brain. Peptides from the gastrointestinal tract (i.e. ghrelin) and adipose tissue (i.e. leptin and adiponectin) penetrate the blood-brain barrier to mediate effect on feeding centrally.[3] Homeostatic regulation of appetite and food intake is regulated by the hypothalamic region.[4,5] Beside this, it is known that food intake is also under the control of cortical areas related to reward and cognition. The mesolimbic dopamin system, is considered the major reward pathway[6] activated by ghrelin.[7-9] The studies have shown that during fasting leptin levels decrease, ghrelin levels get very high and adiponectin levels go down dramatically.[10-13] This study was designed to test the

hypothesis that there could be a difference in these hormone levels between individuals who in the morning have in mind to eat food and who intent to fast all day.

With the aim to test this theory we decided to study if there is a difference in these hormone levels in fasting serum of individuals during Ramadan and after Ramadan.

METHODOLOGY

The study was conducted on forty two non-smoker healthy volunteers. Adults over 18 years old, who are fasting during Ramadan, and who have no life style and weight changes more than 3% within the last six months were included in the study. The study protocol was designed in accordance with the Declaration of Helsinki, and was approved by the local Ethics Committee of the Istanbul Medeniyet University, Goztepe Training and Research Hospital (Decision No. 6C dated 21.10.2010). Written informed consent was obtained from each subject, who was invited to the clinic in two different days. Blood samples were obtained in the morning during the last week of the Ramadan (Sample 1), and during the first week after the Ramadan (Sample 2) with the same duration of fasting.

The quantitative levels of human leptin, adiponectin and ghrelin were measured using a DSL-23100 ACTIVE Leptin Coated-Tube Immunoradiometric Assay Kit, a Ray Bio Human Adiponectin/Acrp 30 ELISA Kit, and a Ray Bio Human/Mouse/Rat Ghrelin Enyzme Immunoassay Kit respectively.

Statistical Analysis: All statistical analyses were made by using the software SPSS for Windows V16.0. The normality of distribution of variables was assessed by Shapiro-Wilk and Kolmogorov-Smirnov tests. Subjects were compared for differences in two measurements using the paired samples t-test or Wilcoxon test. The correlations between variables were determined by Pearson correlation test or Spearman's Rho. Data were expressed as means ± SD. A p-value below 0.05 (two-tailed) was considered statistically significant.

Table-I: Demographic and Clinical data of the study group.

n=42 (22 M, 20 F)	*Mean±SD (Median)*
Age (years)	33.31±8.70
BMI (kg/m2)	24.67±4.05
Waist circumference (cm)	95.68±8.71 (M)
	85.95± 13.69 (F)

RESULTS

Forty two subjects completed the study (22 M and 20 F). The mean age was 33.31 years. Demographic and clinical characteristics of the subjects are provided in Table-I. Ramadan fasting was associated with higher leptin and adiponectin (12.25 ng/ml and 485.19 pg/ml, respectively) and lower ghrelin (15.18 ng/ml) levels as compared to non-Ramadan fasting (11.56 ng/ml, 286.52 pg/ml, 24.07 ng/ml respectively). But the differences were not statistically significant (p=0.317, p=0.282 and p=0.604, respectively). Other laboratory parameters did not show any difference between the two measurements (Table-II).

DISCUSSION

During Ramadan fasting while Muslims are prohibited eating and drinking from dawn until sunset, intention to fast may affect the feeding physiology. We could not find any statistically significant difference between Ramadan and non-Ramadan fasting serum levels. But we think that approximately 50 percent difference in adiponectin and ghrelin levels between Ramadan fasting and

Table-II: Comparing the biochemical and hormonal data of groups in Ramadan fasting and ordinary fasting.

	Ramadan fasting Mean±SD (Median)	*Ordinary fasting Mean±SD (Median)*	*p*
FPG (mg/dl)	83.59±38.17 (80.00)	84.90±33.35 (79.00)	0.09
Triglyceride (mg/dl)	110.76±83.84 (84.00)	127.44±86.00 (97.00)	0.159
HOMA-IR	1.37 ±1.08 (1.03)	1.25 ±0.72 (1.03)	0.926
TSH (mIU/L)	1.27±0.73 (1.10)	1.78±1.36 (1.34)	0.06
GH (mU/L)	0.60±1.31 (0.14)	1.04±2.10 (0.13)	0.791
Leptin (ng/ml)	12.25 ±12.27 (7.92)	11.56 ±12.27(6.45)	0.317
Adiponectin (ng/ml)	485.19 ±893.12 (140.70)	286.52±401.80 (162.40)	0.282
Ghrelin (pg/ml)	15.18 ±19.82 (7.20)	24.07±33.66 (6.98)	0.604

FPG: Fasting plasma glucose, HOMA-IR: homeostasis model assessment of insulin resistance, TSH: Thyroid-stimulating hormone.

non-Ramadan fasting blood samples of the same individuals is noteworthy.

It is known that people who intent to eat become hungry before they start to eat. In this study we expected that non-Ramadan fasting group as they know that they will have a meal after giving blood sample would feel hungry and also the appetite hormone levels would change accordingly. In intended fasting group because of the inspiration of fasting till sunset we expected the leptin, adiponectin and ghrelin linked to brain induced appetite would act as if the individual was full. We observed this effect in ghrelin and adiponectin although partially.

Ghrelin which is produced by neurons in subparaventricular zone of hypothalamus beside stomach is known as an orexigenic hormon[14] and displays strong growth hormone releasing activity through the binding to and activation of growth hormone secretagogue receptor.[15] In this study also growth hormone levels were found lower similar to ghrelin levels in intended fasting days than non-intended fasting days.

Adiponectin is the other adipocyte derived hormone that regulates the metabolism of lipids and glucose, influences the body's response to insulin. Beside these peripheral metabolic effects, adiponectin receptors are also expressed widely in the brain and recent reports indicate that hypothalamic adiponectin-receptor complex is probably involved in the control of food intake, effected by anorexigenic leptin and insulin, and conversely stimulated by orexigenic ghrelin.[16,17] We also think in this study the relatively higher adiponectin and lower ghrelin levels measured during Ramadan fasting could be related to increased sense of hunger. We expected that anorexigenic leptin[10] would be higher during intended fasting but the results in these two different days were nearly the same.

Recently, neuroimaging methods have been used to learn brain activation in response to food stimuli following manipulation of appetite-related hormones. In ghrelin studies; combining i.v. infusions of ghrelin with functional magnetic resonance imaging, measured brain activation in response to pictures (pictures of palatable food versus non-food), postinfusion increase in response to the food pictures were observed in amygdala, orbitofrontal cortex, insula, striatum and orexigenic effect of ghrelin increased in motivational salience of appetising food images.[18] Jerlhag et al reported that ghrelin administrations into tegmental areas were increasing extracellular concentration of dopamine in the nucleus accumbens.[8]

Similar studies with leptin showed leptin related changes in hunger and satiety areas. Taken together, these studies are consistent with a model in which leptin down-regulates hedonic activation in reward areas in response to food stimulation, and simultaneously up regulates homeostatic control by enhancing the central response to peripheral satiety signals.[19,20]

Ramadan has an impact on a number of major metabolic endocrine processes. Although, the major change in the routine was redistribution of meal timing. In the present study, intention to fast up to sun set in the first day may inhibite orexigenic hormones. On the other hand, expectation for the breakfast on the second day may have caused differences in brain activity.

It can also be considered that the spiritual satisfaction by intended religious fasting can reverse the stress-related effects. Stress keeps the central nervous system engaged through activation of physiological and behavioral responses. Hypothalamus and brain stem are also involved in the stress as well as hippocampus and amygdala in the limbic system.[21] Stress increases catecholamines and reduce plasma adiponectin levels, decreasing the anti-inflammatory, insulin sensitizing, thermogenic and fatty acid oxidation effects mediated by adiponectin.[22] In the present study, the relief resulting from intended fasting during the Ramadan had relative positive effect on the adiponectin and ghrelin levels.

The power of this study could be diminished and this can be considered as a limitation of our study as the participants were not invited to breakfast without knowing that they will be asked to give blood. We also think that the awareness of the participants that they will have to give blood samples might act as an intention decreasing the differences although not as strong as in a religious fasting intention.

CONCLUSION

Although we did not find any statistically significant difference, the difference in adiponectin and ghrelin levels reaching to more than fifty percent suggested that there could be an effect of intended fasting during Ramadan, which needs to be investigated with larger samples.

ACKNOWLEDGMENTS

Authors would like to declare that no competing financial interests exist.

REFERENCES

1. Chaudhri OB, Salem V, Murphy KG, Bloom SR. Gastrointestinal satiety signals. Annu Rev Physiol. 2008;70:239-255.
2. Lenard NR, Berthoud HR. Central and peripheral regulation of food intake and physical activity; pathways and genes. Obesity 2008:16(Suppl 3):11-22.
3. Banks WA. The blood-brain barrier: connecting the gut and the brain. Regul Pept. 2008;149(1-3):11-14.
4. Schwartz GJ. Integrative capacity of the caudal brainstem in the control of food intake. Philos Trans R Soc Lond B Biol Sci. 2006;361(1471):1275-1280.
5. Kampe J, Tschop MH, Hollis JH, Oldfield BJ. An anatomic basis fort he communication of hypothalamic, cortical and mesolimbic circuitry in the regulation of energy balance. Eur J Neurusci. 2009;30(3):415-430.
6. Haber SN, Knutson B. The reward circuit. Linking primate anatomy and human imaging. Neuro Psyco Pharmacology. 2010;35:4-26.
7. Jerlhag E, Egecioglu E, Dickson SL, Andersson M, Svensson L, Engel JA. Ghrelin Stimulates Locomotor Activity and Accumbal Dopamine-Overflow via Central Cholinergic Systems in Mice: Implications for its Involvement in Brain Reward. Addiction Biology. 2006,11(1):45–54.
8. Jerlhag E, Egecioglu E, Dickson SL, Douhan A, Svensson L, Engel JA. Ghrelin administration into tegmental areas stimulates locomotor activity and increases extracellular concentration of dopamine in the nucleus accumbens Addiction Biology. 2007;12(1):6–16.
9. Hewson AK, Tung LY, Connell DW, Tookman L, Dickson SL. The rat arcuate nucleus integrates peripheral signals provided by leptin, insulin, and a ghrelin mimetic. Diabetes. 2002;51(12):3412–3419.
10. Keim NL, Stern JS, Havel PJ. Relation between circulating leptin concentrations and appetite during a prolonged, moderate energy deficit in women. Am J Clin Nutr. 1998;68(4):794–801.
11. Inui A, Asakawa A, Bowers CY, Mantovani G, Laviano A, Meguid MM, et al. Ghrelin, appetite, and gastric motility: the emerging role of the stomach as an endocrine organ .FASEB J. 2004;18(3):439–456.
12. Qi Y, Takahashi N, Hileman SM, Patel HR, Berg AH, Pajvani UB, et al. Adiponectin acts in the brain to decrease body weight. Nat Med. 2004;10:524-529.
13. Neary NM, Small CJ, Bloom SR. Gut and mind. Gut. 2003;52(7):918-921.
14. Satya P, Kalra, Naohiko Ueno, Pushpa S Kalra. Stimulation of appetite by ghrelin is regulated by leptin restraint peripheral and central sites of action. J Nutr. 2005;135(5):1331-1325.
15. Van der Lely AF, Tschop M, Heiman ML, Ghigo E. Biological, physiological, pathophysiological, and pharmacological aspects of ghrelin. Endocrine Reviews. 2004;25(3):426–457.
16. Thundyil J, Pavlovski D, Sobey CG, Arumugam TV. Adiponectin Receptor Signaling in the Brain. Br J Pharmacol. 2012;165(2):313-327.
17. Guillod-Maximin E, Roy AF, Vacher CM, Aubourg A, Bailleux V, Lorsignol A et al. Adiponectin receptors are expressed in hypothalamus and colocalized with proopiomelanocortin and neuropeptide Y in rodent arcuate neurons. J Endocrinol. 2009;200(1):93-105.
18. Malik S, Mc Glone F, Bedrossian D, Dagher A. Ghrelin modulates brain activity in areas that control appetite behavior. Cell Metab. 2008;7(5):400-409.
19. Farooqi IS, Bullmore E, Keogh J, Gillard J, O'Rahilly S, Fletcher PC. Leptin regulates strial regions and human eating behavior. Sci. 2007;317(5843):1355.
20. Baicy K, London ED, Monterosso J, Wong ML, Delibasi T, Sharma A, et al. Leptin replacement alters brain response brain response to food cues in genetically leptin-deficient adults. Proc Natl Acad Sci USA. 2007;104(46):18276-18279.
21. Hjemdahl P. Stress and the metabolic syndrome. Circulation. 2002;106:2634-2636.
22. Delpotre ML, Funahashi T, Takahashi M, Matsuzawa Y, Brichard SM. Pre and post-translational negative effect of beta-adrenoreceptor agonists on adiponectin secretion: in vitro and in vivo studies. Biochem J. 2002;277:6214-6222.

Authors' Contribution:

Banu Mesci: Contribution to design, acquisition of the data, drafting the article, final approval.
Aytekin Oguz: Design, revising the article, final approval.
Berrin Erok: Acquisition of the data, revising the article, final approval.
Damla Coksert Kilic: Analysis and interpretation of data, revising the article, final approval.
Arzu Akalin: Interpretation of data, revising the article, final approval.