The Effect of Long-Term Controlled Fasting (The Ramadan Model) on Body Mass Index, Blood Biochemistry and Oxidative Stress Factors

Uzun Süreli Kontrollü Açlığın (Ramazan Modeli) Beden Kitle İndeksi, Kan Biyokimyası ve Oksidatif Stres Faktörlerine Etkisi

Barlas SÜLÜ, MD,[a]
Barış ÖZTÜRK,[b]
Aysel GÜVEN, MD,[c]
Kemal KILIÇ, MD[a]

Departments of
[a]General Surgery,
[b]Nutrition and Dietetics,
Kafkas University Faculty of Medicine,
[c]Department of Biology,
Kafkas University
Faculty of Arts and Sciences, Kars

Geliş Tarihi/*Received:* 28.11.2008
Kabul Tarihi/*Accepted:* 02.04.2009

This study was presented at 6th International Nutrition and Dietetics Congress, Antalya/TURKEY, 2008.

Yazışma Adresi/*Correspondence:*
Barlas SULU, MD
Kafkas University Faculty of Medicine,
Department of General Surgery, Kars,
TÜRKİYE/TURKEY
barlas.sulu36@gmail.com

ABSTRACT Objective: The month of ramadan is holy in Islam. During this month, muslims, in accordance with religious rules, spend most of the day without eating and drinking anything. We may consider this situation as a perfect model in order to detect the alterations that starvation might cause in human body. In this study, being inspired by this model, we have investigated some biochemical and endocrine alterations that long-term fasting might cause in human body and its effect on oxidative stress factors. **Material and Methods:** Anthropometric measures and blood samples of each healthy volunteers were obtained before and after ramadan. Biochemical parameters, thyroid hormones and oxidative stress factors malondialdehyde, glutathione in blood were analyzed. **Results:** Significant changes in body mass index were not observed. At the end of Ramadan month, significant increase in glucose, HDL and albumin levels were observed in both genders. Although a significant decrease was determined in T. bilirubin, D.bilirubin and fT4 levels in males at the end of ramadan, significant increases were identified in total cholesterol, LDL and urea values of females. Malondialdehyde levels increased in both genders, however the increase was statistically significant only in female subjects ($p< 0.05$). Significant changes were observed in glutathione levels in both genders. In male subjects, glutathione levels decreased while significant increases were observed in female subjects ($p< 0.05$). **Conclusion:** The results have shown that long-term controlled fasting (the ramadan model) may be able to cause alterations in parameters revealing metabolic and endocrine conditions and also cause oxidative stress. Some factors such as socio-economic conditions, nutritional habits, daily activities and gender may induce this situation.

Key Words: Antioxidants; nutritional status; lipids; fasting

ÖZET Amaç: Ramazan ayı islam dininde kutsaldır. Bu ayda, milyonlarca müslüman dini kurallar gereği bir ay boyunca günün çoğunu aç kalarak (oruç tutma) geçirirler. Bu durumu, açlığın insan vücudunda yaratabileceği değişiklikleri saptamak için mükemmel bir model kabul edebiliriz. Biz de bu çalışmada, bu modelden yola çıkarak uzun süreli açlığın insan vücudunda yaratabileceği kimi biyokimyasal ve endokrin değişiklikler ile oksidatif stres faktörlerine etkisini araştırdık. **Gereç ve Yöntemler:** Ramazan öncesi ve sonrasında herbir gönüllünün antropometrik ölçümleri ve kan örnekleri alındı. Kanlarda biyokimyasal parametreler, tiroid hormonları ve oksidatif stres faktör malondialdehit glutatyon değerleri saptanarak istatiksel analizler yapıldı. **Bulgular:** Beden kitle indeksinde anlamlı değişiklikler gözlenmedi. Ramazan ayı sonunda her iki cinste glukoz, HDL-kolesterol ve albumin seviyesinde anlamlı artış tespit edildi ($p< 0.05$). Erkeklerde ramazan ayı sonunda, öncesine göre T. bilirubin, D.Bilirubin, fT4 seviyelerinde anlamlı azalma tesbit edilirken, kadınlarda ise total kolesterol, LDL-kolesterol ve üre değerlerinde anlamlı artışlar görüldü ($p< 0.05$). Her iki cinsde de malondialdehit düzeyinde artış gözlenirken, sadece kadın bireylerdeki bu artış istatiksel olarak önemli bulunmuştur ($p< 0.05$). GSH düzeylerinde, cinsiyetlere göre önemli değişiklikler saptanmıştır. Erkek bireylerde glutatyon düzeyleri azalırken kadın bireylerde önemli artışlar gözlenmiştir ($p< 0.05$). **Sonuç:** Bu sonuçlar göstermektedir ki uzun süreli kontrollü açlık (Ramazan modeli) metabolik, endokrin durumu gösteren parametrelerde değişiklik yapabilmekte ve oksidatif strese neden olabilmektedir. Bu duruma sosyo-ekonomik koşullar, beslenme şekli, günlük aktivite ve cinsiyet gibi faktörlerin etkisi olabilmektedir.

Anahtar Kelimeler: Antioksidanlar; beslenme durumu; lipidler; açlık

Turkiye Klinikleri J Med Sci 2010;30(3):855-63

The custom of fasting has been carried out in different religions. Every year millions of people believing in Islam, Christianity, Judaism and Baha'i have been continuing and practicing this tradition. According to this custom, during ramadan month which is one of the 11 months of Islamic calendar, muslims fast for one month from sunrise (sahur) to sunset (iftar). Everyday, within this month, approximately one billion muslims on earth keep themselves away from any type of food, beverage, sex, drug treatment and daily habits like smoking for 12-19 hours in total.[1]

During ramadan month changes in, eating habits, and frequency and al sleep rhythm may lead to metabolic and behavior changes. This subject has attracted the attention of many researchers and the change of nutrition habits and long-term starvation in ramadan has been considered as an appropriate model,[2] therefore; the changes that have effects on human body have been investigated. Few studies established those changes.[1,3,4] However, these results are conflicting.[1,5] Besides, different impacts like oxidative stress have not been evaluated in detail.

As it is known, oxidative stress occurs through the increase of free radicals and reactive oxygen products. This situation leads to disorders in metabolism and physiology by causing various damages in biological macromolecules.[6,7] Oxygen radicals cause the formation of malondialdehyde (MDA) and membrane peroxidation which are harmful for cell function. Peroxidation increases membrane permeability. This means a vital risk for cell liveliness. Carcinogenic effect of MDA in long-term was reported.[8] In order to minimize free radical damage, there is a complex antioxidant defense system. This system contains the prevention of free radicals to form less reactive compound. Antioxidant system protects the organism from its harmful effects by inhibiting the shaping of free radicals. This system consists of glutathione peroxidase (GSH-Px), glutathione-S transferase (GST), superoxide dysmutase (SOD), catalase (CAT), glutathione reductase (GRx), some rare-earth elements and vitamin A, E and C, which resist against oxidative damage.[9]

In the present study, we have examined some biochemical and hormonal changes in blood, depending on stress and occurring on metabolism due to one-month nutrition frequency in ramadan month, nutritional habits, sudden change on sleep mode and abstention from consuming liquid throughout the day. We have compared the pre-fasting and post-fasting values by establishing the values of malondialdehyde (MDA), an indicator of lipid peroxidation, and reduced glutathione (GSH), an indicator of antioxidant defense system. We have also evaluated the changes occuring within this period in BMI (body mass index).

MATERIAL AND METHODS

STUDY DESIGN

The protocol for the study was administered in accordance with the confirmation by Kafkas University Faculty of Medicine Ethical Commission. This study was carried out in 2007, during ramadan month (September and October) on healthy volunteers who had no acute or chronic diseases and working in Kafkas University Faculty of Medicine and in other units of the University. An informed consent form was obtained from each of the subjects. A total of 45 healthy volunteers, 23 males and 22 females, with an average age of 28.7 years (range: 21 to 51 years) were participated in the study. Average age in males was 30.5 ± 7.1 years and in females 26.9 ± 3.8 years. Females who were pregnant and using oral contraceptives were excluded from the study. Each volunteer was informed about the study in advance. The volunteers participated in the study were asked to maintain their lifestyles, daily physical activities, eating habits as they did in other months, during ramadan month, in the time period between sunrise (sahur) and sunset meals (iftar). Those who partly had a break in fasting or completely stopped fasting and who got ill and started drug treatment were excluded from the study. During that month, a weekly visit to the participants was carried out by a team including a doctor and a nutritionist in order to check the health condition of them and to check the discipline of the study.

LABORATORY ANALYSIS

Venous blood samples to be evaluated in the present study were taken from arm prior to Ramadan and after 8-hours fasting (at 10:00) and control bloods were collected on the 28th day of Ramadan and 8 hours after following the last meal (at 12:00). In blood samples, fasting blood glucose (glucose), triglyceride (TG), total cholesterol (TC), low density lipoprotein cholesterol (LDL), high density lipoprotein cholesterol (HDL), very low density lipoprotein cholesterol (VLDL), urea, creatinine, AST (Aspartate aminotransferase), ALT (Alanine aminotransferase), total Bilirubin (T. Bilirubin), direct bilirubin (D.Bilirubin), albumin (measured by OLYMPUS AU600 IVD autoanalyser via kit method), and fT3 (free Triiodothyronine), fT4 (free Thyroxin), TSH (Thyrotropin-Stimulating Hormone) values were (by VIDAS PC BioMerieux via kit method) analyzed.

About 5 cc blood taken from volunteers in order to examine MDA and GSH was used to prepare plasma and erythrocyte packets via centrifuge. These samples were stored at -20°C until laboratory analyses. Plasma MDA levels were established by the method stated by Placer et al.[10] This method is mainly based on the reaction of Tiobarbituric acid (TBA) with MDA which is one of the aldehyde products of lipid peroxidation. Reduced glutathione was carried out according to the method explained by Sedlak and Lindsay.[11]

During the blood taking process also anthropometric measurements were done by another team. BMI was calculated as weight (kg) divided by the square of the height (m^2).[2]

STATISTICAL ANALYSIS

All observations obtained before and after ramadan were statistically analyzed. Statistical analysis was performed with SPSS 15.0 software (SPSS Inc., Chicago, IL). Results were expressed as means and standard deviations (means ± SD). It was determined that, all blood values were normally distributed by statistical method of Kolmogorov-Smirnov Test. Paired-sample t test was used for data analysis. P-value less than 0.05 was considered statistically significant.

RESULTS

In both genders, after ramadan weight loss and insignificant decrease in BMI were observed when compared with pre-ramadan period ($p > 0.05$). (Table 1).

At the end of ramadan month, significant increase was observed in glucose, HDL and albumin levels of both genders ($p < 0.05$). (Table 2a,b).

At the end of ramadan month, whereas significant decrease ($p < 0.05$) was established at T. bilirubin and D. bilirubin levels in males when compared to the values prior to Ramadan, significant increases were observed in TC, LDL and urea values of females ($p < 0.05$) (Tables 2a and b). The decreases detected in TG, VLDL, AST, ALT, urea and creatinine values and increases in TC, LDL values in males were not statistically significant ($p > 0.05$). On the other hand, in females, the decrease in TG, VLDL, creatinine, T.bilirubin, D.bilirubin values and increase in AST, ALT values were not statistically significant ($p > 0.05$).

TABLE 1: Changes of mean (±SD) BMI during Ramadan Fasting.

BMI (kg/m^2)		Mean before ramadan	Mean after ramadan	Mean difference	Standard error of mean difference	t	p-value
	Male	27.1 ± 3.4	27.0 ± 3.4	0.1 ± 0.6	0.2	0.3	0.759NS
	Female	25.4 ± 6.5	25.2 ± 6.7	0.2 ± 1.0	0.3	0.5	0.646NS
	Total	26.2 ± 5.2	26.1 ± 5.3	0.1 ± 0.8	0.2	0.6	0.563

NS: not significant.

TABLE 2a: Some important biochemical blood parameters before and after Ramadan.

		Mean before Ramadan	Mean after Ramadan	Mean difference	Mean standart error	T	p-value
Glucose (mg/dL)	Male	88.6 ± 6.0	94.4 ± 8.1	-5.8 ± 8.7	1.8	-3.2	0.004*
	Female	82.4 ± 7.2	91.1 ± 5.5	-8.7 ± 6.8	1.5	-6.0	0.000*
	Total	85.6 ± 7.2	92.8 ± 7.1	-7.2 ± 7.9	1.2	-6.2	0.000
Triglyceride (mg/dL)	Male	151.2 ± 64.0	131.3 ± 64.5	19.9 ± 51.4	10.7	1.9	0.077NS
	Female	97.4 ± 44.5	79.0 ± 31.7	18.4 ± 42.2	9.0	2.0	0.054NS
	Total	124.9 ± 61.1	105.8 ± 57.1	19.1 ± 46.6	7.0	2.8	0.009
Total cholesterol (mg/dL)	Male	174.3 ± 37.5	183.0 ± 26.8	-8.7 ± 28.1	5.9	-1.5	0.151NS
	Female	176.0 ± 33.4	188.4 ± 41.5	-12.4 ± 20.0	4.3	-2.9	0.009*
	Total	175.2 ± 35.2	185.6 ± 34.5	-10.4 ± 24.3	3.62	-2.89	0.006
LDL (mg/dL)	Male	108.6 ± 26.7	113.7 ± 22.5	-5.1 ± 22.1	4.6	-1.1	0.282NS
	Female	106.6 ± 29.0	116.7 ± 33.4	-10.1 ± 15.6	3.3	-3.1	0.006*
	Total	107.6 ± 27.6	115.2 ± 28.1	-7.6 ± 19.1	2.9	-2.7	0.011
HDL (mg/dL)	Male	40.1 ± 7.9	42.5 ± 5.8	-2.4 ± 4.9	1.0	-2.3	0.029*
	Female	50.1 ± 11.9	55.9 ± 10.9	-5.8 ± 4.7	1.0	-5.8	0.000*
	Total	45.0 ± 11.2	49.0 ± 10.9	-4.0 ± 5.0	0.8	-5.4	0.000
VLDL (mg/dL)	Male	30.2 ± 12.8	27.1 ± 12.0	3.1 ± 9.8	2.1	1.5	0.147NS
	Female	19.4 ± 8.9	15.8 ± 6.4	3.6 ± 8.4	1.8	2.0	0.057NS
	Total	24.9 ± 12.2	21.6 ± 11.1	3.3 ± 9.0	1.4	2.5	0.017

LDL (low density lipoprotein cholesterol), HDL (high density lipoprotein cholesterol) and VLDL (very low density lipoprotein cholesterol).

*: $p < 0.05$

NS: not significant.

In males, a significant reduction was established in fT4, which is one of the thyroid hormones ($p < 0.05$). Yet, other hormonal changes both in males and females were not significant ($p > 0.05$) (Table 3).

In addition, throughout ramadan period, some changes were monitored in MDA and GSH values. Although there was an increase in MDA values in both genders at the end of Ramadan, only the increase in females was significant ($p < 0.05$). At the end of this term again, significant decrease in GSH values in males but increase in females ($p < 0.001$) was observed (Table 4).

The changes in biochemical measurements and hormone levels were in normal ranges.

DISCUSSION

The month of ramadan is holy in Islam as it is in many religions. Those who are fasting in ramadan month eat only in sunset (iftar) and sunrise (sahur). The number, quality, energy amount of food intake within this period differs according to countries, socio-economic status and habits. The features of food consumed during Ramadan and the differences of energy intake were presented in various studies.[12,13] In a study carried out in Saudi Arabia,[12] it was established that the energy gained by food during ramadan month increased (3680 kcal/day) while a decrease of energy occurred in another study conducted in the same country.[14] However, we did not administer any energy adjustment or calculation for the volunteers participated in this research. Thus, we think that the changes on people induced by long-term controlled fasting (ramadan model), which concerns millions of people as a social fact, will be evaluated more objectively.

THE EFFECT OF LONG-TERM CONTROLLED FASTING ON BMI

We identified a decline in body weight and BMI of males and females participated in our study. How-

TABLE 2b: Some important biochemical blood parameters before and after Ramadan.

		Mean before Ramadan	Mean after Ramadan	Mean difference	Mean standart error	t	p-value
AST (U/L)	Male	30.2 ± 8.5	28.4 ± 6.8	1.9 ± 6.3	1.3	1.4	0.170NS
	Female	25.8 ± 7.3	26.2 ± 12.5	-0.4 ± 13.2	2.8	-0.2	0.873NS
	Total	28.0 ± 8.2	27.3 ± 10.0	0.7 ± 10.2	1.5	0.5	0.632
ALT (U/L)	Male	32.1 ± 11.2	30.4 ± 9.8	1.7 ± 8.8	1.8	0.9	0.365NS
	Female	24.3 ± 15.1	27.5 ± 29.3	-3.2 ± 26.2	5.6	-0.6	0.580NS
	Total	28.3 ± 13.7	29.0 ± 2.4	-0.7 ± 19.3	2.9	-0.2	0.818
Albumin (g/dL)	Male	4.4 ± 0.2	4.6 ± 0.2	-0.2 ± 0.2	0.1	-3.1	0.005*
	Female	4.2 ± 0.3	4.4 ± 0.2	-0.2 ± 0.3	0.1	-3.4	0.003*
	Total	4.3 ± 0.3	4.5 ± 0.2	-0.2 ± 0.3	0.1	-4.7	0.000
Urea (mg/dL)	Male	33.0 ± 6.5	31.4 ± 8.2	1.6 ± 6.5	1.4	1.1	0.271NS
	Female	22.0 ± 6.7	24.5 ± 5.9	-2.5 ± 5.2	1.1	-2.3	0.030*
	Total	27.6 ± 8.6	28.1 ± 7.9	-0.5 ± 6.2	0.9	-0.5	0.598
Creatinin (mg/dL)	Male	1.7 ± 2.7	1.0 ± 0.1	0.7 ± 2.7	0.6	1.2	0.232NS
	Female	0.8 ± 0.2	0.7 ± 0.1	0.1 ± 0.2	0.0	1.6	0.135NS
	Total	1.2 ± 2.0	0.9 ± 0.1	0.3 ± 1.9	0.3	1.3	0.188
Total Bilurubin (mg/dL)	Male	1.0 ± 0.6	0.7 ± 0.2	0.3 ± 0.5	0.1	3.6	0.002*
	Female	0.7 ± 0.5	0.6 ± 0.6	0.1 ± 0.6	0.1	0.8	0.415NS
	Total	0.9 ± 0.5	0.6 ± 0.5	0.3 ± 0.6	0.1	2.8	0.008
Direct Bilurubin (mg/dL)	Male	0.2 ± 0.1	0.1 ± 0.1	0.1 ± 0.0	0.1	2.9	0.008*
	Female	0.1 ± 0.1	0.1 ± 0.0	0.0 ± 0.1	0.0	1.6	0.135NS
	Total	0.1 ± 0.1	0.1 ± 0.0	0.0 ± 0.0	0.00	3.1	0.004

AST (Aspartate aminotransferase), ALT (Alanine aminotransferase).

*: $p < 0.05$.

NS: not significant.

ever it was not significant ($p > 0.05$). There was no change in weight or BMI in the study conducted by Beltaifa et al.[15] On the other hand, significant decreases were established in a number of studies.[4,14,16] In another study, as a result of CT evaluation of body fat distribution before and after fasting, significant decrease in visceral fat distribution was established only in females after fasting. Besides, no change was determined in subcutaneous or visceral tissue in males and in both genders there was no significant change in BMI.[17] The result of this study was consistent with that of our study.

THE EFFECT OF LONG-TERM CONTROLLED FASTING ON BLOOD BIOCHEMISTRY

In our study, in lipid profiles at the end of ramadan period, HDL increased in males and TC, HDL and LDL increased in females significantly ($p < 0.05$). However, VLDL did not change ($p > 0.05$). There are some studies supporting our results.[4,16,18] Mittendorfer et al. stated in their research that 10% weight loss leads to 40% decrease in VLDL causing the decrease of systematic (generally obtained from TG lipolysis in subcutaneous tissue) and non-systematic fatty acids (generally obtained from intraperitoneal and intrahepatic TG lipolysis).[19] In the same study, it was also expressed that gender difference accompanied by weight loss might be effective on alteration in VLDL. However, in our study, weight loss in both genders and the alterations in VLDL were not significant. Yet, there was a significant rise in other lipoproteins and cholesterol. Maislos et al. noted that in a condition of declining main course meal numbers within the day (gorging diet, 1-3 meal/day), postprandial lipemia duration and magnitude was longer in comparison with

TABLE 3: Changes of thyroid hormone profiles during Ramadan.

		Mean before Ramadan	Mean after Ramadan	Mean difference	Mean standart error	t	p-value
fT3 (µIU/mL)	Male	4.9 ± 1.3	4.7 ± 0.3	0.2 ± 1.2	0.2	1.1	0.285NS
	Female	4.7 ± 1.1	4.2 ± 0.4	0.5 ± 1.2	0.3	1.9	0.078NS
	Total	4.8 ± 1.2	4.5 ± 0.4	0.3 ± 1.2	0.2	2.1	0.042
fT4 (µIU/mL)	Male	13.6 ± 1.9	12.5 ± 1.4	1.1 ± 2.1	0.4	2.5	0.021*
	Female	12.8 ± 2.5	13.2 ± 2.2	-0.4 ± 3.1	0.7	-0.5	0.636NS
	Total	13.2 ± 2.2	12.8 ± 1.9	0.4 ± 2.7	0.4	1.0	0.335
TSH (µIU/mL)	Male	1.7 ± 1.3	1.4 ± 0.7	0.3 ± 1.0	0.2	1.8	0.080NS
	Female	2.2 ± 1.2	1.8 ± 1.1	0.4 ± 1.0	0.2	1.9	0.071NS
	Total	1.9 ± 1.3	1.6 ± 0.9	0.3 ± 1.0	0.1	2.7	0.011

fT3 (free Triiodothyronine), fT4 (free Thyroxin) and TSH (Thyrotropin-Stimulating Hormone).

*: p< 0.05.

NS: not significant.

TABLE 4: Changes of lipid peroxidation marker MDA and antioxidant marker GSH during Ramadan.

		Mean before Ramadan	Mean after Ramadan	Mean difference	Mean standart error	t	p-value
MDA (nmol/mL)	Male	7.0 ± 3.2	8.9 ± 6.8	-1.9 ± 7.9	1.7	-1.2	0.26 NS
	Female	5.8 ± 2.2	9.3 ± 3.2	-3.5 ± 4.7	1.0	-3.4	0.03*
	Total	6.4 ± 2.8	9.1 ± 5.5	-2.7 ± 6.6	1.0	-2.6	0.01
GSH (µmol/mL)							
	Male	1.1 ± 0.7	0.9 ± 0.6	0.2 ± 0.1	0.0	8.4	0.00*
	Female	0.8 ± 0.1	1.0 ± 0.6	-0.2 ± 0.1	0.0	-6.5	0.00*
	Total	1.0 ± 0.2	1.0 ± 0.9	0.0 ± 0.2	0.0	0.3	0.79

MDA (malondialdehyde), GSH (reduced glutathione).

*: p< 0.05

NS: not significant.

non-gorging nutrition (nibbling diet, 7-17 meal/day).[18] In this case, duration without absorption was going to be longer and lipid levels in blood were going to be high for a longer period (LDL and especially HDL). In another study, it was emphasized that the changes in plasma lipid values depend on dietary habits, amount of fat received via daily diet, exercise and stress.[16] Considering our results, we also think that those factors have same kind of effects. Furthermore, a study carried out in Turkey displayed that, during this period, daily activities of females were less demanding than those of males.[20] It makes us think that this situation is an important cause of higher lipid and cholesterol values in females.

In the studies, the effects of ramadan fasting on glucose levels have revealed disagreements. Beside the studies that argue for the decrease of fasting blood glucose,[14,16,21] there are also studies arguing against that change.[15,22] Our study revealed a significant increase in both genders (p< 0.05). The reason for this is not exactly clear. Nevertheless, the approach[23] stating that glucose absorption go on at maximum rate and long time in gorging diet, which leads to the induction of insulin secretion due to the rise of glucose level in tissues, explains the glucose rise displayed in our study.

In our study, the effect of controlled fasting on liver functions was evaluated as well. At the end of

ramadan fasting, while AST and ALT decreased in males, they increased in females. Yet, those results were not significant ($p > 0.05$). Albumin rise in both genders and bilirubin level decrease in males were significant ($p < 0.05$) but those values were at normal limits. We think that albumin rise is related to nutritional habit since, protein-rich diet takes an important place in eating habits of our region. Significant increase in urea detected in females stems from liquid restriction due to the nature of fasting. This change was also at normal limits and was changeable according to liquid intake of individuals, which agrees with the literature.[1]

THE EFFECT OF LONG-TERM CONTROLLED FASTING ON THYROID HORMONES

In our study, fT4 decrease in thyroid functions of males was significant ($p < 0.05$). In contrast to the studies detecting no significant change in thyroid values,[24] in another study, it was stated that gradual and significant increase was observed in TSH during fasting.[25] Due to the changes in TBG (Thyroxine-Binding Globulin), a decrease in total T3 and T4 in females was reported although fT3 and fT4 remained stable.[1] The relation between thyroid hormone level and nutrition was strongly marked through the presence of leptin.[26,27] It is known that leptin, which is synthesized and secreted from adipose tissue, plays role in a number of physiological events by influencing the hypothalamus and takes part in energy hemostasis and saturation regulation and its amount in circulation is proportional to body fat mass.[28,29] In a study it was noted that there was 20-30% reduction in leptin level during acute caloric abstinence of 2-3 days.[30] In another study, it was stated that the decrease in adiposis tissue affected hypothalamus-pituitary-thyroid axis in order to decrease energy consumotion and pressurized TRH and thyroid functions (especially T4).[31] The result of our study was consistent with the results of those studies. The decrease in BMI affected thyroid functions (especially T4) even if it was not significant.

THE EFFECT OF LONG-TERM CONTROLLED FASTING ON OXIDATIVE STRESS

As it is known, survival of aerobic tissues is provided by a sensitive balance between antioxidant defense mechanisms and cellular systems producing oxidant.[32,33] Oxygen molecule has a high affinity against lipids. Binding of oxygen to double bonds of unsaturated fat acids causes a chemical reaction called lipid peroxidation. Increased lipid peroxidation is an indirect indicator of free radical activation.[34,35]

There are few studies displaying the relation between lipid peroxidation and antioxidants in long-term controlled fasting. Only one study so far reported significantly decreased MDA level at the end of ramadan.[36] On the contrary, in our study an increase was seen. The reason of this difference might stem from the socio-economic condition of the countries, nutrition styles, immune system and metabolic structure of the people. However, our result (increased tendency in lipid peroxidation) shows that oxidative stress may develop depending on the impact of fasting at the end of ramadan period.

In present study, a significant increase of GSH in females, and a significant decrease of GSH in males were observed ($p < 0.05$). Decreased GSH in males is a natural result of oxidative stress developed depending on long-term controlled fasting, because we expect a decrease in antioxidants which are defense systems for broken balance. On the contrary, the reason of the rise in GSH of females is not clear. In our opinion, this difference observed in a working population with similar socio-cultural environment and traditions, stems from different metabolic reactions against stress in different genders. The reason might be hormonal. The major estrogen in reproduction period of females is estradiol (E2). In the studies carried out, it was stated that in ovariectomized patients E2 treatment reduced the increasing oxidative stress and functioned as an antioxidant thanks to this feature.[37,38] Phenolic structure of estrogen was pointed out as a reason of this effect.[39] Yet, on the contrary, in an experimental study administered by Aydilek et al. it was expressed that the testosterone, which is a dominant hormone in males, increased oxidative stress and decreased GSH.[40] Those studies have supported our findings. We might assert that the females, who are in reproduction period and

included in our study group are more advantageous, in comparison to the males, against stress depending on long-term fasting and due to the hormonal effect.

In this study, there were some limitations. The most important one was that we did not have data on the nutritional habits during the ramadan fasting. Additionally, the levels of the sex hormones in both gender could be valuable data that we would use in the discussion. The other point which limited us was the lack of evaluating the blood leptin levels and changes in the proportion and distribution of the adipose tissue in the body. In this way, we could discuss the relationship between adipose tissue-leptin thyroid hormone levels in detail.

CONCLUSION

The effect of ramadan fasting on the body was evaluated in some studies although they were not sufficient. Besides, those studies could not go further than being an experimental study or researches of a few days after fasting period in human. Considering ramadan fasting as a model, even if it is partial, we have investigated some effects of fasting on humans. We have established that it causes different effects in males and females at the end of the present study. We think that in addition to the socio-economic condition, nutritional habits, and daily activities, gender diversity might also be a determining factor in the formation of this effect. Further studies are needed to enlighten details on this matter.

REFERENCES

1. Azizi F. Research in Islamic fasting and health. Ann Saudi Med 2002;22(3-4):186-91.
2. Maislos M, Khamaysi N, Assali A, Abou-Rabiah Y, Zvili I, Shany S. Marked increase in plasma high-density-lipoprotein cholesterol after prolonged fasting during Ramadan. Am J Clin Nutr 1993;57(5):640-2.
3. Chamsi-Pasha H, Ahmed WH. The effect of fasting in Ramadan on patients with heart disease. Saudi Med J 2004;25(1):47-51.
4. Fedail SS, Murphy D, Salih SY, Bolton CH, Harvey RF. Changes in certain blood constituents during Ramadan. Am J Clin Nutr 1982;36(2):350-3.
5. Kapıcıoglu S, Danaoglu A, Çetiner M, Koptagelli İ. [The relationship between Ramadan And upper gastrointestinal system bleeding] Turkiye Klinikleri J Gastroenterohepatol 1996;7(1):1-5.
6. Hasselbaink DM, Glatz JF, Luiken JJ, Roemen TH, Van der Vusse GJ. Ketone bodies disturb fatty acid handling in isolated cardiomyocytes derived from control and diabetic rats. Biochem J 2003;371(Pt 3):753-60.
7. Abou-Seif MA, Youssef AA. Evaluation of some biochemical changes in diabetic patients. Clin Chim Acta 2004;346(2):161-70.
8. Yeh CC, Hou MF, Tsai SM, Lin SK, Hsiao JK, Huang JC, et al. Superoxide anion radical, lipid peroxides and antioxidant status in the blood of patients with breast cancer. Clin Chim Acta 2005;361(1-2):104-11.
9. Brambilla D, Mancuso C, Scuderi MR, Bosco P, Cantarella G, Lempereur L, et al. The role of antioxidant supplement in immune system, neoplastic, and neurodegenerative disorders: a point of view for an assessment of the risk/benefit profile. Nutr J 2008;7:29.
10. Placer ZA, Cushman LL, Johnson BC. Estimation of product of lipid peroxidation (malonyl dialdehyde) in biochemical systems. Anal Biochem 1966;16(2):359-64.
11. Sedlak J, Lindsay RH. Estimation of total, protein-bound, and nonprotein sulfhydryl groups in tissue with Ellman's reagent. Anal Biochem 1968;25(1):192-205.
12. Frost G, Pirani S. Meal frequency and nutritional intake during Ramadan: a pilot study. Hum Nutr Appl Nutr 1987;41(1):47-50.
13. Roky R, Chapotot F, Hakkou F, Benchekroun MT, Buguet A. Sleep during Ramadan intermittent fasting. J Sleep Res 2001;10(4):319-27.
14. Khalid Al-Numair. Body weight and some biochemical changes associated with Ramadan fasting in healthy Saudi men. J Med Sci 2006;6(1):112-6.
15. Beltaifa L, Bouguerra R, Ben Slama C, Jabrane H, El-Khadhi A, Ben Rayana MC, et al. [Food intake, and anthropometrical and biological parameters in adult Tunisians during fasting at Ramadan]. [Article in French] East Mediterr Health J 2002;8(4-5):603-11.
16. Ziaee V, Razaei M, Ahmadinejad Z, Shaikh H, Yousefi R, Yarmohammadi L, et al. The changes of metabolic profile and weight during Ramadan fasting. Singapore Med J 2006;47(5):409-14.
17. Yucel A, Degirmenci B, Acar M, Albayrak R, Haktanir A. The effect of fasting month of Ramadan on the abdominal fat distribution: assessment by computed tomography. Tohoku J Exp Med 2004;204(3):179-87.
18. Maislos M, Abou-Rabiah Y, Zuili I, Iordash S, Shany S. Gorging and plasma HDL-cholesterol--the Ramadan model. Eur J Clin Nutr 1998;52(2):127-30.
19. Mittendorfer B, Patterson BW, Klein S. Effect of weight loss on VLDL-triglyceride and apoB-100 kinetics in women with abdominal obesity. Am J Physiol Endocrinol Metab 2003;284(3):E549-56.
20. Karaağaoğlu N, Yücecan S. Some behavioural changes observed among fasting subjects, their nutritional habits and energy expenditure in Ramadan. Int J Food Sci Nutr 2000;51(2):125-34.
21. Larijani B, Zahedi F, Sanjari M, Amini MR, Jalili RB, Adibi H, et al. The effect of Ramadan fasting on fasting serum glucose in healthy adults. Med J Malaysia 2003;58(5):678-80.
22. Dowod TAHM. Effects of Ramadan fasting on blood lipids and sugar. Pak J Med Sci 2004;20(4):308-10.
23. Rashidi MR, Mahboob S, Sattarivand R. Effects of nibbling and gorging on lipid profiles, blood glucose and insulin levels in healthy subjects. Saudi Med J 2003;24(9):945-8.
24. Sulimani RA. The effects of Ramadan fasting on thyroid functions in healthy male subjects. Nutr Res 1988;8(5):549-52.

25. Sajid KM, Akhtar M, Malik GQ. Ramadan fasting and thyroid hormone profile. J Pak Med Assoc 1991;41(9):213-6.

26. Fontana L, Klein S, Holloszy JO, Premachandra BN. Effect of long-term calorie restriction with adequate protein and micronutrients on thyroid hormones. . J Clin Endocrinol Metab 2006;91(8):3232-5.

27. Kaptein EM, Fisler JS, Duda MJ, Nicoloff JT, Drenick EJ. Relationship between the changes in serum thyroid hormone levels and protein status during prolonged protein supplemented caloric deprivation. Clin Endocrinol (Oxf) 1985;22(1):1-15.

28. Gale SM, Castracane VD, Mantzoros CS. Energy homeostasis, obesity and eating disorders: recent advances in endocrinology. J Nutr 2004;134(2):295-8.

29. Al-Harithy RN. Relationship of leptin concentration to gender, body mass index and age in Saudi adults. Saudi Med J 2004;25(8):1086-90.

30. Chan JL, Mantzoros CS. Role of leptin in energy-deprivation states: normal human physiology and clinical implications for hypothalamic amenorrhoea and anorexia nervosa. Lancet 2005;366(9479):74-85.

31. Ahima RS, Osei SY. Molecular regulation of eating behavior: new insights and prospects for therapeutic strategies. Trends Mol Med 2001;7(5):205-13.

32. Bast A, Haenen GR, Doelman CJ. Oxidants and antioxidants: state of the art. Am J Med 1991;91(3C):2S-13S.

33. Enkvetchakul B, Bottje W, Anthony N, Moore R, Huff W. Compromised antioxidant status associated with ascites in broilers. Poult Sci 1993;72(12):2272-80.

34. Freeman BA, Crapo JD. Biology of disease: free radicals and tissue injury. Lab Invest 1982;47(5):412-26.

35. Güven A, Güven A, Gülmez M. The effect of kefir on the activities of GSH-Px, GST, CAT, GSH and LPO levels in carbon tetrachloride-induced mice tissues. . J Vet Med B Infect Dis Vet Public Health 2003;50(8):412-6.

36. Asgary S, Aghaeı A, Naderı GA, Kelıshadı R, Gharıpour M, Azalı S. Effects of Ramadan Fasting on Lipid Peroxidation, Serum Lipoproteins and Fasting Blood Sugar. Medical Journal of Islamic Academy of Sciences 2000;13(1):35-8.

37. Oztekin E, Tiftik AM, Baltaci AK, Mogulkoc R. Lipid peroxidation in liver tissue of ovariectomized and pinealectomized rats: effect of estradiol and progesterone supplementation. Cell Biochem Funct 2007;25(4):401-5.

38. Muñoz-Castañeda JR, Montilla P, Muñoz MC, Bujalance I, Muntané J, Túnez I. Effect of 17-beta-estradiol administration during adriamycin-induced cardiomyopathy in ovariectomized rat. Eur J Pharmacol 2005;523(1-3):86-92.

39. Moosmann B, Behl C. The antioxidant neuroprotective effects of estrogens and phenolic compounds are independent from their estrogenic properties. Proc Natl Acad Sci USA 1999;96(16):8867-72.

40. Aydilek N, Aksakal M, Karakilçik AZ. Effects of testosterone and vitamin E on the antioxidant system in rabbit testis. Andrologia 2004;36(5):277-81.