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Effect of Fasting with Two Meals on BMI and Inflammatory Markers of Metabolic Syndrome

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Abstract: The metabolic syndrome has been recognized as a proinflammatory state and inflammatory markers are associated with an increased risk for subsequent cardiovascular disease and type 2 diabetes. The aim of this clinical trial study was to evaluate the effect of Ramadan fasting on High-sensitive C-reactive Protein (hs-CRP) and fibrinogen levels in metabolic syndrome. Sixty five male with metabolic syndrome who were admitted to Hospital were selected for the study. Waist circumference, BMI, FPG, HDL-C, TG, fibrinogen and hs-CRP were evaluated before and after month of Ramadan. The duration of study was thirty days. The dietary intake was estimated by 24 h recall before and after fasting. Metabolic syndrome was diagnosed using the ATP III criteria. FPG, HDL-C, fibrinogen, hs-CRP, BMI and waist circumference were decreased significantly after study ($p = 0.005$, $p = 0.002$, $p = 0.02$, $p = 0.01$, $p = 0.01$, $p = 0.01$, respectively). There was no change in serum TG level ($p = 0.21$). Simple linear regression analysis demonstrated that after fasting, hs-CRP was related to waist circumference and BMI ($r = 0.388$, $p = 0.01$ and $r = -0.439$, $p = 0.02$, respectively). Change in the number and timing of meals and portioning the entire intake into two without changing the total energy consumption may have beneficial effects on anthropometry measures and inflammatory markers of metabolic syndrome.

Key words: High sensitive C-reaction protein, fibrinogen, Ramadan fasting, metabolic syndrome

INTRODUCTION

The metabolic syndrome has been recognized as a proinflammatory state, associated with elevated levels of High sensitive C-reactive Protein (hs-CRP) and Interleukin-6 (IL-6) (Ridker *et al.*, 2003; Festa *et al.*, 2002; Ridker *et al.*, 2004; Rutter *et al.*, 2004). Inflammatory markers are associated with an increased risk for subsequent cardiovascular disease and type 2 diabetes (Festa *et al.*, 2002; Pradhan *et al.*, 2001; Hu *et al.*, 2004). CRP is an acute phase protein that is produced predominantly by hepatocytes under the influence of cytokines such IL-6 and tumor necrosis factor- α . Fibrinogen is an acute phase reactant, with levels increasing as part of the acute inflammatory response (Woloshin and Schwartz, 2005).

Several dietary approaches have been advocated for treatment of the metabolic syndrome. These diets decrease levels of markers of inflammation and improve endothelial function (Esposito *et al.*, 2004).

It has been shown that many different diets such as Mediterranean diet, the Dietary Approach to Stop Hypertension (DASH) diet, Foods with low glycemic index and low saturated fat diet, independent of weight loss, by reducing insulin resistance may be effective in improving the metabolic syndrome (Minehira and Tappy, 2002). These diets are also effective in lowering hs-CRP (Koh *et al.*, 2005). During the month of Ramadan (The ninth month of the Islamic calendar), Muslims fast every day from dawn to sunset. They refrain from drinking and eating for about 12 h intervals. As there was no study to determine the effect of two meals per day pattern of feeding on metabolic syndrome, the effect of Ramadan fasting on hs-CRP and fibrinogen levels were evaluated in these subjects.

MATERIALS AND METHODS

The present study was a clinical trial which was carried out in a university hospital. Sixty five male

volunteers, aged between 29 and 55 (40.14±10.8) with metabolic syndrome were included in this study. A participant was defined to have the metabolic syndrome if three or more of the following criteria were met, according to the National Cholesterol Education Program recommendations (NCEP/ATPIII, 2001), (1) abdominal obesity, i.e., waist circumference = 90 cm (the Caucasian criterion for abdominal obesity (Inoue *et al.*, 2000), (2) hypertriglyceridaemia: = 150 mg dL⁻¹ (1.70 mmol L⁻¹), (3) low HDL cholesterol (HDL-C), i.e., <40 mg dL⁻¹ (1.04 mmol L⁻¹), (4) high blood pressure: = 130/85 mmHg; (5) high Fasting Plasma Glucose (FPG): = 110 mg dL⁻¹ (6.1 mmol L⁻¹). Exclusion factors were females, any addiction or drug therapy and conditions which cause changes in hs-CRP and fibrinogen levels including Subjects with a current or prior history of infection, infarction, inflammatory arthritis and various neoplasm. The males were selected for the study because females exempt from fasting during their menstrual period. The study protocol was approved by responsible ethic committee and informed consent was obtained from all participants. All subjects were encouraged to continue their usual lifestyle and activities before and during Ramadan. The duration of fasting was approximately 17 h from sunrise to sunset (the time of abstinence from food) during a 30 day period in the Northern hemisphere summer season. The subjects had two meals per day; one early in the morning about 30 min before sunrise and the second immediately after sunset.

After a 12 h overnight fast, a fasting blood sample was taken for determination of Triglyceride (TG), HDL-C, FPG, fibrinogen and hs-CRP a day before Ramadan and a day after Ramadan. Fibrinogen levels were measured by turbidimetry (Ral coagulometer, Spain) and hs-CRP levels were measured using a CRP ELISA Kit (Immunodiagno, Bensheim, Germany). At the same time Body Mass Index (BMI) and waist circumference were measured. Weight was measured while the subjects were minimally clothed without shoes using digital scales and recorded to the nearest 0.1 kg. Height was measured in a standing position without shoes using a tape meter while the shoulders were in a normal state. Waist circumference was measured above the iliac crest, using an outstretched tape meter, without any pressure to body surface and measurements were recorded to the nearest 0.1 cm. The dietary intake was calculated through 24 h recall before intervention for three non-holiday, nonconsecutive, non-fasting days and repeated for days of 10, 20 and 30th of the fasting period in two groups.

Statistical methods: Results are reported as Means±SD. Paired t test was used for comparisons of variables before

and after intervention. Demographic data and baseline values and outcome measures between two groups were compared with student's t test. Simple linear regression analysis was performed for analysis of association among inflammatory markers as dependent variables with BMI and waist circumference as independent variables. A value of p≤0.05 was considered statistically significant.

RESULTS

A total of 65 male volunteers were included in the study. The mean age of subjects was 40.14 years (range: 29-55, SD: 10.8). Clinical characteristics and laboratory data of subjects in two groups are shown in Table 1.

Analysis of nutritional intake variable indicated that there was no significant difference in total calorie intake before and after fasting. Percent of BMI and waist circumference reduction after trial were 3.3 and 2.7%, respectively and their decline was statistically significant. Values of FPG and HDL-C were decreased significantly after the study period (p = 0.005, p = 0.002) but there was no change in serum TG levels (p = 0.21).

Values of hs-CRP and fibrinogen were significantly decreased after trial (p = 0.01, p = 0.02).

At baseline, mean CRP levels for those with 3, 4, or 5 characteristics of the metabolic syndrome in subjects were 0.63, 0.78 and 0.89 mg L⁻¹, respectively (p<0.001). After trial these values were 0.60, 0.72 and 0.84 mg L⁻¹, respectively (p<0.001). These values for fibrinogen at baseline were 235, 250.2 and 270.1 mg dL⁻¹ (p<0.05) and after fasting were 219.2, 232.2 and 267 mg dL⁻¹, respectively (p<0.05).

Correlation coefficients of hs-CRP with BMI and waist circumference before and after fasting period are shown in Table 2. Simple linear regression analysis showed that there was a linear decrease in hs-CRP levels with a decrease in BMI and waist circumference after fasting (hs-CRP = 5.57×waist+0.19, p = 0.02 and hs-CRP = 1.44 × BMI + 0.31, p = 0.01, respectively).

Table 1: Clinical and laboratory characteristics of the subjects before and after fasting

| Characteristics | Mean±SD of fasting | | p-value |
|-------------------------------------|--------------------|--------------|---------|
| | Before | After | |
| Total energy (kJ) | 12700±767.7 | 12625±659.8 | 0.4 |
| BMI (kg m ⁻²) | 28.62±4.79 | 27.87±3.34 | 0.01 |
| Waist (cm) | 96.41±8.22 | 93.8±6.40 | 0.01 |
| HDL-C (mg dL ⁻¹) | 41.53±5.45 | 46.66±5.50 | 0.002 |
| Triglyceride (mg dL ⁻¹) | 229±85.60 | 232.78±88.87 | 0.216 |
| FBS (mg dL ⁻¹) | 101.45±28.79 | 81.21±17.84 | 0.005 |
| hs-CRP (mg L ⁻¹) | 0.766±0.11 | 0.72±0.11 | 0.01 |
| Fibrinogen (mg dL ⁻¹) | 251.7±39.89 | 239.4±30.06 | 0.02 |

Table 2: Correlation coefficients of hs-CRP with BMI and waist circumference in fasting

| Group | Before fasting period | | After fasting period | |
|---------|-----------------------|-------|----------------------|-------|
| | BMI | Waist | BMI | Waist |
| hs-CRP | 0.554 | 0.564 | 0.439 | 0.388 |
| p-value | 0.001 | 0.001 | 0.020 | 0.010 |

DISCUSSION

The present study demonstrate that Ramadan fasting led to some beneficial changes in anthropometric measures and inflammatory markers of subjects with metabolic syndrome. Both hs-CRP and fibrinogen decreased significantly after trial and a linear decrease in hs-CRP levels with a decrease in BMI and waist circumference was seen. Also our results show a linear increase in CRP levels with an increase in the number of metabolic disorders. CRP is a sensitive marker for systemic inflammation and is produced by the liver. In an Insulin Resistance Atherosclerosis Study (IRAS), there was a linear increase in CRP levels with an increase in the number of metabolic disorder (Festa *et al.*, 2000). In a study of 40 healthy volunteers of normal weight, prolonged intermittent fasting in a model like Ramadan has some positive effects on the inflammatory markers of CRP and IL-6 (Aksungara *et al.*, 2007). It is supposed that subclinical inflammation and moreover elevated concentrations of CRP, produced by adipose tissue and other tissues, are shown to be associated with insulin resistance and metabolic syndrome (Festa *et al.*, 2000; Ridker *et al.*, 2004) and It has been reported that Ramadan fasting increases insulin sensitivity in subjects with metabolic syndrome (Shariatpanahi *et al.*, 2008). In our study FPG and serum HDL-C were decreased significantly after fasting period, the result that is reported in some studies (Salehi and Neghab, 2007). As there was no significant decrease in energy consumption in our study group regardless of significant decrease in BMI and waist circumference, we suppose that they may be due to pattern of eating in Ramadan. Fasting during the month of Ramadan is a unique metabolic model that includes abstinence from food and fluid intake during the period from dawn to sunset. Change in the number and timing of meals and portioning the entire intake into two (instead of the usual three or five) could have beneficial effects on patients with metabolic syndrome. It has been established that a given nutrient ingested at an unusual time can induce different metabolic effects (Nelson *et al.*, 1973). During Ramadan fasting the sleep-wakefulness cycle is also altered. Long-lasting modifications in the circadian rhythm of the body may result in various changes in metabolism and Ramadan fasting is known to have an impact on metabolic endocrine processes (Kassab *et al.*, 2004; Bogdan *et al.*, 2001).

CONCLUSION

In conclusion, this study has demonstrated that change in the number and timing of meals and portioning of the entire daily intake into two meals without changing the total energy consumption may decrease inflammatory markers in metabolic syndrome. Therefore, Ramadan fasting provides an excellent opportunity to study the effects of the prolonged reduction of meal frequency on body metabolism.

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ABBREVIATIONS

hs-CRP : High-sensitive C-reactive protein
HDL-C : High density lipoprotein cholesterol
IL-6: Interleukin-6
DASH : Dietary approach to stop hypertension
NCEP : National cholesterol education program recommendations
FPG : Fasting plasma glucose
TG : Triglyceride
BMI : Body mass index
IRAS : Insulin resistance atherosclerosis study

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