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Augmented Plasma Adiponectin after Prolonged Fasting During Ramadan in Men

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ABSTRACT

Background: Intermittent fasting during Ramadan entails major changes in metabolism and energy expenditure. This study sought to determine effect of the Ramadan fasting on serum levels of adiponectin and tumor necrosis factor-α (TNF-α) as two inter-related peptides involved in cells sensitivity to insulin and glucose metabolism.
Methods: Total of seventy healthy men, with age range equal or greater than 30, with at least three type2 diabetes mellitus (DM) risk factors were selected. Serum lipid profile, anthropometric indices and plasma glucose levels were determined using conventional methods. Also, serum adiponectin and TNF- α concentrations were assessed using Enzyme-linked Immunosorbent Assay. Data were analyzed by paired t-test.
Results: Ramadan fasting resulted in a significant increase of serum adiponectin ($P< 0.000$), fasting glucose ($P< 0.000$) and triglycride ($P< 0.001$). Body mass index was lowered during the fasting ($P< 0.000$). Finally, no remarkable decrease was found in serum TNF-α levels ($P= 0.100$).
Conclusion: Ramadan fasting resulted in augmented adiponectin levels which may help in improving metabolic stress induced by insulin resistance in men with predisposing factors of type2 DM.

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Introduction

Intentional abstention from foods is a frequent practice among followers of many religions including Muslims. These behavioral changes provide a great forum for researchers who interested in life style modification strategies to look for its effects on individuals' health status. The month of Ramadan, as a specific model of intermittent fasting, is associated with very profound alteration in life style of the observers including dietary patterns and physical activity. The fasting is known to affect many aspects of metabolism such as body composition and glucose and lipid profile.

Adipokines play as key coordinators in many aspects of body metabolisms including energy expenditure pathways. Adipocytes are the most frequent source of production for these active polypeptides.[1] Adiponectin, a 30-KD protein, is one of the most abundant

adipokines that is involved in modulation of both glucose and fatty acid metabolism. It has a specific conformational structure consisting four domains; an N-terminal signal sequence, a specific variable region, a collagen-like domain and a carboxy-terminal globular domain. Interestingly, the latest domain, has partial structure similar to tumor-necrosis factor-α (TNF-α).[2,3] However, they down regulate each others' secretion implying their important role on pathogenesis of diabetes mellitus (DM), obesity and also chronic inflammatory diseases.[4-6]

A high plasma level of adiponectin is associated with augmented insulin sensitivity in peripheral tissues. Adiponectin may be involved in activation of AMP activated protein kinase which in turn down regulates lipogenesis. Moreover, adiponectin suppresses expression of enzymes responsible for gluconeogenesis in mRNA level and subsequently liver and muscular glucose load.[3] Besides, it is efficiently able to impede damage of β-cells in endocrine pancreas which is usually induced by either autoimmune components or lipid peroxidation.[7] On the contrary, TNF-α produced by macrophages, mononuclear lymphocytes and adipose tissue posses a potent pro-inflammatory effect.[8] Thus, it is thought to play a major role in the etiology of insulin resistance through inhibition of insulin signaling pathways followed by termination of insulin responsiveness.[9]

Adiponectin levels could be increased through both pharmaceutical and lifestyle modifications.[10] In addition, the most successful therapeutic managements of type 2 DM patients are strongly correlated with significant elevation of adiponectin via control of sensitivity to insulin.[11] Collectively, up-regulation of plasma adiponectin levels plays a major role in reduction of insulin resistance and metabolic syndrome.[12,13] It seems that TNF-α and adiponectin antagonize each other, regulating expression of the other and acting in an antagonist manner in modulating many aspects of insulin action.[3, 14] Fasting during Ramadan, ninth lunar month is the religious duty of all healthy adult Muslims. During this month, Muslims abstain eating and drinking from dawn to sunset. This mode of fasting is a unique model of intermittent daily fasting for one month and is distinct from experimental fasting. This alteration in daily eating patterns and meal frequency influences many metabolic and physiologic aspects of human body.[15] Most importantly, the Ramadan intermittent fasting entails major changes in sleep pattern, physical activity and eating habits which may cause changes in cytokines balance.

The aim of current study was to elucidate alterations of adiponectin and TNF-α among men observing Ramadan fasting with three risk factors of type 2 DM.

Materials and Methods

This study was performed during Ramadan of 2012 (July-August). Ethical approval of this study was gained from the Research Ethics Committee. Females were excluded from the study, because they are not allowed to observe fasting during menstruation. Men who were suffering from obesity, defined as body mass index (BMI) greater than 30, DM, cardiovascular diseases, liver diseases including hyperbilirubinemia, high levels of aspartate aminotransferase, alanine aminotransferase and alkaline phosphatase, acute or chronic inflammatory disease or any other known disease were excluded from the study. Healthy men who had at least three risk factors of type 2 DM; overweight ($25<BMI<30$), age $\geq$ 30 years and a sedentary lifestyle were included in the study. Participants with physical activity of less than 20 minute a day and with frequencies of less than three times a week were considered to be sedentary. The obese men were also excluded because it could affect adiponectin production.[4]

All the participants were interviewed face to face and a full demographic and medical history was collected. Body weight of the participants was measured pre and post Ramadan with a precision of 0.1 kg. The height was measured to the nearest 0.5 cm at the

same time intervals. All of the subjects fasted for at least 25 days during Ramadan and had two main meals named as Iftar and sahur.

Venous blood was taken twice; once at first or 2nd day of Ramadan and the other at last 3 days of the fasting period after an average day time fasting of between 10 to twelve hours. Serum was separated by centrifugation at 3000 rpm for 10 min and stored at −20°C until completion of the study. All serum samples were analyzed on the same run soon after the end of the study to avoid inter-assay variations.

Adiponectin and TNF-α concentrations were determined using an Enzyme-linked immunosorbent assay from Mediagnost, and Id Labs™ Inc Biotechnology, respectively. The blood samples were also analyzed for fasting glucose, plasma triglycerides (TG), total cholesterol (TC), high density lipoprotein (HDL-C), and low density lipoprotein (LDL-C) by enzymatic colorimetric method using Pars Azmoon reagent kits and BT3000 Autoanalyser.

Statistical Analysis

Normality of data was checked using Kolmogorov-Smirnov test. Data were presented as mean ± SD. Paired t-test was used to compare pre and post Ramadan fasting variables. Differences were considered significant when *P* values were less than 0.05. All analyses were performed using SPSS 17.

Results

Seventy healthy overweight volunteer males were included in this study. The mean age of the participants was 47.88 years ranging from 30 to 70.

As shown in Fig. 1, there was a significant increase in serum level of adiponectin ($P < 0.001$) and an unremarkable decrease in TNF-α ($P = 0.100$) after Ramadan as compared to pre-Ramadan. As shown in Table 1, no significant changes were observed on total cholesterol, LDL – C and HDL – C after Ramadan as compared to pre-Ramadan. In contrast, plasma concentrations of glucose ($P < 0.001$) and triglyceride ($P < 0.001$) were significantly increased. After Ramadan subjects BMI ($P < 0.001$) were significantly decreased than pre Ramadan.

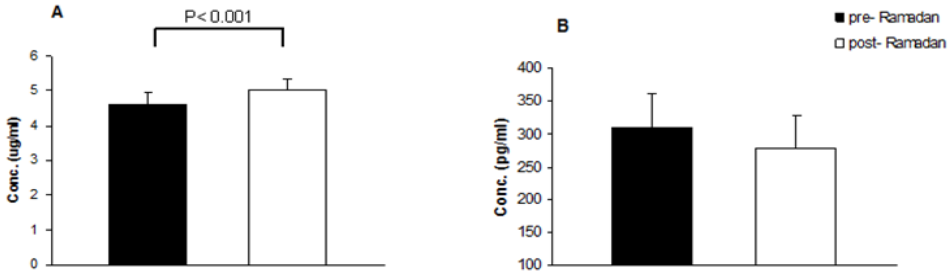

Fig. 1: Effect of Ramdan fasting on serum levels of Adiponectin (A) and TNF-alpha (B). The data are presented as mean (SEM)

Table 1: Effect of Ramadan fasting on blood glucose, lipid profile and body mass index

Component	Pre Ramadan (mean ± SD)	Post Ramadan (mean ± SD)	*P*
Glucose (mg/dl)	96.7±17.29	106.56±24.67	0.001
Triglyceride (mg/dl)	139.85±89.31	165.14±84.96	0.001
Total Cholesterol (mg/dl)	207.91±33.89	213.37±30.31	0.009
HDL (mg/dl)	57.74±9.70	57.88±8.62	0.825
LDL (mg/dl)	118.47±28.26	120.4±27.07	0.437
Weight (kg)	79.77±8.95	77.93±8.93	0.001
Body Mass Index	27.98±1.38	27.35±1.51	0.001

***P* values based on Paired *t* tests**

Discussion

The current study revealed that intermittent fasting of Ramadan was associated with significant increase in serum level of adiponectin among men with risk factors of type 2 DM. It has been reported that an increase in serum adiponectin was followed by improvement in insulin sensitivity[3] and also cells protection against injuries induced by autoimmunity and lipotoxicity.[7] It has been shown that higher adiponectin levels were consistently associated with a lower risk of type 2 DM in prospective studies of diverse populations.[3] Adiponectin is a promising target for reducing risk of type 2 DM.[16] It seems that fasting during Ramadan in men with risk factors for type 2 DM may attenuate development of the disease.

We also found a significant decrease in BMI of the participants after the Ramadan fasting. Production of some adipokines including adiponectin is correlated to body fat mass.[17] Therefore, we speculate that augmented adiponectin levels in post Ramadan can be attributed to weight loss and decreased body fat percentage. However, our finding is not correspondent with a report that no significant change of adiponectin levels existed after Ramadan fasting in trained young men.[18]

On the contrary to previous reports,[19-20] we did not observe any significant decrease in serum levels of TNF-α after Ramadan fasting. Besides, the fasting is associated with alteration in classically activated macrophage regulation/signaling and increase macrophage function and of proinflammatory cytokines and immune cells in healthy subjects.[21,22] Adiponectin with its immune function and anti-inflammatory action[23] can help this beneficial balance of cytokines during the fasting.

Levels of total cholesterol, LDL and HDL did not increase significantly during Ramadan. Interestingly, the serum level of triglyceride significantly increased during the fasting period. It should be mentioned that there are contradictory data regarding effect of Ramadan fasting on lipid profile in previous studies.[24-26] These discrepancies might be attributed to very fluctuant dietary habits and variable physical activity levels and sleep patterns of participants in different study plans. Effect of the Ramadan fasting on plasma glucose levels is intensively reviewed by many research groups. We found a significant increased level of plasma glucose concentrations during the fasting period. Ramadan fasting has no significant changes on serum glucose.[20,23,26,27] While, others reported either higher[25] or lower[22] blood glucose levels after the month of the fasting. These controversies may be due to different food habits, total calorie intake, number of fasting days, period of daily fasting, time of sampling, genetic differences and different daily activity levels.[23] However, the most important limitation of this study was that we were unable to assess the impact of dietary patterns and physical activity levels and also the sleep patterns on profile of adipokine production.

Conclusion

Intermittent fasting during Ramadan can cause adiponectin elevation in men have risk factors of diabetes type 2 and may be of help to decrease risk of type- 2 diabetes. Further studies are needed to better clarify effect of intermittent fasting on profile of adipokines and cytokines related to metabolic disorders including diabetes mellitus.

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Competing interests

The authors declare that there is no conflict of interest.

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