The Effect of Ramadan Fasting on IGF-1 and IGFBP-3 in Pre-menarche Girls

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Abstract

Background: The metabolic and endocrine effects of fasting have been studied in healthy adults but not in adolescent children. The purpose of this study was to determine the effects of Ramadan fasting on the serum of insulin-like growth factor -1 (IGF-1) and IGF-binding protein-3 (IGFBP-3) among pre-pubertal girls.

Methods: This study was performed during Ramadan of 2012. Fifty-eight girls aged 9-13 years old who either fasted or did not fast as per their own choice participated. Anthropometric and hormonal assessment was undertaken before and after Ramadan. Body composition was measured using bio-impedance analyzer method and tanner stages were determined following examination by an endocrine pediatrician. Serum IGF-1 and IGFBP-3 were measured using Radio Immunoassay and ELISA kit, respectively.

Results: Ramadan induced a significant decrease in BMI and weight in the fasting group (P=0.005, P=0.044, respectively) while a significant increase was observed in the non-fasting group (P<0.001). After Ramadan, IGFBP-3 concentration decreased in the fasting group but increased in the non-fasting group; although the changes were not statistically significant (P>0.05 for both). However, serum IGF-1 concentration increased significantly after Ramadan in the non-fasting group (P=0.005). IGF-1 concentration increased in the fasting group although this was not significantly different from baseline the fasting group (P>0.05).

Conclusions: In the present study, no difference was observed in IGF-1 and IGFBP-3 concentrations between fasting and non-fasting groups in pre menarche girls; however, a significant increase of IGF-1 was found in the non-fasting group after Ramadan compared to before Ramadan.

Keywords IGF-1; IGFBP-3; Pre-Menarche; Ramadan fasting

Introduction

Many religions around the world recommend a period of fasting per year. During the Ramadan, Muslims are expected to fast due to Islamic beliefs; they refuse fluid and food from sunrise to sunset each day for one month.

During Ramadan, the majority of Muslims eat two principal meals; one before sunrise (Sahari) and another immediately after sunset (Iftar). Islamic fasting is a special model of fasting which may cause metabolic and hormonal changes in the body [1], which may differ from other kinds of fasting.

One of the most important growth hormones that may be affected by fasting is insulin-like growth factor -1 (IGF-1); whose production in the liver is stimulated by growth hormone. IGF-1 concentration is also affected by thyroid function and nutritional status [2]

IGF-1 has indirect effects on many of physiological functions of growth hormone; therefore, IGF-1 plays an important role in growth and metabolism during puberty [3]. IGF-I availability is regulated by IGF binding proteins [4] and binds mostly to IGF-binding protein-3 (IGFBP-3) [5].

Islamic fasting as a compulsory law for Muslim girls must be started from the age of nine years old if they are in full health [6]. To the best of our knowledge, the effect(s) of fasting on the hormonal changes and especially on IGF-1 and IGFBP-3 have not been previously studied in pre pubertal girls. Thus, the present study was designed to compare the growth hormone in fasting and non-fasting young girls before and after Ramadan.

Material and Methods

Participants

This prospective study was performed during Ramadan of 2012 (July-August) in Mashhad, Iran. Sixty-five healthy girls aged 9-13 years, were selected from families affiliated with a Charity. Of 65 participants, 34 fasted and 31 did not fast based on their own choice.

The inclusion criteria were: 9-13 year old healthy girls living in Mashhad, willingness to contribute to the project, absence of menarche (menarche diagnosis was based on clinical history). Girls in tanner stages 4 and 5 were excluded from the study. Subjects were advised to keep their regular life style, including diet and physical activity during the course of study. All procedures involving human subjects were approved by the ethical committee of the Research Deputy of the Mashhad University of Medical Sciences, Mashhad, Iran (approval code of IR.MUMS.fm.REC.1391.306). The study aims and methods were explained to the participant's parents and written informed consent was obtained before participation of their child in the study.

Measurements

Demographic variables including age, education, number of fasting days, and past medical history were recorded through interview with participants and their mothers. The participants' tanner stages were determined by the endocrine pediatrician based on clinical examination and were categorized from stage 1 to stage 3 [3]. Height was recorded by a standard clinical stadiometer (Seca 720, Germany) with an accuracy of 0.1 cm with the subject stretching to the maximum height, without shoes and the head positioned in the Frankfort plane. Weight was measured with light clothes and without shoes by a bio impedance analyzer (BIA; BC-418 MA, Japan) and was recorded to the nearest 100 g. Body mass index (BMI) was calculated as weight in kilograms, divided by height in meters squared.

Biochemical assessments

After 12 h of fasting, a 5 CC blood sample was obtained for measurement of IGF-1 and IGFBP-3, three days before Ramadan and one day after Ramadan. Thirty minutes after sampling, the blood samples were centrifuged (3-30K, Sigma, Germany) to separate serum at 3000 rpm in 4°C for 10 minutes and stored at - 80°C in the central laboratory of Mashhad University of Medical Sciences until the second sampling procedure. Serum IGF-1 and IGFBP-3 concentration were measured with Radio Immunoassay (RIA) method using Biosource company kits (KIP1588) and ELISA kits respectively (DE/CA40/00809/22, mediagnost, Germany, respectively).

Statistical analysis

Kolmogorov-Smironov test was used to assess the distribution of the variables. Categorical and continuous variables with normal distribution were expressed as percentages and mean ± SD, respectively. To compare continuous variables between fasting and non-fasting groups and to compare variables before and after Ramadan, independent t-test and paired t-test were used, respectively. Categorical variables were compared using Pearson's chi-square test between the two study groups. SPSS (version 11.0; SPSS Inc., Chicago, IL, USA) was used for data analyses and P values<0.05 were considered statistically significant. Tanner stage was adjusted in generalized linear models.

Results

During the study, three subjects were excluded from the fasting group because of menarche incident and fasting less than 20 days, and four subjects were excluded from the non-fasting group because of menarche incident, and not providing the follow-up measurements. Eventually, 58 participants completed the study (31 in the fasting and 27 in the non-fasting groups). The mean age and BMI of the participants was 11.1 ± 1.1 years and 16.8 ± 2.7 kg/m², respectively. The baseline characteristics of adolescents according to study groups are shown in Table 1. No significant differences between the groups were seen for age, weight, height, BMI, and tanner stages. The mean IGF-1and IGFBP-3 in fasting and non-fasting groups before and after Ramadan is shown in Table 2. There were no significant changes in IGFBP-3 concentrations in the two groups during the Ramadan period. There was also no statistically significant difference between the two groups in IGFBP-3 concentrations before and after Ramadan and no differences in the changes from baseline. Adjusting for tanner stages did not change the IGFBP-3 concentrations (data not shown). There was a significant increase in serum IGF-1 after Ramadan compared to baseline values in the non-fasting group (227.5 ± 115.4 vs. 175.3 ± 61.0, P value=0.005) only. The mean change of serum IGF-1 concentration did not significantly differ between the two groups (P value=0.58). Again, as with IGFBP-3, adjusting for the tanner stages did not result in changes in the IGF-1 concentrations between the two groups (data not shown).

Table 1: Baseline characteristics of participants according to fasting and non-fasting groups.

Variable	Total	Fasting group (n=31)	Non-fasting group (n=27)	P-value*
Age (years)	11.0 ± 1.2	11.1 ± 1.1	10.9 ± 1.3	0.58
Height (cm)	142.0 ± 7.8	143.2 ± 7.4	140.7 ± 8.1	0.23
Weight (kg)	34.2 ± 8.0	35.6 ± 8.0	32.6 ± 7.8	0.16
Body mass index (BMI) (kg/m2)	16.8 ± 2.7	17.2 ± 2.8	16.3 ± 2.5	0.19

Tanner stages n (%)				
1	14 (24.2)	5 (16.1)	9 (33.3)	
2	22 (37.9)	12 (38.7)	10 (37.0)	0.25
3	22 (37.9)	14 (45.2)	8 (29.7)	

Data presented as mean ± standard deviation for continuous variables or n (%) for categorically distributed variables

Taner 1: The first stage of breast development (before breast growth)

Taner 2: The second stage of breast development

Taner 3: The third stage of breast development

*P-value according to independent sample t-test and Chi-square

Table 2: IGFBP3 and IGF1 in fasting and non-fasting groups before and after Ramadan.

Variables	Before Ramadan	After Ramadan	Mean difference	P-value*
	(mean ± SD)	(mean ± SD)		
IGFBP3 (mg/L)				
Fasting group	8.78 ± 1.78	8.35 ± 2.15	-0.42 ± 2.20	0.28
Non-fasting group	7.93 ± 2.52	8.08 ± 2.08	0.14 ± 2.20	0.74
P-value**	0.14	0.63	0.32	
IGF1 (pg/dl)				
Fasting group	206.4 ± 60.5	238.8 ± 122.6	36.7 ± 117.7	0.11
Non-fasting group	175.3 ± 61.0	227.5 ± 115.4	52.3 ± 87.5	0.005
P-value**	0.06	0.72	0.58	

IGFBP3: insulin like growth factor banding protein 3; IGF1: insulin-like growth factor 1

* P-value according to paired t-test

** P-value according to independent sample t-test

Discussion

In the present study, no difference was observed in IGF-1 and IGFBP-3 concentrations between fasting and non-fasting groups in pre menarche girls; however, a significant increase of IGF-1 was found in the non-fasting group after Ramadan compared to before Ramadan. This was an unexpected finding since the period was short to expect any changes in maturation. However, since Ramadan fasting is an integral part of the Islamic religion, it is important to further study these hormonal changes at this crucial period of childhood and adolescence.

Nearly all nations and religions have some kind of fasting, although the length of fasting and type of food consumed differ greatly between religions [7]. The fasting obligation limits the daily calorie intake in one or two meals or limits the types of foods consumed. From a physiological viewpoint, Islamic fasting provides a unique fasting model. It is distinct from experimental fasting by the fact that the observant of the fast does not drink during fasting which may reach more than 12 hours. Therefore, one may assume that physiological changes occurring during Ramadan fasting would be different from those noted during an experimental fast [8,9].

Animal and human studies have shown that short-term food restriction (48-72 h) resulted in reduction in serum IGF-1 concentrations [10-12]. Unlike our finding on serum IGF-1, an in vivo study performed by Amstalden and colleagues resulted in reduced IGF-1 levels during acute food deprivation [12]. Another study in Sweden also showed that serum IGF-1 decreased (246 ± 29 mcg/L (pre-fast) to 87 ± 10 mcg/L (after fasting)) in healthy adults [13]. However, similar to our findings, Sanjari et al. in Iran found that Ramadan fasting for at least 25 days, produced no significant changes in serum IGF-1 [14].

In addition, Ramadan fasting induced no significant change on IGF-1 and IGFBP-3 during sub maximal exercise in male athletes [15]. Furthermore, in a study of spontaneous GH secretion to distinguish GH-deficient and normal adults, no significant changes in serum concentrations of IGF-1 and IGFBP-3 were observed after 36-h fasting [16].

In the present study, fasting lasted for 15-15.5 h each day and a total of 20-30 days. It is worth mentioning that the half-life of free-form of IGF-1 is 6 minutes; however, the half-life of [IGF-1-IGFBP-3] complex is longer at about 16 h [17], which covers almost the fasting duration of the study. If sufficient protein was consumed in the Iftar (breaking fasting at sunset), serum IGF-1 concentration would rapidly return to the concentration observed before fasting [18]. It is worth noting that overall,

findings of the studies conducted in humans and animals are contradictory which may be related to disparities in people's response due to differences in the number of days of fasting, the participants' age and gender, physical activity, and the diet during Ramadan.

Conclusion

In the present study, no difference was observed regarding IGF-1 and IGFBP-3 between fasting and non-fasting groups among 9-13 years healthy girls before the age of menarche. However, IGF-1 increased significantly in the non-fasting group after Ramadan. This was an unexpected finding since the period was short to expect any changes in maturation. However, since Ramadan fasting is an integral part of the Islamic religion, it is important to further study these hormonal changes at this crucial period of childhood and adolescence.

What is already known on this topic?

IGF-1 has indirect effects on many of physiological functions of growth hormone; therefore, IGF-1 plays an important role in growth and metabolism during puberty.

IGF-I availability is regulated by IGF binding proteins and binds mostly to IGF-binding protein-3 (IGFBP-3).

To the best of our knowledge, the effect(s) of fasting on the hormonal changes and especially on IGF-1 and IGFBP-3 have not been previously studied in pre pubertal girls.

What this study adds?

This study was designed to compare the growth hormone in fasting and non-fasting young girls before and after Ramadan.

In the present study, no difference was observed regarding IGF-1 and IGFBP-3 between fasting and non-fasting groups among 9-13 years healthy girls before the age of menarche. However, IGF-1 increased significantly in the non-fasting group after Ramadan. This was an unexpected finding since the period was short to expect any changes in maturation. However, since Ramadan fasting is an integral part of the Islamic religion, it is important to further study these hormonal changes at this crucial period of childhood and adolescence.

Study limitations

The present study has both strengths and limitations. To our knowledge, this is the first study evaluating the effect of fasting on IGF-1 and IGFBP-3 concentration among pre-menarche girls. In addition, the current study included a control group, whereas previous studies did not. However, the current study was performed on a particular population and only among girls; thus it is suggested that future studies involve various population groups of both girls and boys and from all pubertal stages. Furthermore, future studies should involve a larger population to confirm the current findings. In the current study, it was recommended that the subjects keep their regular life style, including diet and physical activity. Diet, however, was not assessed and it is recommended that dietary questionnaires are used in future studies to remove confounding dietary factors. Additionally, it would have been better to assess long-term effects of Ramadan fasting by re-assessing the concentrations of IGF-1 and IGFBP-3 one month after the end of Ramadan and even at regular time periods in the year in fasting and non-fasting pre-menarche girls.

Conflict of Interest

The authors declare no conflict of interest.

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