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SERUM LEVELS OF PROLACTIN, THYROTROPIN, THYROID HORMONES, TRH RESPONSIVENESS, AND MALE REPRODUCTIVE FUNCTION IN INTERMITTENT ISLAMIC FASTING

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ABSTRACT

During the Islamic lunar month of Ramadan millions of Muslims abstain from drinking and eating from dawn to sunset. The objective of this study was to investigate the effect of intermittent Islamic fasting on reproductive function, hypothalamic-pituitary-thyroid axis and the peripheral metabolism of thyroid hormones in men.

We measured serum levels of FSH, LH, testosterone, prolactin, TSH, T4, T3 and T3 uptake, and prolactin and TSH responses to TRH, before, at 10th, 20th and 29th days of Ramadan and four weeks after fasting month was terminated. Subjects were nine healthy men who fasted 17 hours a day for 29 days. There were no significant changes in serum levels of any of measured hormones during Ramadan. Prolactin and TSH responses to TRH were also unaltered. The only positive finding was increased serum T4 of 1.5 to 2.8 μg/dl and increased free T4 index (FT4I) in five of nine subjects in the last days of Ramadan.

We conclude that 1) Intermittent abstinence from food and drink for 17 hr a day, as is observed in Islamic fasting, does not alter male reproductive function, hypothalamic-pituitary-thyroid axis, or peripheral metabolism of thyroid hormones. 2) In some subjects slight increase in serum T4 may occur in the last days of Ramadan.

INTRODUCTION

Intermittent fasting from dawn to sunset is obligatory for all adult and healthy Muslims during the whole month of Ramadan every year. The majority of Muslims have two good size meals, one immediately after sunset and the other just before dawn. They are allowed to eat and drink between sunset and dawn but they neither eat nor drink after dawn. Since the Islamic calendar employs a lunar cycle, the Islamic year contains 345 days. Therefore, Ramadan moves back eleven days every year and may be situated in any of

four seasons, making the length of fasting hours variable. The month of Ramadan usually contains 29 days, and every few years 30 days.

Several studies have demonstrated the effect of total food abstinence on the peripheral metabolism of thyroid hormone and hypothalamic-pituitary-thyroid axis,[1-13] and male reproductive function.[14,15] Although there are more than one billion Muslims in the world and many millions of them fast during Ramadan, only one article has recently studied serum levels of thyroid hormones on the first and the last days of Ramadan and found small but significant increase in serum T4 but no change in serum T3 levels.[16] However, values of free thyroid hormone indices, serum TSH, or TSH response to TRH were not studied.

In the present paper, we report that Islamic fasting had no effect on serum concentrations of FSH, LH, testosterone, prolactin, TSH, T3, and free T3 index (FT3I) values, and TSH and prolactin responses to intravenous administration of TRH. As a group, mean ± SD of T4 and FT4I were also unchanged. However, five of nine subjects studied showed increase in T4 and FT4I during Ramadan.

MATERIALS AND METHODS

Nine male volunteers aged 23 to 54 yr (mean 35) were studied during Ramadan in Tehran. They fasted each day from dawn to sunset for 29 days. The length of each day of fast was approximately 17 hr (3 AM to 8 PM). They had two regular meals, one after sunset and another just before dawn, and were allowed to eat and drink in the interim.

Experiments were performed immediately after sunset, one week before Ramadan and on the first, 10th 20th and 29th day of Ramadan, and four weeks after fasting month. Before Ramadan, samples were taken after 8 hr fast, from 12 noon to 8 PM. Since all the results of studies done before and on the first day of Ramadan were similar, the results of the first day of Ramadan were expressed as values before Ramadan. On each night of experiment, a baseline blood sample was drawn for measurement of serum FSH, LH, testosterone, prolactin, TSH, T4, T3 and T3 uptake. Thereafter, 250 μg of TRH was administered intravenously. Additional blood samples were drawn at 10, 20, 30, 45 and 60 minutes after TRH injection, for measurement of serum prolactin and TSH concentrations.

Serum concentrations of FSH, LH, testosterone, prolactin, TSH, T4 and T3 were performed by commercial kits, as was T3 uptake test. FT4I and FT3I were then calculated.[17] The results were evaluated with student's and paired t tests.

RESULTS

During Ramadan there was a significant fall in body weight in every subject. Mean body weight was 65.4±9.1 before and 61.6±9.0 kg at 29th day of Islamic fasting ($P<0.001$). Four weeks after Ramadan body weight increased in every subject and reached near prefasting value (64.8±8.5 kg).

There were no significant changes in serum concentrations of FSH, LH and testosterone before, during and after Ramadan (Table I). Serum concentrations of prolactin, TSH, T3, and FT3I values, and prolactin and TSH responses to TRH were also unchanged (Table II).

Serum T4 concentration increased more than 1 μg/dl in five subjects (55%) and was equivocal or decreased in another four subjects. Mean±SD of serum T4 concentration was 8.7±2.1, 9.2±2.0, 9.1±1.6, 9.8±1.8 μg/dl, before and at 10th, 20th and 29th days of Ramadan, respectively (Table III). The changes were not statistically significant. Values for FT4I showed increases in five subjects at the 29th day of Ramadan. Mean±SD of all nine subjects for FT41 before and during Ramadan was not significantly changed.

In five subjects who showed increased T4 and FT4I,

Tabl I. Body Weight and Serum Concentrations of FSH, LH and Testosterone Before, During and After Ramadan

	Before	DAYS OF RAMADAN			After*
		10	20	30	
Body weight (kg)	65.4 ± g.1	63.3 ± 9.2	62.9 ± 8.9	61.6 ± 9.0	64.8 ± 8.5
Serum constituent					
FSH (mU/ml)	12.2 ± 7.7	11.9 ± 6.3	13.4 ± 9.2	13.4 ± 8.2	12.6 ± 7.5
LH (mU/ml)	8.3 ± 2.1	8.1 ± 2.0	10.1 ± 2.8	8.7 ± 3.0	8.6 ± 3.1
Testosterone (ng/dl)	626 ± 263	691 ± 223	711 ± 240	625 ± 228	568 ± 163

* Four weeks after Ramadan
\+ Compared to values before Ramadan by paired t test, none of the values were significant.

Table II. Serum Concentrations of Prolactin, TSH and T3, FT3I Values and Prolactin and TSH Responses to TRH Before, During and After Ramadan

Serum constituent	Before	DAYS OF RAMADAN			After*
		10	20	29	
Prolactin (ng/ml)					
Basal	13.9 ± 5.5	11.6 ± 4.2	13.2 ± 3.1	15.3 ± 6.1	14.3 ± 4.1
△**	38 ± 13	47 ± 21	44 ± 18	44 ± 17	43 ± 19
TSH (μU/ml)					
Basal	2.7 ± 1.0	3.0 ± 1.4	2.0 ± 1.2	2.6 ± 0.8	2.8 ± 1.3
△	9.7 ± 3.6	9.3 ± 4.1	9.9 ± 4.0	8.8 ± 4.1	10.5 ± 4.1
T3 (ng/dl)	130 ± 16	129 ± 26	135 ± 16	140 ± 24	134 ± 14
FT3I	123 ± 14	114 ± 23	123 ± 15	123 ± 20	122 ± 10***

* Four weeks after Ramadan.
** △ = Peak minus basal after TRH injection.
*** Compared to values before Ramadan by paired t test, none of the values were significant.

Table III. Serum T4 Concentrations and FT4I Values in Nine Male Volunteers Before, During and After Ramadan

		Before	DAYS OF RAMADAN			After*
			10	20	29	
Serum T4 (μ/dl)	1	7.2	7.6	7.6	7.6	7.2
	2	13.0	13.0	10.5	12.2	11.5
	3	7.2	7.2	8.0	6.6	7.0
	4	7.2	9.8	9.0	10.0	8.0
	5	10.0	11.0	11.5	11.5	10.0
	6	8.0	8.2	8.6	9.8	8.0
	7	7.2	7.2	8.0	9.8	9.0
	8	11.0	10.5	11.5	10.5	11.0
	9	7.6	8.2	7.6	10.5	6.6
Mean ± SD		8.7 ± 2.1	9.2 ± 2.0	9.1 ± 1.6	9.8 ± 1.8	8.7 ± 1.8
FT4I	1	7.8	8.6	8.3	6.7	7.2
	2	11.3	11.3	9.5	9.0	9.4
	3	6.0	6.1	7.3	6.1	6.0
	4	7.6	10.2	9.3	10.7	7.6
	5	9.3	9.2	10.4	10.7	9.5
	6	7.3	7.3	7.1	8.4	7.1
	7	7.0	6.6	6.6	8.7	8.3
	8	9.6	10.3	10.1	9.3	8.9
	9	7.5	7.5	6.8	8.8	6.2
Mean ± SD		8.2 ± 1.6	8.6 ± 1.8	8.4 ± 1.5	8.7 ± 1.5	7.8 ± 1.3+

*Four weeks after Ramadan.
+ Compared to values before Ramadan by paired t test, none of the values were significant.

mean ± SD of serum T4 concentration was 8.0 ± 1.2 μg/dl before, and increased to 8.9 ± 1.5 (NS), 8.9 ± 1.5 ($P<0.05$), and 10.3 ± 0.7 μg/dl ($P<0.005$) at 10th, 20th and 29th days of Ramadan, respectively. Corresponding values for FT4I were 7.7 ± 0.9, before; 8.2 ± 1.5, at 10th day (NS); 8.0 ± 1.7, at 20th day (NS); and 9.4 ± 1.1, at 29th day ($P<0.01$). Four weeks after Ramadan, serum T4 (8.3 ± 1.8 μg/dl), and FT4I (7.7 ± 1.2) had returned to pre-Ramadan values. In these five subjects, serum TSH concentration and its response to TRH was not significantly changed during or after Ramadan.

DISCUSSION

Several of the world's great religions recommend a period of fasting or abstinence, and of these the Islamic fast during the month of Ramadan is strictly observed. One whole month of intermittent fasting every year is particular to Islam. The experience of fasting teaches Muslims self-discipline and self-restraint and reminds them of the feelings of the impoverished.[18] Fasting is not obligatory for children. Menstruating women, as well as sick and travelling people are excused, and pregnant and lactating women are permitted to postpone fasting of Ramadan; however they should fast during another month of the year, when they have no reason for exemption.

From the physiological standpoint, Islamic fasting provides a unique model of intermittent fasting everyday for one month. It is also distinct from regular voluntary or experimental fasting by the fact that the observant of the fast does not drink during fasting hours. Therefore, one may assume that hormonal changes occurring during Islamic fasting would be different from those seen during regular fast. The results of the present study are in accord with this assumption.

The effects of regular fasting on reproductive function in men have previously been studied. Serum FSH and testosterone concentrations may be normal[14] or decreased[15] after fasting in over weight and obese men. Basal serum LH concentration and its response to GnRH infusion does not change, but serum FSH response to GnRH infusion is blunted during fasting.[15] Our results clearly demonstrate that Islamic fasting had no effect on serum concentrations of FSH, LH and testosterone in men. Basal serum prolactin is not altered during regular fast,[5,6] and prolactin response to TRH may be normal[5] or decreased.[19] In the present study, we did not find any impairment in the basal prolactin level and its response to TRH.

We and others have found profound alterations in both peripheral thyroid hormone metabolism and the hypothalamic-pituitary-thyroid axis during regular fasting. Decreased peripheral conversion of T4 to T3, due to inhibition of 5′-monodeiodination results in a decrease in serum T3 and an increase in serum rT3.[1-12] Basal serum TSH may be normal,[5,9] or decreased,[1,4-6,8,9,11,13] and, despite lower serum T3 concentrations, most studies have shown a blunted TSH response to TRH during fasting, both in euthyroid[1,4,5,13] and hypothyroid[2] subjects. Refeeding with carbohydrate, but not protein or fat, returns serum T3, as well as TSH responsiveness to TRH, to normal values,[1] and supplementation of glucose, but not aminoacids, during fasting prevents subnormal TSH responsiveness to TRH.[20] Therefore, most changes seen during regular fasting appear to be due to carbohydrate deprivation.

In Islamic fasting, the length of intermittent fast is not adequate to cause any change in serum T3, TSH and TSH responsiveness to TRH. Although dietary regimen varies in different muslim countries, the majority of diets contain bread, rice and sweets, hence preventing fall in serum T3 and decreased thyrotroph responsiveness. Conflicting data have been presented concerning the effect of regular fast on serum T4. Most reports have indicated that serum T4 remains unchanged,[3,6,7,21] others have found either rise,[1,11] or fall,[7,5] in serum T4. The only study concerning the possible effect of Ramadan on serum T4 has found that small but significant increase in serum T4 occurs on the last day of Ramadan as compared to values on the first

day.[16] However, there was no mention of FT4I, serum TSH and TSH response to TRH. In the present study, in a group of nine subjects, there were no statistically significant changes in serum T4 and FT4I values during Ramadan. However, analysis of data showed that in five subjects, significant increases in serum T4 and FT4I had occurred by the last day of Ramadan. Serum T4 concentrations appeared to increase at 20th day as well, which must have been due to increased TBG binding, as FT4I values were unchanged. The reason for the increase in serum T4 and FT4I in some subjects is not clear. Since their serum TSH was unchanged and TSH response to TRH was not blunted, increased production is not likely. A decreased peripheral metabolism may be assumed. However, serum T3 concentration was unchanged and serum rT3 was not measured.

We conclude that no significant changes occur in reproductive and pituitary-thyroid axis in men during Islamic fasting. However, physicians working in Muslim countries and those caring for Muslims in other regions should be aware that serum T4 may increase up to 2.8 µg/dl in some individuals in the last days of Ramadan.

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