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The Effect of Ramadan Fasting on Endocrine System

Nadia Boroumand[1], Seyed Isaac Hashemy[2]*

1. Department of Clinical Biochemistry, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
2. Surgical Oncology Research Center, Imam Reza Hospital, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran

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ABSTRACT

In the religion of Islam, fasting is obligatory for healthy adults during Ramadan. Millions of Muslims around the world practice fasting in this holy month which may cause different metabolic and hormonal changes due to the restrictions in regular caloric intake. Despite various studies regarding the impact of Islamic fasting on a number of hormonal values, yet there is not any obvious consensus on its impact on human health. This review was aimed to explain some possible effects of Ramadan fasting on the endocrine system which has a great impact on physiological and cellular processes through a wide variety of hormones. In conclusion, this article recommended normal people to continue fasting during this holy month because despite the modifications that occur in the secretion pattern of some hormones, it causes no major alteration in the health of normal subjects; it is also effective for maintenance of remission in some diseases.

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Introduction

Ramadan is a religious occasion for more than a billion Muslims around the world (1). It is a time to practice self-restraint and self-reflection. Fasting is seen as a way for spiritual purification during this holy month. During the fasting Muslims totally abstain from food, drink, smoking, and sexual intercourse from breaking of dawn to setting of the sun (2, 3). The length of fasting can vary from 12 to 19 hours per day depending on the geographical position and the season in which Ramadan is placed (4). Ramadan fasting is obligatory for adult Muslims, but there are some exceptions such as suffering from an illness, being on travel, pregnancy, breastfeeding, going through menstrual bleeding, etc (5, 6). Ramadan fasting is distinct from regular voluntary fasting, since it is a month per year through which Muslims have two principal meals, a pre-dawn meal *(suhoor)* and a meal right after the sunset *(iftar)* (3, 7). Therefore, this long-lasting fasting accompany with sleep time alteration may cause different metabolic and hormonal changes from regular caloric restriction (8, 9). Because of the importance of endocrine system in health and disease, and Ramadan as a major religious duty, we aimed to review the effects of Ramadan fasting on the endocrine parameters.

Effect of Ramadan Fasting on Pineal Gland

Pineal gland, a small endocrine gland located in epithalamus, secrets melatonin which is responsible for controlling sleepiness and wakefulness (10, 11). Since the sleep time is altered during Ramadan, it can be expected that level of melatonin would change in Ramadan; but to our knowledge, the studies regarding assessing this issue are limited. In the study conducted by Bogdan et al, a statistically significant time-related alteration was found for melatonin concentration. During Ramadan, melatonin's night pick is lower than before Ramadan, which may be the result of a longer exposure to artificial light in Ramadan;

* *Corresponding author:*Isaac Hashemy, Surgical Oncology Research Centre, Imam Reza Hospital, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.Email:hashemyi@mums.ac.ir

although the investigators emphasized that since the experiment was performed in winter, there was only one hour longer exposure to artificial indoor light in Ramadan rather than the control period. Also, delay in the onset of increasing concentration was observed which is in accordance with the altered sleep schedule in Ramadan (12).

Effect of Ramadan Fasting on Pituitary Gland

Pituitary gland, a pea-sized structure gland, involves in controlling various processes such as body metabolism, reproduction, growth and maturation, blood pressure, etc. It consists of two lobes: anterior lobe producing Follicle-stimulating hormone (FSH), Luteinizing hormone (LH), Adrenocorticotropic hormone (ACTH), Growth hormone (GH), Prolactin (PRL), Beta-endorphin as well as Thyroid-stimulating hormone (TSH), and posterior lobe producing antidiuretic hormone (ADH) and Oxytocin.

Studies on the effects of Islamic fasting on serum concentrations of some Pituitary gland hormones have provided valuable data that are as the follows.

FSH and LH are glycoprotein hormones, secreted by gonadotropes of the anterior pituitary gland. FSH is one of the hormones essential for pubertal maturation and reproductive processes of the body. In women, FSH stimulates the growth of ovarian follicles in the ovary. It also increases estradiol production. LH is involved in development of the corpus luteum. Besides, an acute rise of LH triggers ovulation. In men, FSH is responsible for spermatogenesis and LH stimulates Leydig cells in the testes to produce testosterone (13-15). In a case control study on 58 pre-menarche girls divided in fasting and non-fasting groups, Bahreyni et al assessed the level of FSH and LH before and after Ramadan. The result showed a significant increase in FSH and LH levels of non-fasting group after Ramadan while there was no significant rise in FSH and LH concentration of fasting group after Ramadan (9). Moreover, in another study, Zangeneh et al showed no significant difference in the levels of FSH and LH in women with Polycystic Ovary Syndrome during Ramadan fasting (16). Besides, Shahabi et al reported that Ramadan fasting results in no significant changes in the serum concentration of FSH and LH around ovulation days (14th day of menstruation). They concluded that food restriction in Ramadan could not affect the occurrence of ovulation (17).

ACTH, also known as corticotropin, is a polypeptide hormone, secreted by corticotroph cells of the anterior pituitary gland. It is often produced in response to biological stress which leads to production and release of cortisol by the cortex of the adrenal gland. Few studies have evaluated the effect of Islamic fasting on the level of ACTH as a stress-response hormone. El-Migdadi et al claimed that fasting as a stress condition for body causes remarkably increase in ACTH serum levels (18).

GH, also known as somatotropin, is a peptide hormone, secreted by somatotroph cells of the anterior pituitary gland. GH stimulates growth and cell regeneration and maintains body's normal metabolism. Growth hormone release is not continuous, and its pulsatile secretion is critical for its effect. GH level can be affected by sleep timing, stress, exercise, glucose level, etc. The study conducted by Bouhlel et al showed that the levels of resting GH and GH after exercise do not significantly change during Ramadan. The authors mentioned that plasma samples were not collected at the same time, which is a limitation of this study (19). Moreover, André Bogdana et al reported no significant changes in the secretion pattern of GH during Ramadan (2). However, Hartman et al found an increase in GH secretion by 2 days of total fasting during which the participants fed water, a multivitamin tablet and potassium chloride (20 meq/day)(20). It can be concluded that the long-term fasting in Ramadan could not affect the GH significantly whereas short-term fasting could.

PRL is a polypeptide hormone, also known as luteotropic hormone, secreted by lactotroph cells of the anterior pituitary gland. It has a crucial role in females' lactation. It also has a wide range of other functions such as roles in metabolism, regulation of the immune system, and pancreatic development. Among the studies that assessed the PRL level, Azizi F reported no alteration in the level of PRL caused by Ramadan fasting in male subjects fasting 17 hours per day (21). Besides, Cağlayan et al reported that the concentration

of prolactin does not change remarkably and stay within the normal values in women during Islamic fasting (22).

Beta endorphin is a neuropeptide found in neurons of the hypothalamus, as well as the pituitary gland secreted by corticotroph cells. It is an opioid receptor agonist causing the pain to be felt as a numb or dull pain. It has been confirmed that acute exercise and training could increase the level of beta endorphin (23). Furthermore, the relationship between beta endorphin and immune function and its role in reproduction has been confirmed (24-26). To assess the effect of Ramadan fasting on beta endorphin level, Zangeneh et al observed that Islamic fasting in women with Polycystic Ovary Syndrome does not affect the beta endorphin concentration significantly (16). However, ArdikLahdimawan, reported that Islamic fasting enhances the level of beta endorphin which had advantageous effects on body defense mechanism against *Mycobacterium tuberculosis* (27). These conflicting results may be due to different situation such as sleep, nutrition, and physical activity pattern of the subjects or differences in immune system abilities between the participants. Further investigations with elimination of confounding variables are needed to obtain a valid result.

The effect of Ramadan food restriction on TSH values secreted by the pituitary gland will be discussed in the following section.

Effect of Ramadan Fasting on Thyroid Gland

Thyroid gland is one of the largest endocrine glands located in the front of the neck, below the Adam's apple. It has two lobes connected by a narrow strip of thyroid tissue called isthmus. It secrets thyroxine (T4) and triiodothyronine (T3) in response to TSH, and is involved in controlling body organs' metabolism. TSH has a rhythmic pattern of secretion resulting in a circadian serum concentration which should be taken into consideration in evaluating its level. Moreover, the duration of fasting and the number of days of being fasted should be counted as effective factors. Available data demonstrated that there is no major alteration in the levels of T3, T4 and TSH during the Islamic fasting. A study carried out on 42 healthy men showed no significant change in the level of T3, but a mild decrease in T4 level in Ramadan fasting period (28). On the other hand, Bahrayni et al found that Islamic fasting induces a significant decrease in the level of T3, although it stayes within the normal range. They reported a slight decrease and increase in the level of T4 and TSH, respectively in both case and control groups; but no remarkable difference was reported in the T4 and TSH concentration before and after Ramadan between these two groups (29). Furthermore, an experiment conducted by Bogdan et al showed no considerable change in the levels of free T3 and free T4 during Ramadan fasting. Nevertheless they reported that Islamic fasting flattens the amplitude of TSH circadian rhythm (2). Similarly, in a case-control study conducted by Sajid et al, no notable variation was seen in the level of T3 and T4 between the fasting and non-fasting groups. However, a gradual reduction was observed in TSH levels in fasting group which decreases after Ramadan and re-attains the pre-Ramadan levels at about two months after Ramadan (30).

Effect of Ramadan Fasting on Adrenal Gland

Adrenal glands are triangular-shaped organs located on top of the kidneys. Like other organs, they also have vital roles in body such as regulating metabolism, blood pressure, controlling the body in physical and emotional stress, etc. Each adrenal gland contains two distinct parts: the outer part called the adrenal cortex secreting glucocorticoids (such as cortisol), mineralocorticoids (such as aldosterone), and androgens, and the inner part, known as the adrenal medulla secreting hormones such as adrenaline and noradrenaline in response to stress situations . As mentioned before, fasting can be counted as a stress situation for body, thus the effect of Ramadan fasting has been assessed on some hormones of adrenal glands by investigators.

Cortisol, a steroid hormone, is secreted in response to ACTH. It has crucial roles in psychological and physiological stresses, inflammation, as well as in carbohydrate, fat and protein metabolism, etc. In a study by Dikensoy et al, maternal serum cortisol was assessed in 36 healthy women with

uncompleted pregnancy of 20 weeks or more as the fasting group, and 29 healthy pregnant women as the non-fasting group. Maternal serum cortisol levels were notably higher on 20th day of Ramadan in fasting group in compare with its levels in 1 week before Ramadan. The investigators suggested that alteration in sleep and eating schedules may influence the maternal cortisol levels in fasting pregnant women (31). Nevertheless, Zangeneh et al reported that Ramadan fasting causes a remarkable decrease in cortisol levels in fasting women with polycystic ovary syndrome in compare with non-fasting group (16). Moreover, a significant time-related alteration in the levels of serum cortisol was observed in a case-control study on healthy non-smoking men. The results showed that cortisol concentration raises in the afternoon but the elevation of cortisol in the morning seemingly delays. In addition, higher morning values and spiky drop occur during Ramadan in view of the fact that there are day and time modifications during Ramadan (2). In addition, Al-Hadramy et al reported that there is a reversal in the morning/midnight ratio of cortisol during Islamic fasting or shortly after that, therefore, single-point cortisol levels during this month can be misleading (32).

Concerning the adrenaline and noradrenaline alteration by Islamic fasting, Zangeneh et al reported that the serum levels of noradrenalin decrease significantly in fasting women with polycystic ovary syndrome in compare with control group, while the serum levels of adrenalin showed a decrease that was not significant. They assumed that significant decline in the levels of noradrenaline may be due to the hormonal and metabolic characteristic of the syndrome (16).

The effect of Ramadan fasting on androgens will be discussed in the “sex hormone” section.

Effect of Ramadan Fasting on Endocrine Pancreas

Pancreas is an exocrine and endocrine gland. The endocrine part contains several hormone-producing cell types classified by their secretion: α cells secrete glucagon, β cells secrete insulin, δ cells secrete somatostatin, ϵ-cell secret ghrelin, and PP cells or γ cells, secrete pancreatic polypeptide (33). Insulin, a peptide hormone, regulates the metabolism of carbohydrates and fats by elevating the cell uptake of glucose and stocking fat instead of be used for energy. Several studies has evaluated the correlation between Ramadan fasting and the serum levels of insulin and glucose. Zangeneh et al reported that there is no notable difference in concentration of insulin between fasting and non-fasting women with polycystic ovary syndrome during this month (16). Furthermore, Bouhlel et al revealed that Ramadan fasting does not have any significant effect on the plasma levels of insulin and glucose in trained men either at rest or right after exercise (19). On the other hand, Gnanou et al in a study on 20 healthy Muslim men showed that the insulin and glucose levels decrease significantly during Ramadan fasting. They also reported that Islamic fasting causes a considerable increase and decrease in insulin sensitivity and resistance, respectively. They concluded that Ramadan fasting can have a positive impact on improving insulin sensitivity (34). Moreover, decreasing insulin resistance was supported by M’GUIL et al in a study on type 2 diabetic subjects; however, they reported that insulin secretion markers (HbA1c and C-peptide) are not remarkably affected by Ramadan fasting (35).

Effect of Ramadan Fasting on Sex Hormones

Estrogen is responsible for appearing and developing secondary sex characteristics of women and maturation of reproductive organs. Progesterone is involved in lining the uterine to be prepared for pregnancy. This two hormones work together to regulate menstrual cycles. As some pregnant women fast in Ramadan month, some studies have evaluated the effects of Ramadan food restriction on mentioned hormones. In a study by Khoshdel et al on 30 fasting pregnant women, a statistically significant increase was observed in the levels of estrogen during the food restriction; but it decreased dramatically after Ramadan. They also reported that progesterone values elevated during this holy month. This pick continued until two weeks after Ramadan (36). It can be concluded that food restriction during Ramadan is not recommended for pregnant women since

it may have some risks for their pregnancy as data confirmed; although further studies on different populations with different food intake habits are needed in order to obtain more reliable results (36).

Studies regarding the effect of Islamic fasting on androgens' concentration are few. With respect to the testosterone levels during Ramadan fasting, no significant difference was found between the fasting and non-fasting groups of women with polycystic ovary syndrome (16). However, significant time related alterations in the levels of serum testosterone were reported in a study on healthy non-smoking men between fasting and non-fasting groups, in which, a lower slope of decline and a delay in the evening rise were observed in the fasting group (2).

Bahrayni et al in a case-control study on 58 pre-menarche girls showed that dehydroepiandrostenedione (DHEA) concentration decrease significantly in fasting and non-fasting groups while its changes are not significantly different between the two groups, which can be concluded that fasting do not have a notable effect on DHEA levels (P=0.58) (9).

Effect of Ramadan Fasting on Insulin-like Growth Factor 1 (IGF1)

IGF1, also known as somatomedin C, is a protein hormone produced primarily by the liver as an endocrine tissue. It has been thought that it has a key role in childhood growth and has anabolic effects in adults. Studies regarding the effect of Ramadan fasting on the concentration on IGF1 are few. In a study by Bouhlel et al, no significant alteration was found in the level of IGF1 in trained men during Ramadan fasting either following doing exercise or at rest (19). However, Forbes et al reported that IGF1 levels elevate in response to overfeeding. The difference between the results seems to be due to the different energy deficiency and physical fitness of the participants (37).

Effect of Ramadan Fasting on Adiponectin

Adiponectin is a protein hormone secreted from adipose tissue and placenta (38, 39). It regulates glucose metabolism by inducing glucose uptake in striated muscles (cardia and skeletal) and preventing liver from generating glucose, hence reducing serum glucose levels. Moreover, it elevates fatty acid oxidation by cardiac and skeletal muscles and liver (40). Limited studies have assessed the changes of adiponectin during Ramadan. Feizollahzade et al in a study on 20 healthy male subjects who had at least 3 risk factors of type 2 diabetes, observed that Islamic fasting dramatically increase the serum level of adiponectin (P< 0.000), fasting blood sugar (FBS) (P< 0.000) and triglyceride (P< 0.001) (8). About the effect of Ramadan fasting on FBS, the author believed that it might be dute to different caloric intake, duration of fasting, physical activity and genetic factors. According to this study and the role of adiponectin in reducing the risk of type 2 diabetes through the amelioration of insulin sensitivity, it can be concluded that Ramadan fasting has a positive effect on treating type 2 diabetes (8). Conversely, another study on 20 healthy Muslim men showed a considerable reduction in the serum level of adiponectin, glucose and insulin. Investigators emphasized that fall in adiponectin levels is positively correlated with the reduction in body weight (P< 0.05). However, they also declared that Islamic fasting can improve the insulin sensitivity and reduce the insulin resistance which could be resulted from loss of body weight in this study (P< 0.01) (34).

Effect of Ramadan Fasting on Leptin and Ghrelin

Leptin, a protein hormone also known as satiety hormone, has been considered to play a crucial role in regulating energy balance and food intake. It is produced by adipose cells and signals to the hypothalamus in order to generate a feeling of satiety (41, 42). It has been suggested that the diurnal rhythm of leptin secretion reaches its highest level between 22 and 3 o'clock in normal subjects and its lowest levels are between 8 and 17 o'clock (43, 44). On the other hand, ghrelin, a peptide hormone also known as the hunger hormone, plays a role in regulating appetite and use of energy by triggering ghrelin/growth hormone secretagogue receptor (GHSR) in the brain. Ghrelin is generated by ghrelinergic cells

in the gastrointestinal tract (41, 45). There are some conflicting results regarding the correlation between Ramadan fasting and the levels of leptin and ghrelin. Alzoghaibi et al evaluated the effect of Ramadan fasting on the levels of leptin and ghrelin while controlling some interfering variables such as sleep duration and sleep/wake schedule. They found no significant change in leptin levels during Ramadan except a remarkable reduction at 22 o'clock which can be considered as the result of meal time changes. Besdies, no significant difference was observed in the level of ghrelin by fasting (46). Moreover, M'GUIL et al showed that Islamic fasting do not have major effects on the levels of serum leptin in peoples with type 2 diabetes (35). In contrast, in a study by Khoshdel et al on fasting pregnant women, unusual changes were observed in the levels of leptin; it reduced until the second week of Ramadan, elevated at the end of this month and then decreased again two weeks after Ramadan. The investigators concluded that because of diminished food intake in Ramadan by pregnant women, the reduction in leptin occurred rapidly in this month (36).

On the other hand, increased levels of leptin during the Islamic fasting were observed by Kassab et al. They declared that this significant elevation in leptin levels is correlated with an increase in insulin level of the subjects which might be due to an increased caloric intake in Ramadan (47). Nevertheless, in a study on 56 stable cardiac patients, no remarkable change was observed in leptin level by diurnal fasting in Ramadan month (48).

Conclusion

In conclusion, although the modifications in lifestyle habits in Ramadan, particularly in sleep schedule, cause a number of changes in rhythmic pattern of some hormones secretion, but it causes no major alteration in the health of normal subjects. Furthermore, it seems to have some positive effects in particular diseases.

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