Review

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Physiological and Chronobiological Changes during Ramadan Intermittent Fasting

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Key Words

Islamic fasting · Fasting, meal schedule · Ramadan, circadian and hormonal changes · Ramadan, food intake · Ramadan, sleep patterns · Sleepiness during Ramadan

Abstract

Background and Aims: During the month of Ramadan, Moslems refrain from drinking and eating between sunrise and sunset. This review aimed to analyze the effects of Ramadan fasting on physiological and behavioral variables in healthy subjects. ***Methods:*** Articles included in this paper were taken from Medline, three international congresses on health and Ramadan, and in several cases from local journals. ***Results:*** Ramadan fasting did not dramatically affect the metabolism of lipids, carbohydrates and proteins, or the daily mean of hormonal serum levels. An increase in serum urea and uric acid was frequently reported and this could be attributed to dehydration during this month. Some changes, such as the increase of HDL and apoprotein A1, and the decrease in LDL, could be beneficial for the cardiovascular system. However, the chronobiological studies have shown that Ramadan fasting affects the circadian distribution of body temperature, cortisol, melatonin and glycemia. The amplitude of most of these rhythms decreased and the acrophase shifted. Nocturnal sleep, daytime alertness and psychomotor performance were decreased. ***Conclusion:*** The major changes during Ramadan fasting are chronobiological and behavioral. They could be responsible for the high incidence of road traffic accidents and the reduction of working hours during the month of Ramadan.

Introduction

Each year during the lunar month of Ramadan, adult Muslims refrain from eating, drinking, smoking or having sexual relationships during the daytime. This fasting is complete, intermittent and does not require caloric restriction. Free eating is allowed from sunset to dawn. Since Ramadan is a lunar month, its occurrence changes with time. Each year the Ramadan month occurs 11 days earlier. Consequently, each 9 years, Ramadan happens in a different season; the length and the temperature of the fasting days also change. During the last 20 years, several studies were undertaken to elucidate the effects of Ramadan fasting in healthy subjects. Their results showed discrepancies which could have several explanations. The most important one is the difference in protocols. The non-fasting control, choice of the experiment day during Ramadan and the timing of blood sampling were not always comparable. Other explanations could be related to

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the difference in nutritional customs and habits as well as the climate specificities and the seasonal occurrence of the Ramadan month.

In this review, a critical analysis of these results was undertaken in order to elucidate the Ramadan effects on biochemical, hematological, hormonal parameters and behavioral changes. A particular interest was focused on the chronobiological changes as shown by some recent studies. Articles included in this paper were taken from Medline, from three international congresses on health and Ramadan, and in several cases from local journals.

Meals and Energy Intake and Body Weight during Ramadan

The major changes in Ramadan fasting concern meal schedule and frequency. Meals are exclusively nocturnal and less frequent [1–4]. The quality and quantity of meal changes during Ramadan were related to local feeding habits. Total food intake generally decreased [1, 5, 6] but a slight increase was reported in Moroccan and Saudi populations [2, 7]. In several studies an increase in protein [2, 8–11] and lipid [2, 9, 12] intakes was observed. However, in the Moroccan population, lipid intake did not increase [7, 8]. Carbohydrate intake usually increased [1, 7, 11] but not in the Tunisian population [9, 13, 14]. Water and vegetable intake decreased during Ramadan [10–12, 15].

Body weight slightly decreased during this month [2, 5, 7, 12, 13, 16–23]. Some authors suggested that this decrease in body weight could be attributed to the decrease in fluid intake [12, 24].

Glucose, Lipids and Protein Level during Ramadan (table 1)

Several studies [16, 25, 26] have demonstrated that fasting serum glucose did not change during Ramadan. However, in the protocols of these studies, the baseline value of fasting serum glucose was taken at 8:00 or 10:00 h and compared to the Ramadan value taken at 16:00 h. The comparison of two different circadian-time values could be erroneous. When the circadian variation of glucose blood levels was determined with the blood sampling done every 2 h (except in the time of sleep which was from 2:00 to 8:00 h), the results showed that this parameter increased at 2:30 and 8:00 h and decreased at 17:30 h. The 24-hour mean decreased during Ramadan in comparison to the control day before the fasting [27]. Another study, where the blood samples were taken at 16:00 h both before and during Ramadan, confirmed the decrease in the afternoon blood glucose [28].

Studies of lipid blood level showed an increase of the total cholesterol [5, 16, 18, 24, 29–31], HDL [7, 13, 16, 31], and a decrease of LDL [7, 16, 32] and LDL/HDL [33] during Ramadan. These changes could be beneficial for the cardiovascular system [7] since HDL is protective against coronary heart disease. However, in clinical studies, the blood pressure in treated hypertensives [34, 35] and the incidence of stroke [36] did not decrease during Ramadan. In several studies, triglycerides did not vary during this month [18, 37]. However, different results were reported and some authors have demonstrated that triglycerides decreased in healthy [7, 24, 32, 37] and in obese hypercholesterolemic subjects [37, 38]. When fasting Muslims were encouraged to use low-fat and low-calorie diets, plasma cholesterol [38], LDL [39], triglycerides [38, 40] and HDL [39, 40] decreased during Ramadan compared to a non-fasting reference group following the same diet [39]. The increase of apoprotein A1 and its ratio to apoprotein B and to HDL showed in healthy [8] and in hyperlipidemic subjects [41] is another beneficial metabolic change that occurs during Ramadan.

Concerning serum protein levels, an increase was demonstrated for total proteins [16, 28, 29, 42], albumin [5, 16, 29, 42, 43], creatinine [5, 16, 31, 42–44], bilirubin [16] and hematocrit [5]. The most important change observed during Ramadan was the increase of serum uric acid [13, 18, 24, 42, 44–47], urea [32, 40, 48, 49] and serum osmolarity [42, 50]. These changes were attributed to dehydration. The increase in uric acid could also be due to an excessive breakdown of RNA tissue during Ramadan [24, 46]. A regression analysis, indicating a negative relationship between changes in uric acid level and changes in body weight [47], strengthens this hypothesis.

Electrolyte changes were also seen during Ramadan as there was a decrease in calcium, iron and magnesium [14, 42, 44, 50, 51] and an increase in phosphate blood levels [14, 16, 29]. In physically active subjects, serum osmolarity did not increase and serum iron and calcium levels did not decrease in comparison to sedentary subjects [50].

Urinary Excretion

As water intake is usually decreased, the 24-hour urine output showed a decline and urinary osmolarity showed an increase during Ramadan [21, 45] (table 1). The maximum fluid deficit occurred at the third week of Ramadan

Table 1. Biochemical variations during the beginning and the end of Ramadan month in comparison to the period before and after fasting

Variable	Before Ramadan	Beginning of Ramadan	End of Ramadan	After Ramadan	p value	Ref.
Body weight	67 ± 2.8	64 ± 2.4	65 ± 2.7	67 ± 2.7	0.0024	57
	67.6 ± 1.3	66.1 ± 1.3	65.5 ± 1.3		<0.001	20
Plasma glucose, mmol/l	5.1 ± 0.5	4.4 ± 0.28	4.38 ± 0.39	5.1 ± 0.5	<0.001	7
	5.2 ± 0.37	3.7 ± 0.61	3.8 ± 0.46		<0.001	28
	4.62 ± 0.39	4.33 ± 0.17	3.99 ± 0.11		<0.05	23
HDL, mmol/l	0.91 ± 0.21	1.01 ± 0.26	1.04 ± 0.08	1.12 ± 0.26	<0.001	7
	1.22 ± 0.2	1.22 ± 0.2	1.33 ± 0.2		<0.05	13
	0.91 ± 0.28	0.95 ± 0.23	1.13 ± 0.27	0.97 ± 0.26	<0.001	26
LDL, mmol/l	2.91 ± 0.39	2.68 ± 0.23	2.57 ± 0.23	2.57 ± 0.26	<0.001	7
LDL mg/dl	130 ± 23		91 ± 28		<0.05	32
Triglycerides, mmol/l	1.0 ± 0.42	0.76 ± 0.29	0.7 ± 0.28	0.82 ± 0.33	<0.001	7
	0.86 ± 0.09	0.38 ± 0.03	0.98 ± 0.15		<0.005	24
Apoprotein A1	2,37 ± 0.28		2,82 ± 0.23		<0.003	13
Total proteins, g/l	66.2 ± 2.9	66.5 ± 3.8	67.2 ± 2.9	65 ± 3.1	<0.05	39
Plasma uric acid, mmol/l		0.25 ± 0.01	0.3 ± 0.02		<0.05	18
	0.26 ± 0.01	0.27 ± 0.01	0.32 ± 0.02		<0.01	24
	0.29 ± 0.07	0.32 ± 0.07	0.32 ± 0.05		<0.05	44
Plasma osmolarity, mosm/l	281 ± 3.7	284 ± 4.1	286 ± 5.7	282 ± 7.3	<0.01	39
	281 ± 1.8	286.6 ± 0.5	287.6 ± 1.5		<0.05	50
	297 ± 3.2	301 ± 2	301.5 ± 3.6	299.8 ± 2.1	<0.01	21
Hematocrit, %	38 ± 4.6	42.7 ± 5	39.8 ± 4.6	39.5 ± 4.3	<0.01	21
	44.5 ± 0.8	44.8 ± 1.6	45.2 ± 0.9		<0.05	23
Urine osmolarity	754 ± 44	874 ± 38	873 ± 46	739 ± 50	<0.05	48
	881 ± 158	1,022 ± 88	920 ± 109	898 ± 91	<0.05	24
Iron, mmol/l	22.3 ± 3.7	17.6 ± 3.8	16.96 ± 1.5	19.8 ± 6.6	<0.01	39
	24.1 ± 1.3	17.0 ± 1.5	16.7 ± 0.9		<0.05	50
Hemoglobin	9.8 ± 0.7		9.1 ± 0.6		<0.02	5
Coagulation time, min	5.8 ± 1.7	6.6 ± 1.7	7.6 ± 1.7		<0.005	28
Total T cells	77.8 ± 9.4	74.6 ± 8.6	73.6 ± 4.1	75.4 ± 5.9	<0.005	53

Only significant changes are reported.

and was corrected at the end of this month [45]. These results were obtained in relatively dry countries (Sudan and Tunisia). In humid countries such as Malaysia, Ramadan fasting did not result in changes in the pattern of fluid exchange [48]. A decline in 24-hour urine acidity and in urine urea concentration was also observed [48].

Hematological Changes

Although some studies concluded that these variables did not change during Ramadan [44, 46], others have shown a decrease in hemoglobin [5, 14, 16, 31], glycated hemoglobin [52] and T-lymphocyte cells [53, 54] (table 1). Moreover, the platelet count [50] and responses to different aggregation agents decreased, leading to an increase in bleeding and coagulation time [28, 55, 56]. Antithrombin III also decreased in the morning and in the afternoon [56]. The circadian distribution of plasminogen activator inhibitor activity was altered by Ramadan fasting with an increase at 9:00 h [55]. In a recent work, the effect of Ramadan on the body's hematological balance was studied. The relationship between apoprotein, lipoprotein and the coagulation factors was analyzed. The authors concluded that Ramadan fasting altered this balance, favoring an increase of atherothrombosis complications [33]. These latter were not confirmed by a survey on the hospital admission frequency of patients with stroke [36].

Circadian and Hormonal Changes during Ramadan

Body temperature, cortisol and melatonin circadian variations are the most relevant parameters related to the circadian system. The effects of Ramadan intermittent fasting on the circadian distribution of these variables are demonstrated by several recent studies [57, 58]. The circadian analysis of data obtained each 2 min, during 48 h, showed a 2-hour delay in the acrophase, a decrease in the amplitude and no variation in the mesor of the body temperature circadian rhythm during Ramadan [57]. The shift in the acrophase and the invariability of the 24-hour mean are also demonstrated for the cortisol circadian rhythm [58, 59]. Moreover, the nocturnal increase [59–61] and the diurnal decrease in cortisol serum levels [59, 61, 62] suggest that the amplitude of cortisol rhythm is also decreased. An increase in the cortisol level at 15:00 h was also reported in a recent study where blood sampling was carried out at that point only [63].

Circadian changes in melatonin level were assessed every 4 h, and the 2:00 h point was omitted to preserve sleep [58]. This study demonstrated that the amplitude of the melatonin rhythm decreased. Omission of the 2:00 h point did not allow the analysis of the shift in the acrophase whereas the authors suggested a nocturnal shift. In the same study, the circadian changes of prolactin, GH, LH, testosterone, TSH and FSH were determined. The results showed that the circadian rhythm of TSH was flattened while that of testosterone shifted. The evening peak of PRL was enhanced [58]. The circadian rhythm of GH, LH and FSH did not change during Ramadan [58, 61].

It has previously been demonstrated that the circadian rhythm of glucose, insulin gastrin, gastric pH and calcium were altered during Ramadan [27]. The decrease in glucose was observed on the 10th day of Ramadan only, but the other circadian changes were observed at the beginning and at the end of Ramadan. The 24-hour means of gastric pH, calcium and glucose were decreased in healthy subjects and the 24-hour mean of gastrin was decreased in healed duodenal ulcer patients. Daytime insulin was decreased but the 24-hour mean was not changed. Parathyroid hormone, calcitonin, corticotrophin and β-endorphins were assessed at 9:00, 16:00, 21:00 and 4:00 h during Ramadan. The results showed that calcitonin and β-endorphins did not change while parathyroid hormone and corticotrophin were increased at 9:00 h [64]. The circadian distribution of hepatic enzymes, such as γ-glutamyltransferase, alkaline phosphatase, creatine kinase and glutamic transaminase, was also altered by Ramadan fasting. In this study, a decrease in the amplitude and a shift in the acrophase were also observed [65]. In another study with four blood sampling points (7:00, 13:00, 19:00, 21:00 h), testosterone dropped gradually during Ramadan with a significant decrease at 7:00 and 13:00 h, and an increase at 21:00 h at the end of the month [61].

From these hormonal and physiological circadian variations, it could be concluded that the major chronobiological changes during Ramadan are the flattening and the shift in the circadian rhythms. The shift is also observed in sleep-wake cycle [57].

Other studies have determined the effect of Ramadan on the blood levels of PRL, GH, LH, T_3, and T_4, using one daily blood sample. The results were controversial. Some studies showed that serum GH, LH, T_3, and T_4 concentrations did not change during Ramadan [66–68]. However, other authors reported an increase of serum thyroxine [18] and T_4 [69]. In women, both T_3 and T_4 decreased [69]. The authors hypothesized that this decrease is due to a decline in protein binding of thyroid hormones. PRL and LH levels increased during Ramadan [70].

Sleep and Alertness

In two epidemiological studies on 264 young adults [4] and 150 workers [15], bedtime sleep was significantly delayed (table 2). The percentage of people who went to sleep after midnight increased during Ramadan, as compared to the month before. Sleep duration was less than 6 h in 68% of the workers during Ramadan and 37% before Ramadan. Bad sleep was more important (65%) than thirst (19%) and hunger (7%) in causing daytime working difficulties [15]. The effect of Ramadan on sleep was also examined using the polysomnographic recordings before, at the beginning, at the end and after Ramadan [57]. Sleep latency increased and total sleep time decreased in the 10th and the 24th days of Ramadan. The proportion of non-rapid eye movement sleep increased during Ramadan, particularly stage 2 which represents the light sleep. Slow-wave sleep (deep sleep) duration and rapid eye movement sleep duration decreased [57].

As a consequence of these nocturnal sleep alterations, daytime functioning is affected by Ramadan fasting. In fact, subjective alertness, evaluated by the visual analogue scale, decreased at 9:00 and 16:00 h and increased at 23:00 h. The circadian variation of alertness was not significant during Ramadan, whereas, during the non-

Table 2. Sleep parameters, alertness, and road accident frequency during the beginning and the end of Ramadan month in comparison to the period before and after fasting

Variables	Before Ramadan	Beginning of Ramadan	End of Ramadan	After Ramadan	p value	Ref.
Bedding time, h ± min	23:48 ± 7	00:36 ± 11	00:41 ± 13	23:52 ± 15	0.0018	57
Arising time, h ± min	08:03 ± 6	08:52 ± 17	09:08 ± 18	08:32 ± 16	0.0003	57
Total sleep time, min	418 ± 12.8	374 ± 20.4	362 ± 25.9	404 ± 7.4	0.0009	57
Slow-wave sleep, min	84.7 ± 4.8	73.2 ± 8.6	64.9 ± 6.5	81.3 ± 9.3	0.0038	57
REM sleep, min	102 ± 6.7	70.1 ± 7.6	76 ± 5.9	92 ± 4.2	0.0007	57
Alertness (MSLT), min	16.7 ± 1.8	14.8 ± 2.0	11.2 ± 2.3	14.9 ± 2.0	0.007	72
Road accident frequency	21 ± 2.6	38 ± 4.8	35 ± 4.3	21 ± 2.9	0.056	86
Road accident frequency	37		68	20		84

Only significant changes are reported. MSLT = Multiple Sleep Latency Test; REM sleep = rapid eye movement sleep.

fasting period, the time effect was significant with the highest alertness rated at 9:00 and 16:00 h and the lowest at 13:00 and 23:00 h [71]. Objective measure of alertness by the multiple sleep latency test confirmed these results. Sleep latency, which is inversely proportional to sleepiness, increased during the daytime, particularly at 10:00, 12:00 and 16:00 h [72]. Psychomotor performances, such as critical flicker fusion [73] and choice reaction time [71], were especially impaired by Ramadan fasting in the first week of this month. A decrease in memory and work performance was also demonstrated in university students [11, 73]. Other studies have also demonstrated an increase in irritability [74] and a decrease in mood rating [71]. These last changes were more important in regular smokers and coffee consumers. An epidemiological study did not confirm this detrimental effect of Ramadan on mood. In fact, a study on a Jordanian population has reported that suicidal behavior decreased during Ramadan [75].

Physical and Sportive Performances

Only a few studies are available concerning the alteration of physical performance during Ramadan, and they concerned sedentary and sportive subjects. During Ramadan, sedentary subjects usually practice a recreational physical activity in the afternoon, before the breaking of fast meal. It was then important to quantify the physiological changes in this situation. Heart rate did not change in sedentary subjects during a submaximal exercise. However, the respiratory exchange ratio during steady-state submaximal exercise decreased markedly by the end of the month of Ramadan [50]. During a moderately heavy aerobic exercise, the heart rate and ventilatory responses were significantly reduced. Systolic but not diastolic blood pressure increased by the end of Ramadan [76–78]. The submaximal oxygen consumption and respiratory rate decreased during Ramadan in subjects walking at 2.5 mph and 4% grade [12]. In this case, ventilation rate and heart rate did not change. The decrease in VO_{2max} may be attributed to dehydration [79].

In sportive subjects, both physiological changes and sportive performances were reported. Sportive students' diets were low in fat and carbohydrates and normal in protein. A 24% decrease in the daily energy intake was observed [80]. Sportive performance decreased in high school sport students tested in 100- and 800-meter races [81]. In fighter pilots, two studies have demonstrated that Ramadan fasting has deleterious effects on muscle performances and on orthostatic tolerance [23, 82]. This effect persisted during several days after Ramadan. Finally, in young men of the Senegalese army, the capacity of the human organism and its thermoregulation to endure submaximal exercise during the Ramadan fast in hot climates (Sahelian area) was tested. The heart rate and mechanical power were measured before and during 30 min of submaximal exercise. In both cases, muscular activity was well tolerated, but the physical performance produced during 30 min was significantly lower during Ramadan [83]. The authors generally suggested that these physiological responses and such decreases in sportive performance are attributed to dehydration, to the daily refraining from food consumption and to modification of the sleep-wake cycle [50, 77, 78].

Road Accidents

Human factors such as lower alertness and higher irritability shown during Ramadan represent a risk for traffic accidents (table 2). A study in the accident and emergency department in a Saudi hospital reported that the highest attendance of traffic accident victims is observed during Ramadan [84]. The same result was obtained in an emergency hospital in the United Arab Emirates [85] and in a hospital in London where accident-related attendances among Muslims were higher compared to non-Muslims and to the attendances before Ramadan [86]. Consequently, measures are necessary to prevent traffic or work accidents during Ramadan. Such measures can only be achieved by adapting special working conditions for the fasting month of Ramadan, particularly for people whose work requires extreme alertness. Some of these people, like long-distance drivers and pilots, have the religious permission to refrain from fasting.

Conclusion

Ramadan fasting did not result in health-harmful changes of the lipid, carbohydrate and protein metabolism, or in the daily mean of hormonal serum levels in healthy subjects. Some changes, such as the increase of HDL and apoprotein A, and the decrease in LDL, could be beneficial for the cardiovascular system. However, the chronobiological effects of Ramadan intermittent fasting could result in a decrease of sleep quality, diurnal alertness, psychomotor and physical performances. These latter changes are responsible for the high incidence of road traffic accidents, performance at work and reduction of working hours during the month of Ramadan.

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