Effect of intermittent fasting and chronotherapy on blood pressure control in hypertensive patients during Ramadan

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Abstract

Background: During Ramadan, repeated cycles of fasting, associated with alterations in the daily patterns of sleep, activities and medication timing might contribute to changes in blood pressure (BP) and heart rate among hypertensive patients. Studies on the effects of fasting on the blood pressure of hypertensive patients are rare, and have provided inconclusive results. The aim of this study was to examine the effect of medication timing during Ramadan on blood pressure and heart rate in hypertensive individuals taking their treatment once daily.

Material and methods: The study prospectively recruited 44 hypertensive patients between April and June 2019, followed up at the cardiology department of Habib Thameur Hospital in Tunis. A 24-hour blood pressure monitoring was carried out during two periods: prior to Ramadan and during the last ten days of Ramadan. We compared the average values of 24-hour awake and asleep systolic and diastolic blood pressure and 24-hour awake and asleep heart rate.

Results: We studied 29 women and 15 men, mean age was 58.7 years. Fifteen patients were diabetics, 20 had dyslipidemia and 7 patients had coronaropathy. Twenty patients were on monotherapy, 19 on dual therapy and 5 on a triple antihypertensive therapy. During Ramadan, 25 patients took their treatment during the dinner (group1), whereas 19 took their treatment during the S'hour (group 2). Average 24-hour blood pressure in the whole group was 129 ± 18/74 ± 10 mm Hg before Ramadan and 129 ± 19/74 ± 10 mm Hg during Ramadan ($p > 0.05$). Daytime and night-time mean values of systolic and diastolic blood pressure as well as mean values of heart rate were not different between both periods regardless of age and gender. However, during Ramadan, those who took their treatment after dinner had significantly higher values of 24-hour systolic BP, awake systolic and diastolic BP, asleep systolic and diastolic BP than those who took their treatment with the S'hour ($p < 0.05$).

Conclusions: In this study, there were no significant changes in systolic and diastolic blood pressures or in heart rate during the 2 periods. However, during Ramadan, a slight superiority of taking the treatment with the S'hour is observed.

Key words: hypertension; fasting; ambulatory blood pressure monitoring; chronotherapy

Arterial Hypertens. 2022, vol. 26, no. 2, pages: 67–72
DOI: 10.5603/AH.a2021.0019

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Introduction

Fasting during Ramadan means abstention from food, liquids, tobacco, medication (oral, inhaler or injection) and sexual activity from sunrise to sunset. The S'hour is the last meal of the night, taken before dawn. Food and fluids are consumed only at night.

During this month, repeated cycles of fasting, associated with alterations in the daily patterns of sleep, activities and medication timing might contribute to changes in blood pressure and heart rate among hypertensive patients.

Fasting can lead to worsening of cardiovascular disease, dehydration, hypoglycemia, hyperglycemia, and hypertensive peaks [1]. Each year, doctors have to decide with patients with high cardiovascular risk their ability to fast, as well as their therapeutic adaptations to be made, and the methods of the monitoring [2].

Studies on the effects of fasting on the blood pressure and heart rate of hypertensive patients are rare, and have provided inconclusive results.

It is therefore essential for any cardiologist to objectively assess the safety of fasting during this holy month, in order to improve the care of his/her patients and guarantee their physical and psychological well-being.

The aim of this study was to examine the effect of medication timing during Ramadan on blood pressure and heart rate in hypertensive patients taking their treatment once daily.

Materials and methods

This was a descriptive cross-sectional, single-center study including 44 known, reliable and compliant hypertensive patients. After giving their informed consent, they were enrolled between April and June 2019 (one month before and during the month of Ramadan) and followed up at the cardiology department of Habib Thameur Hospital in Tunis.

Tunisia is a country in Northern Africa, bordering the Mediterranean Sea. Tunisia has a highly homogeneous population, almost entirely of Arab and Berber descent. The climate is Mediterranean in the north and along the coast, semi-arid in the interior and arid in the south.

The month of Ramadan took place in the spring, from May 05 to June 05, 2019. Fasting started at 3:30 a.m. and ended at 7:30 p.m., an average of 16 hours a day. The average temperature was 21°C with extremes ranging from 18 to 24°C.

We received the ethical approval from the Bioethics Committee of Habib Thameur hospital.

We included hypertensive patients over 18 years old taking their treatment once daily. The non-inclusion criteria were patients who do not fast during Ramadan and those with diabetes treated with insulin. We excluded patients who did an incomplete fast during Ramadan, and those who had less than two usable ambulatory blood pressure monitoring (ABPM).

We performed an individual interview with each patient, during which a clinical examination was carried out [age, gender, body mass index (BMI), age at diagnosis of the hypertension, comorbidities, treatment, and lifestyle].

The following blood tests were requested for each patient: blood sugar levels, glycated hemoglobin (HbA_{1c}), serum electrolytes and creatinine, hemoglobin, total cholesterol level (TC), low-density lipoproteins (LDL), high-density lipoproteins (HDL), and triglycerides (TG).

A 24-hour blood pressure monitoring was carried out during two periods: prior to Ramadan and during the last ten days of Ramadan, using an ambulatory blood pressure monitoring (GIMA 2018, ABPM 50, Contec Medical Systems Co., Ltd.).

All the monitoring sessions started at approximately the same time in the morning at 10 am (within a 2-hour interval). The cuff was placed on the non-dominant arm and removed after 24 hours for the monitoring of the blood pressure and heart rate. Calibration was checked by comparing the auscultatory results with those by a mercury sphygmomanometer, which were verified to be in close agreement (5 mm Hg). Blood pressure was measured three times per hour between 7.00 am and 11.00 pm, and twice per hour between 11.00 pm and 7.00 am. Subjects were instructed to immobilize their arms during cuff inflation.

The data were then analyzed using the following software: ABPM V4.5.0, Copyright © 2015. A minimum of 70% usable BP recordings are required for a valid ABPM measurement session.

For both periods (period A: ABPM one month before Ramadan, and period B: ABPM during the last ten days of Ramadan) we compared the average values of 24-hour systolic and diastolic blood pressure; awake systolic and diastolic blood pressure; asleep systolic and diastolic blood pressure; 24-hour, awake and asleep heart rate. The software R version 3.6.3 was used to perform the statistical analysis. We used the Student's t-test to compare data within the periods. We verified the normality of distribution by a Shapiro-Wilk test.

P-value < 0.05 was considered statistically significant for all tests.

Results

Our population was made up of 29 women and 15 men, with an average age of 58.7 years. The average BMI of our patients was 28.75 ± 4.67 kg/m² with extremes ranging from 21.07 to 41.31 kg/m². Thirty-seven patients were at least overweight, of whom 19 were obese.

Among our patients, 15 were diabetics, 20 had dyslipidemia, 7 had a coronaropathy, and 17 were active smokers.

The patients in our study have been hypertensive for a period ranging from 1 to 30 years, with an average of 7.15 years. If we consider the treatment, 20 were on monotherapy (10 patients taking ACE inhibitors, 7 taking ARBs, 2 patients taking calcium channel blockers and one patient on a beta-blocker), 19 on dual therapy (13 patients taking a combination of a calcium channel blocker and an ACE inhibitors, 6 patients taking a combination of an ARB and a diuretic) and 5 on triple antihypertensive therapy (a calcium channel blocker + an ACE inhibitor or an ARB + a diuretic).

During the month of Ramadan, the antihypertensive treatment schedule differs from one patient to another. Twenty-five patients took their treatment after dinner (group 1), and 19 during the S'hour (group 2).

All patient biological parameters are summarized in Table 1.

In our study, the average 24h ambulatory blood pressure in the whole group was 129 ± 18/74 ± 10 mm Hg before Ramadan and 129 ± 19/74 ± 10 mm Hg during Ramadan (p > 0.05). Daytime and night-time mean values of systolic and diastolic blood pressure as well as the mean values of heart rate were not different between the periods.

Regardless of age, we found a significantly higher value of average asleep systolic blood pressure in women in comparison with men before Ramadan.

We also compared the average values of blood pressure and heart rate according to age (older/younger than 60 years old), BMI (over than 25 kg/m² or less), duration of hypertension with a cutoff of 5 years, medical history such as the presence of diabetes, dyslipidemia, coronaropathy, smoking and diet. We found out that there are no significant differences between the groups in both periods.

By comparing groups 1 and 2 during the last 10 days of Ramadan, we found significant higher values of 24-hour systolic average BP, awake systolic and diastolic average BP, asleep systolic and diastolic average BP in the patients who took their treatment during dinner (p < 0.05).

The average values are summarized in Table 2.

Table 1. Biological parameters of the patients

Parameters	Average and standard deviation	Extremes
HbA_{1c} [%]	6.07 ± 0.81	[4.1–7.95]
Glycemia [mmol/L]	6.27 ± 1.44	[4.41–13.32]
Creatinine [μmol/L]	68.95 ± 17.43	[36–119]
Natremia [mmol/L]	138.6 ± 2.4	[134–144]
Kaliemia [mmol/L]	3.9 ± 0.3	[3.4–5]
TC [mmol/L]	5.00 ± 0.93	[2.76–6.93]
TG [mmol/L]	1.25 ± 0.51	[0.30–3.71]
HDL [mmol/L]	1.18 ± 0.23	[0.80–1.90]
LDL [g/L]	1.19 ± 0.32	[0.46–1.90]
Hemoglobin [g/dL]	13.2 ± 1.4	[9.80–16.50]

HbA_{1c} — glycated hemoglobin, TC — total cholesterol; TG — triglycerides; HDL — high-density lipoproteins; LDL — low-density lipoproteins

Table 2. Comparison of groups 1 and 2 during Ramadan

	Group 1	Group 2	p
24 hour systolic average BP [mm Hg]	134 ± 23	122 ± 6	0.017
24 hour diastolic average BP [mm Hg]	76 ± 12	70 ± 5	0.052
Awake systolic average BP [mm Hg]	138 ± 23	125 ± 6	0.012
Awake diastolic average BP [mm Hg]	79 ± 12	73 ± 5	0.044
Asleep systolic average BP [mm Hg]	127 ± 26	114 ± 12	0.030
Asleep diastolic average BP [mm Hg]	71 ± 13	65 ± 7	0.045
24 hour average heart rate [bpm]	71 ± 7	70 ± 6	0.524
Awake average heart rate [bpm]	76 ± 7	74 ± 7	0.322
Asleep average heart rate [bpm]	65 ± 7	65 ± 7	0.931

BP — blood pressure; bpm — beats per minute

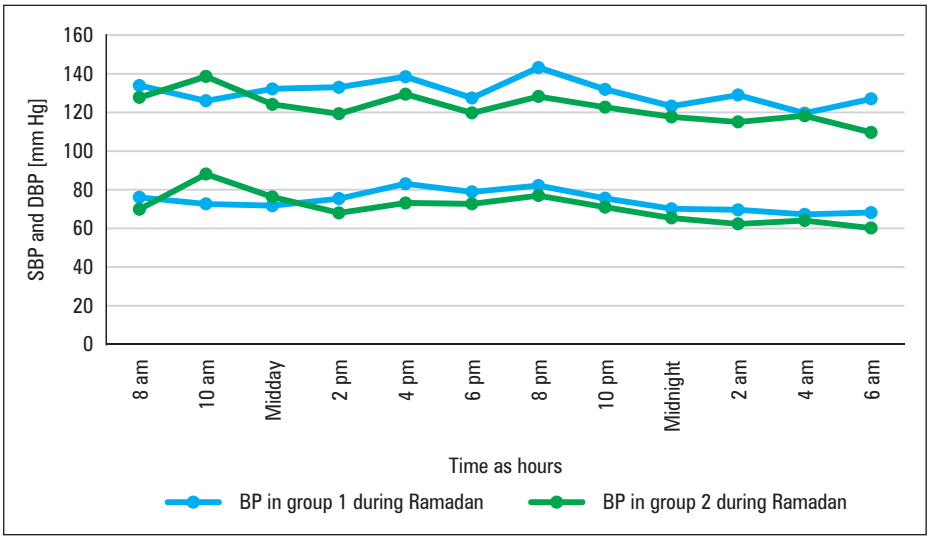

Figure 1. 24-hour profile of blood pressure (BP) values during the last ten days of Ramadan in groups 1 and 2. SBP — systolic blood pressure; DBP — diastolic blood pressure

Figure 1 is a representation of the 24-hour profile of blood pressure values during the last ten days of Ramadan in groups 1 and 2.

Discussion

Characteristics of the study population

Gender and BMI

Our population was made up of 29 women and 15 men. Women were certainly more willing to perform multiple visits than men. Regardless of age, we found a significantly higher value of average asleep systolic blood pressure in women in comparison with men in period A. In contrast to our results, several studies have shown that there is a significant difference between men and women where men have a higher prevalence of hypertension and higher values of blood pressure from 20 to 65 years then the difference between the two genders is narrowed [3].

However, as far as we know, there are no large-scale studies that have yielded results powerful enough to change recommendations about hypertension according to gender [4].

The average BMI of our patients was 28.75 ± 4.67 kg/m² with extremes ranging from 21.07 to 41.31 kg/m².

Several studies showed that a normal BMI was associated with a lower prevalence of cardiovascular diseases [5]. The link between obesity and hypertension is complex. A high BMI is one the principal risk factors for hypertension [6, 7] and as a result the prevalence of hypertension increases with a rising BMI [8, 9].

Medical history

In our study, 15 patients were diabetics, 10 under treatment and 5 on a diet. In a study carried out in Algeria, in Ain Taya, involving 1511 patients, Biad et al. found that the prevalence of diabetes in the population of hypertensive patients was 22.7% [10].

As we all know, type 2 diabetes and hypertension are often present as part of the metabolic syndrome [11].

Moreover, 20 patients were dyslipidemic, 15 on lipid-lowering therapy and 5 on a diet.

By analyzing three reports from the National Health and Nutrition Examination Surveys from 1988 to 2010, Egan et al. [12] showed that 60.7 to 64.3 % of hypertensive patients also had hypercholesterolemia.

If we consider the hypotensive treatment, among our patients, 20 were on monotherapy, 19 on dual therapy and 5 on a triple antihypertensive therapy.

Our results are in line with those of the French Mona Lisa study that has involved 4825 hypertensive patients of which 47% received monotherapy, 34% were on dual therapy and 19% on a triple therapy [13]10 year-age group (35–74 years).

Chronotherapy

Many functions of the organism, such as heart rate and blood pressure, are subject to fluctuations during the day [14].

In healthy subjects, we can see a nocturnal decrease in blood pressure (10 to 20 mm Hg) called dipping. In some patients, however, this daily rhythm is abolished, resulting in an insufficient decrease or even an increase in their blood pressure during the night [15].

The day/night cycle of blood pressure and heart rate may vary due to activities. It has been demonstrated that subjects with variable work shifts have a reversed circadian rhythm. This adaptation is rapid since it can be observed from the first day of change (from daytime to night-time break, for example) [16].

A number of published trials have reported that taking the treatment in the morning or at night, may interfere with the efficiency, the duration of action and the safety profile of the antihypertensive drugs [17].

Taking at least one hypotensive medication in the evening may improve the control of blood pressure and reduce the risk of significant cardiovascular morbidity and mortality [17].

Given the importance of chronotherapy in hypertension, and the significant changes in the circadian rhythm during the month of Ramadan, it is necessary to know the therapeutic adaptations to be made to avoid or to minimize cardiovascular morbidity and mortality.

During Ramadan, patients have to take their treatments between sunset and sunrise, trying to keep the same therapeutic pattern as before this month.

Among our patients, 20 were on monotherapy, 19 on dual therapy and 5 on a triple antihypertensive therapy. Mzoughi et al., in 2006, included 20 hypertensive patients and compared their BP before and during Ramadan. This study found that the sub-group of the patients under monotherapy had significant increase in the average night-time BP (systolic asleep BP during Ramadan 119.5 ± 15 *vs.* 113.5 ± 14.3 before Ramadan ; p = 0.05 and diastolic asleep BP during Ramadan 67 ± 14.4 *vs.* 63 ± 15 before Ramadan; p = 0.02) [18].

In our study, patients were divided into two groups: 25 took their treatment during dinner and 19 during the S'hour.

During Ramadan, those who took their treatment after dinner had significant higher values of 24-hour average systolic blood pressure (SBP), average awake SBP and diastolic blood pressure (DBP), average asleep SBP and DBP than those who took their treatment with the S'hour ($p < 0.05$).

This is a further proof that chronotherapy, especially during the month of Ramadan, is an essential element that needs to be studied in greater depth in order to provide better management of hypertensive patients.

Study limitations

The weak points of our study were:

- the single-center nature of the study with a low population size;
- the limited repeatability of the ABPM;
- the lack of accurate data on patient dietary surveys: the nutritional value of food could not be objectively assessed as it was based on patients' self-reporting;
- for technical reasons, we were unable to carry out systematic medical laboratory tests during the month of Ramadan to compare the results in both periods;
- we studied the impact of the month of Ramadan when it occurred during summer, the hot season, which did not allow us to generalize the results;
- no power analysis was performed prior the study. The number 44 was not determined before the start of the study. These are the patients who consented to come to the hospital for the ABPM 2 times.

Conclusion

In this study, there were no significant changes in systolic and diastolic blood pressures as well as heart rate during the 2 periods. However, during Ramadan, a slightly better result is observed when taking the treatment with the S'hour. In order to elaborate recommendations on the management of patients with cardiovascular risk during Ramadan, it would be necessary to conduct an international randomized single-center study.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of interests

None declared.

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