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Research Article

The Effect of Zeitgeber (Fasting and Exercise) on Phase Advance Blood Glucose Circadian Rhythms in Endurance Athletes

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Abstract

Objectives: Fasting is usually associated with changes in the metabolic, psychological and physiological responses of athletes; advancing and/or delaying their biological clock and therefore, affecting their sport performance. The aim of this study was to assess the effect of Ramadan fasting on blood glucose level, mean arterial pressure (MAP), heart rate (HR) and skin temperature in 11 experienced endurance athletes.
Methods: The study was conducted during the third and fourth weeks of Ramadan (26 May - 24 June 2017). Eleven northwest African male endurance runners volunteered to participate in this study (mean $\pm$ SD: Age 32 $\pm$ 8 years, mass 64 $\pm$ 5 kg, and height 1.72 $\pm$ 0.05 cm). All participants regularly trained between 18:00 - 19:00; aiming to complete their training close to the time of breaking of fast to allow for rapid rehydration and avoiding any health complications. Blood finger-pricking, blood pressure (BP), HR and skin temperature samples were taken every 2 hours over a 24-hour period during the 3rd or 4th weeks of Ramadan. Data were analysed using a two-way repeated measures ANOVA with Bonferroni-adjusted post hoc tests.
Results: A clear within-day variation was revealed in blood glucose concentrations and HR ($P < 0.05$). Blood glucose concentration variation was directly associated with exercise and food intake but significant peaks were also observed prior to breaking fast. These peaks corresponded to the start of athlete's usual daily routine and suggest the athletes were able to phase advance blood glucose circadian rhythms.
Conclusions: The data presented demonstrates the combination of exercise and fasting phase shifted and adjusted the blood glucose concentration to start rising prior to training session.

Keywords: Blood Glucose, Fasting, Circadian Rhythm

1. Background

Numerous studies have shown the benefits of fasting in the general population in terms of overall health, weight loss and sports performance (1-3). In contrast, there is a shortage of evidence-based support for the effect of fasting in phase shifting and advancing physiological measures in experienced athletes.

Muslim athletes are required to totally abstain from both food and drink from sunrise to sunset during the 29/30 days of Ramadan. This form of food restraint is likely to have implications for both training and performance of competitive athletes (4). A reduction in the composition of the diet and total energy intake may occur during Ramadan, with a late evening meal and an early breakfast causing sleep interruption or deprivation (5). However, most individuals observe an overnight fast on a daily basis, and the human body copes well with this short fasting duration (6). In the absence of physical activity, this type of fasting has little or no effect on muscle glycogen stores. Because muscle glycogen stores are not depleted by fasting, it does not appear to negatively affect performance on most types of exercise (7).

There are clearly psychological and physiological changes associated with periods of fasting but limited evidence of it having an effect on exercise performance (8). The evidence suggests that the effects of fasting vary depending on the individuals and/or the sport in which they partake. More experienced athletes develop effective coping strategies to accommodate their food restraint or total intake allowances within their competition and training programs. There is growing evidence that supports the role of nutrition intake in promoting the adaptive responses of athlete muscle tissues to a training

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stimulus and affect gene expression in the post-exercise period (9, 10). It is also well known that exercise improves insulin sensitivity post-exercise through multiple adaptations in glucose transport and metabolism. Fasting has little effect on resting blood glucose in non-athletic individuals, showing only a mild decrease in the early weeks of Ramadan, but remaining within clinical limits (11, 12). Whereas, in athletic populations, Faye (13) reported missing breakfast will lead to a progressive decrease in blood glucose during the daytime, which may lead to a severe pre-race or training hypoglycaemia. In this regard, it was recommended that a higher intensity of exercise is required during the warm-up session in the fasted state, as this triggers a rapid breakdown of liver glycogen and the mobilized glucose could then be used as supplementary energy for muscular contractions during the training session or competition (5).

Regardless of exercise intensity, experts recommend that training sessions during daytime in Ramadan do not last longer than 75 minutes to avoid developing hypoglycaemia (14). This is due to the fact that endogenous muscle glycogen will not deplete and will affect exercise capacity and performance (9). In addition, athletes encountered a higher risk of musculoskeletal injury when they experiencing greater levels of fatigue; with fatigue more likely during periods of fasting during which energy stores are depleted (15).

One theory for the impact of fasting or meal skipping on blood glucose levels in conjunction with exercise is the existence of circadian rhythms. Fasting is similar to the way other physiological changes are regulated and controlled by the biological clock. The existence of circadian rhythms has been found to occur in a wide range of cell functions (16). The mechanism of a cell's circadian rhythms is still not fully understood, but protein synthesis is critical to the process. The secretions of glucose and insulin (a hormone important for regulating the metabolism of glucose) exhibit circadian rhythms, with peak blood glucose waking time. There 21:00 in non-fasting individuals (17). Circadian rhythms are self-sustaining or "free-running" under constant environmental conditions, but this rhythmicity can be altered by changes in these conditions. For example, changes in light intensity and/or duration can result in these rhythms shifting over time (Aschoff's rule) (18). Another effect that may confound interpretation of rhythm waveforms in humans is masking, where a circadian rhythm is temporarily influenced by exogenous components such as fasting. The failure to control the masking factors has a large impact on the result of each study, and hence the true influence of circadian rhythmicity on sporting performance (19, 20).

It is well documented that Ramadan fasting affects circadian rhythm patterns, impacting physiological, metabolic, and endocrine function as well as blood glucose and body temperature (21-23). To our knowledge, no investigators have studied the effect of zeitgeber (time giver) in blood glucose circadian rhythms in endurance athletes during a 24 hour period (with a minimum of 6 training sessions a week and for a duration of no less than 1 hour in each running session).

2. Objectives

Our study was designed to examine the effect of fasting during Ramadan on blood glucose levels in highly trained athletes, considering the influence of circadian rhythms in other physiological parameters including heart rate, mean arterial pressure and skin temperature.

3. Methods

The study was conducted during the third and fourth weeks of Ramadan (26 May - 24 June 2017). Excluding the initial two weeks of fasting allows for the body to adapt to fasting and prevents any bias. The average fasting time was 16 hours ± 12 mins. The local meteorological conditions during the investigative period were as follows: Mean temperature 27 ± 1.4 °C, humidity 73 ± 5.2. Eleven northwest African male endurance runners volunteered to participate in this study (mean ± SD: Age 32 ± 8 years, mass 64 ± 5 kg, and height 1.72 ± 0.05 cm). All participants were injury free with no chronic or short-term illness reported.

All participants regularly trained between 18:00 - 19:00; aiming to complete their training close to the time of breaking of fast to allow for rapid rehydration and avoiding any health complications. The inclusion criteria included all participants were endurance runners, running between 10 - 20 km for daily training sessions and a minimum of 80 km per week. Approximately, 20 - 40% of each daily training session involved high-intensity training. All participants provided fully informed consent before engaging with the experiment and were free to withdraw from the study at any stage. All procedures performed in studies involving human participants were in accordance with the ethical standards with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

3.1. Skin Temperature

Using a skin infrared device (Testo, 380-TI-UK) on the forehead, the temperature was measured using the method described in the instruction manual of the device by placing the infrared on the forehead waiting 3 seconds for the digital reading to occur and recording the reading. The reading was collected every 2 hours for a period of 24 hours.

3.2. Blood Pressure and HR

Every 2 hours for a period of 24 hours, at resting state (BP) blood pressure was measured in the seated position using an electronic mercury sphygmomanometer (Wrist, Omron, 5-1, Japan). Participants were advised to wear loose-fitting clothes such as a t-shirt to allow the sleeve to be pushed up comfortably if needed. The same arm was used for measurement each time. With the arm extended in a relaxed position and the palm facing up, a blood pressure cuff was placed approximately 5 cm above the elbow joint. Afterwards blood pressure was automatically measured and the result was displayed on the device screen. Mean arterial pressure was calculated using Equation 1:

$$MAP = \frac{(2 \times diastolic) + systolic}{3} \quad (1)$$

The device used to measure BP was also designed to read HR and the HR result was recorded at the same time as BP measurement.

3.3. Blood Glucose Measurement

Blood glucose measurement was conducted in accordance with Pickering and Marsden method (24). Subjects were instructed to self-monitor blood glucose using finger-prick blood samples, test strips, and a portable Abbott Optium Xceed blood glucose meter (Freestyle Optium). The reading was collected every 2 hours for a period of 24 hours.

3.4. Statistical Analysis

Prior to statistical analysis, all data were checked for normality. Data were analysed using a two-way repeated measures ANOVA with Bonferroni-adjusted post hoc tests to determine the difference at which time point the diurnal variation occurred (SPSS20 statistical software, IBM, UK). Statistical significance was accepted at $P < 0.05$. Results are represented as mean values $\pm$ standard deviation (SD).

4. Results

There was a circadian rhythm in HR ($P < 0.02$, partial $\eta^2 = 0.9$) (Figure 1A). A peak HR was recorded at 18:00 due to zeitgeber with a nadir recorded during the daytime at 14:00. MAP did not show a significant difference ($P > 0.05$) (Figure 1B). However, the peak value was recorded at 18:00 coinciding with the HR peak and nadir was recorded at 08:00 at waking time. There was no circadian rhythm in skin temperature ($P > 0.05$) (Figure 1C). However, the mean nadir skin temperature was recorded at 18:00 and the mean peak skin temperature was reported at 14:00. A significant diurnal difference was reported in blood glucose concentration ($P < 0.01$, partial $\eta^2 = 0.9$) (Figure 1D). The nadir and the peak were recorded at 16:00 and 20:00, respectively. The amplitude between the nadir and the peak of blood glucose was 27%. Another peak of blood glucose concentration was recorded at 04:00, which coincided with pre-sunrise breakfast.

5. Discussion

Our findings add to the existing literature by defining a major impact of circadian rhythm on exercise performance during Ramadan fasting (7, 11, 12). Our study is unique because most studies have evaluated circadian variations under conditions of continuous food intake or glucose infusion, especially with a clinical population. This research has assessed the effect of Ramadan fasting on glucose level circadian rhythm in 11 well-trained endurance runners during a 24-hour period in the third and fourth week of Ramadan. Blood glucose peaked at 20:00 and 04:00, which is directly related to food intake (20:00 breaking-of-fasting, 04:00 early breakfast) and the nadir level was recorded at 16:00, which was directly affected by the duration of fasting (12 hours since last food intake). Skin temperature, HR and MAP were directly controlled by physical activity or rest. HR and MAP peaked at 18:00 coinciding with the athletes' training time. In addition, a fall in skin temperature during the initial stage of training was recorded at 18:00 and a peak at 12:00. This was probably associated with the cutaneous vasoconstrictor response to exercise (25).

During exercise, a slight drop in blood glucose circulating in the bloodstream is known to occur. The body responds to this slight decrease by producing glucagon and epinephrine, stimulating the liver and muscles to convert the stored glycogen into glucose and releasing it into the bloodstream for immediate use during exercise (26). Surprisingly, in our study, pre-anticipation of exercise caused the body to release glycogen into the bloodstream pre-exercise (17:00 - 19:00). Our participants' pre-training rise in the level of blood glucose is unexplainable, and to the best of our knowledge, this is the first study to report this finding. This glucose secretion into the bloodstream was at least 1 hour prior to the training session, which contradicts the expected daily nadir in blood glucose concentration due to the length of fasting hours at pre-training phase (< 12 hours). In other words, due to the time of the

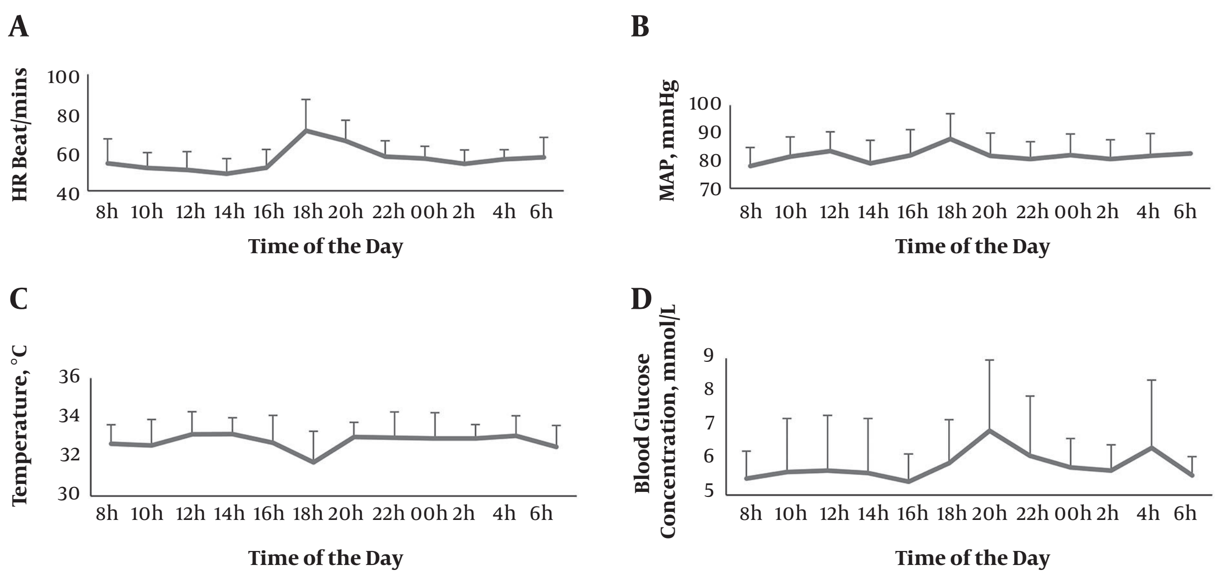

Figure 1. Variations in A, HR; B, MAP; C, Temperature; D, blood glucose concentration during a 24 hour period. Values show mean and standard deviation.

training session, the athlete's body was able to phase advance blood glucose circadian rhythms. It is important to note that the research was conducted in the 3rd and 4th weeks of Ramadan, allowing for adaptation to fasting to have occurred. This finding may indicate that daily afternoon training during Ramadan in our participants has the potential to retrain their circadian pacemaker through phase advancing.

Athletes are required to produce optimal performance or be at their best at a specific time of day and including long fasting hours during Ramadan. However, it has been suggested that the effects of zeitgebers may influence psychological functioning (27). Mental preparation may have had a direct effect on the pre-training rise in blood glucose that occurred in the absence of food intake. Kobrick and Johnson (20, 27) stated that environmental changes may influence the psychological aspects before they affect physiological factors. This suggests that in our study mental preparation triggered blood glycogen to be released in the athlete's muscles prior to the training session. This type of chemical change within the body has been observed to some extent by Miyazaki (28) who found that, in participants who exercised, plasma melatonin was phase-advanced significantly during the waking period, whereas melatonin rhythmicity did not change in non-exercising participants. However, to date, it is still not fully understood whether this phase shift is directly affected by exercise or a combination of other factors, such as the increase in body temperature as a response to exercise.

Despite our findings, we acknowledge a number of limitations. Firstly, within the field setting of this study, participants were exposed to different zeitgeber and we are unable to determine the exact mechanism underlying our findings due to complex and interrelated interactions. However, measuring other hormonal variables such as cortisol and melatonin would help bring clarity to these results, elucidating further the prevailing mechanisms causing this phase advance in blood glucose. The absence of a control group is also a limiting factor in this study, which was unavoidable due to Ramadan being observed by all available athletes.

The mechanism(s) that induced physical exercise to phase shift the circadian rhythm is not yet known. Our study's findings suggest that timed physical exercise during Ramadan fasting produced phase-advance shifts in our participant's blood glucose. In addition, these findings suggest that physical exercise during fasting is useful to adjust the circadian rhythm to external time cues, especially in highly trained athletes. These findings could be applied within populations with chronic diseases such as diabetes, by using exercise and fasting for therapeutic use or timing of medication administration.

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Footnotes

Authors' Contribution: Study concept and design: Boukhemis Boukelia, Abdelhakim Sabba and Mark Fogarty. Analysis and interpretation of data: Boukhemis Boukelia.

Conflict of Interests: The authors were wholly responsible for the research conducted in this paper and present the work without conflict of interest.

Ethical Considerations: This study is ethically approved by Test4sport limited.

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