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Review

Ramadan and diabetes: What we see, learn and understand from continuous glucose monitoring

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Abstract

Abstinence from eating and drinking from dawn to sunset characterizes the holy month of Ramadan. For the 50 million Muslims worldwide with diabetes who adhere to this religious fast, the practice results in marked changes in glucose homoeostasis. The sunset meal (*Iftar*) that breaks the fasting state is followed by exaggerated surges in blood glucose and sustained overnight hyperglycaemia in cases of nocturnal overfeeding. The predawn meal (*Suhoor*) frequently results in prolonged glucose decay over the daylight hours. These glycaemic disturbances are particularly marked in insulin-treated patients, in those with unsatisfactory diabetes control during the pre-Ramadan period and in patients who are poorly compliant with lifestyle recommendations. Whether such patients should be exempt from the Islamic fast remains an open debate, which might be partially resolved by long-term controlled studies using the technology of continuous glucose monitoring in large populations of patients with diabetes.
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1. Introduction

Among the 1.6 billion Muslims in the world's population, 5% (approximately 80 million) are affected by diabetes [1,2]. Considering that two-thirds of them fast during Ramadan [3], it may be estimated that more than 50 million Muslim people with diabetes participate in the religious fast every year [4]. Although all religions provide recommendations to their congregations for spiritual fasting periods [5], Islam is probably the only one that sets its adherents upon such long periods of fasting, characterized by abstinence from eating and drinking from dawn to sunset during the holy month of Ramadan. In people with diabetes, such periods of intermittent fasting affect both the regularity and contents of meals. At least in insulin-treated patients, any disruption of the recommended stable dietary planning [6] is at risk of triggering adverse effects on glycaemic control, as the timing and doses of insulin injections are set according to mealtimes and amounts of carbohydrates ingested at each consistent meal. When the fasting state during Ramadan exceeds several hours, striking metabolic disorders, characterized by an increased mobilization of fatty acids from adipose tissue, can arise [7]. In type 2 diabetes (T2D), the release of fatty acids contributes to an increase of insulin resistance in muscles and other target sites [8], as well as to an additional impairment of glucose homoeostasis.

Bringing all these observations together, it appears that either permission for or exemption from fasting should be decided upon after carefully weighing the respective advantages and disadvantages. In 1995, experts at an international consensus meeting held in Casablanca [9] stated that patients with stable T2D without progressive comorbid pathology and treated with oral antidiabetic agents could safely receive authorization for undertaking the Islamic fast. Nevertheless, many other situations

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were left open to debate. The present review aims to revisit the usual guidelines by integrating new scientific findings that have arisen from recent studies using the technology of continuous glucose monitoring [10–12].

2. Chronic Ramadan dysglycaemia: lessons from observational studies

Acute adverse events such as severe hyperglycaemia or hypoglycaemia are usually reported during Ramadan [3]. Such events are probably due to inappropriate handling of dosages of oral or injectable agents and dietary intakes [4,13,14]. Beyond acute events, there arises the question of whether Ramadan can result in sustained chronic glucose disorders—so-called 'ambient hyperglycaemia'. In this case, it should first be borne in mind that the Ramadan period has a 1-month duration and, second, that any abnormally prolonged exposure of several weeks to high glucose levels can result in deleterious effects, such as a sustained increase in HbA_{1c} levels and excess glycation of the structural proteins in blood vessel walls [15,16]. The latter can have a subsequent 'legacy' effect, with the development of adverse cardiovascular outcomes several years later [17]. In fact, a 1-month exposure to abnormally high glucose levels, if repeated every year, can produce, after 24 years, the same deleterious vascular damage as sustained hyperglycaemia over a continuous 24-month period. For this reason, our recently published reports [12,18] merit particular attention.

2.1. Continuous 24-h glucose profiles during Ramadan when pre-Ramadan diabetes control is satisfactory

In 56 patients with relatively well-controlled diabetes (mean ± SD non-Ramadan HbA_{1c} levels = 55 ± 9 mmol/mol, 7.2 ± 1.2%) investigated by continuous glucose monitoring during Ramadan, interruption of the fasting state coupled with sudden refeeding at the sunset meal (*Iftar*) was marked by a rapid rise in glucose of approximately 5 mmol/L above premeal values (Fig. 1) [12]. This increase persisted overnight until dawn. The predawn meal (*Suhoor*), taken before sunrise, then contributed by reactivating the hyperglycaemia and maintaining glucose at abnormally high levels. During daylight hours, glucose concentrations returned to baseline levels, which were near-normal in the population as a whole, but remained elevated in those using insulin regimens (Fig. 1) [12]. Glucose nadirs were only observed at the end of the afternoon after a slow progressive glucose decline at a constant rate throughout the period of abstinence from eating and drinking. In this observational study, it is noteworthy that insulin-treated patients behaved differently from those treated with either oral antidiabetic agents or diet alone. This was particularly evident when the prescription of oral antidiabetic agents was limited to metformin and/or dipeptidyl peptidase (DPP)-4 inhibitors, drugs without risk of triggering hypoglycaemia.

2.2. Continuous 24-h glucose profiles during Ramadan when pre-Ramadan diabetic control is unsatisfactory

A few years ago, our team investigated a patient with a body mass index (BMI) of 31 kg/m^2, an HbA_{1c} level of 68 mmol/mol (8.4%) and T2D treated with insulin [18]. Ambulatory continuous glucose monitoring during the Ramadan period showed that the dietary intake at the sunset meal was followed by rapid and exaggerated glucose increments that were similar over the three consecutive study days (Fig. 2). Within a time interval of < 2 h, glucose concentrations rose from premeal levels of between 5.5 and 7.2 mmol/L to postmeal peaks ranging from 16.7 to ≥ 22.2 mmol/L. However, nocturnal glucose patterns were markedly different on study days 2 and 3 (Fig. 2). On study day 2, the postmeal peak was quickly followed by a decrease in glucose concentrations that further fluctuated around an average level of 11.1 mmol/L overnight until the predawn meal taken at 07:00 h. On study day 3, glucose concentrations plateaued at an average level of 22.2 mmol/L overnight until dawn. On both study days, slow progressive decays of glucose

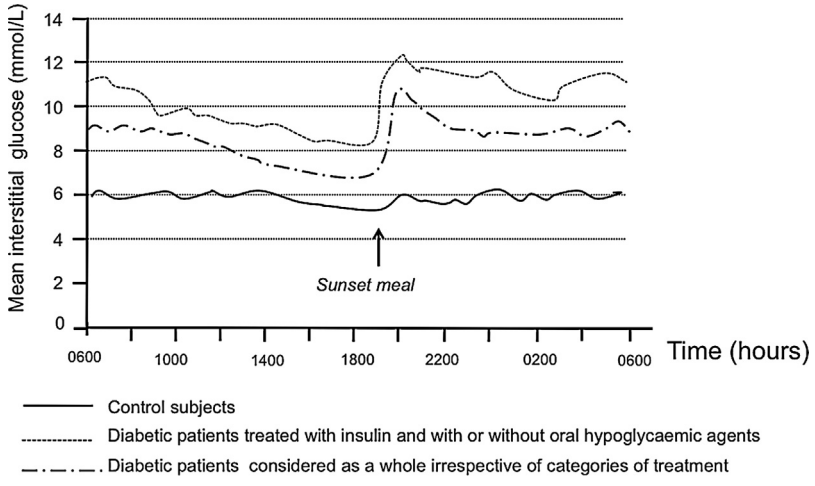

Fig. 1. Mean 24-h glycaemic profiles during Ramadan. Seven healthy, nondiabetic subjects (solid line) and 56 diabetic patients (broken and dotted lines), irrespective of treatment categories, were investigated. Among these patients, 13 (dotted line) were treated with insulin: six had type 1 diabetes and seven had type 2 diabetes [12].

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