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Diabetes mellitus and Ramadan. A narrative review of literature

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Abstract
Background: The medical ramification of fasting among patients with diabetes is largely unknown; the purpose of the review is to find out how diabetes mellitus is managed during the month of Ramadan.
Methods: Literature published on diabetes management during the month of Ramadan in the Middle-East are aimed at getting a global picture of this condition at a time when diabetes is having an adverse effect on health care delivery. I hope the review will be a useful and comprehensive source on the subject (diabetes mellitus) for researchers, academics and clinicians who care for the increasing number of diabetic patients and help health care providers curb the tide of the diabetes epidemic. The search includes available articles published, by using the keywords "Diabetes Mellitus", "Ramadan" and "fasting" covering epidemiology, clinical, management and complication profile.
Results: Studies have shown that fasting among diabetic patients carries the potential risk of dangerous hypoglycaemia and hyperglycaemia, diabetic ketoacidosis and thrombosis. The EPIDIAR study was the largest study where 50% of the whole sample changed their treatment and hypoglycemia was the only observed event. There are also few studies which evaluated specific management modalities.
Conclusion: It follows from this review that Ramadan fasting is acceptable for well balanced diabetic patients, conscious of their disease and compliant with their diet and drug intake. Patients willing to fast must be advised to undertake control of their glycaemia several times a day to prevent hypoglycemia risks during daytime fasting or hyperglycemia during the night.

Key words: diabetes mellitus, Ramadan, fasting

Introduction

Each year, Muslims around the world observe a period of fasting during Ramadan, the ninth lunar month of the Islamic year [1]. Fasting in Ramadan is obligatory for all healthy Muslim adults [2], This involves refraining from eating, drinking, smoking or taking medications (orally or parentally) from dawn to sunset each day – approximately 11 to 20 hours, depending on the geographic location and season for 28 to 30 days. Two meals are taken during Ramadan, one before dawn (Suhur) and the other at sunset (Iftar) [1,3,4]. Between Iftar and Suhur, there is no restriction on the intake of food or fluids [5]. If an individual has a medical condition that would be adversely affected by fasting during Ramadan, the rules of Islam exempt this individual from the obligation to fast for as many days as necessary [3, 5-7]. Patients with type I diabetes mellitus fall into this category and their physicians generally advise them not to fast because of difficulties in maintaining glycaemic control and the potentially serious complications that may arise [3,5]. However, some patients may be determined to fast, even against the advice of their physicians and some may not consult their physician at all. According to the Epidemiology of Diabetes and Ramadan study, a population-based retrospective survey conducted during Ramadan in 13 countries, 42.8% of patients with type I diabetes fasted for at least 15 days. Of these patients, 10.3% were not monitored by a specialist, and 76% were reported to obtain advice about diabetes care from relatives [8].

The medical ramification of fasting among patients with diabetes is largely unknown. Due to the limited information available from prospective or retrospective studies on the effects of fasting during Ramadan, a group of endocrinologists and Diabetologists from a number of Muslim and non-Muslim countries met to exchange information and opinions and to propose a set of recommendations. Although recommendations

for the management of diabetes in patients who elect to fast during Ramadan were proposed in 1995 at a conference in Casablanca [9], the effort was prompted by data from EPIDIAR (Epidemiology of Diabetes and Ramadan)

Study [8] showing that fasting is quite common among Muslims with diabetes and by the increasing awareness that this represents a global medical issue. The purposes of the recommendations that follow are threefold: 1) to invite an open dialogue on this important topic, 2) to offer a set of medical opinions and suggestions and 3) to identify topics of research needed to answer important medical questions regarding fasting during Ramadan.

The aim of this review is to obtain a global picture of Diabetes Mellitus patients during the month of Ramadan in Middle-East and to find out the current practices regarding the management of this clinical condition with the aim of improving them, since diabetes is still having an adverse effect on health care delivery.

Materials and methods

The review included relevant English-language articles that were identified through searches of three databases [PubMed, Medline and Embase (all, 1990-2010)] conducted in September 2010 using the keywords "Diabetes Mellitus", "Ramadan" and "fasting". Original research and review articles related to adult patients with diabetes mellitus were considered for the review, excluding pregnant women and patients with poorly controlled diabetes.

Inclusion criteria comprised reports of data from original studies and review articles related to adult patients with diabetes mellitus, including data from the control period before or after Ramadan, and data from the period during Ramadan.

Exclusion criteria comprised of case studies, letters to editors , studies in children and pregnant women, and articles reporting data from the periods before and after Ramadan only.

Search strategy and selection criteria of the comprehensive literature review

Firstly, a literature search with special emphasis on research findings published over the past 20 (1990 to 2010) years on Diabetes Mellitus was carried out using PubMed, Medline and Embase databases. PubMed and Medline contain citations published mostly from 1995 to 2010, whereas Embase database dates from 1990 to 1995. The following keywords were employed to search the above mentioned databases: "Diabetes Mellitus", "Ramadan" and "fasting"

Secondly, this search was complemented with an iterative proceeding in which I consistently reviewed reference lists of all those publications that were of relevance to address the main objective. The bibliographies of all these recovered manuscripts were retrieved again and the searching strategies repeated until no new information was forthcoming.

Thirdly, I also performed search of the websites of the following organizations: World Health Organisation (WHO) and American Diabetes Association (ADA).

Fourthly, dissertation abstracts were reviewed. They were searched in the following databases (assessed on 22.09.2010):

- www. google. com
- ProQuest Digital Dissertation

The same keywords as described before for the peer-reviewed literature search were used for this search.

A flow chart of the search strategy and selection criteria of the comprehensive literature review is given below in Figure 1, according to the PRISMA statement [10]

Results

The major potential diabetes related complications of fasting include dangerously low blood glucose level (hypoglycaemia), excessively high blood glucose level (hyperglycaemia), diabetic ketoacidosis and thrombosis.

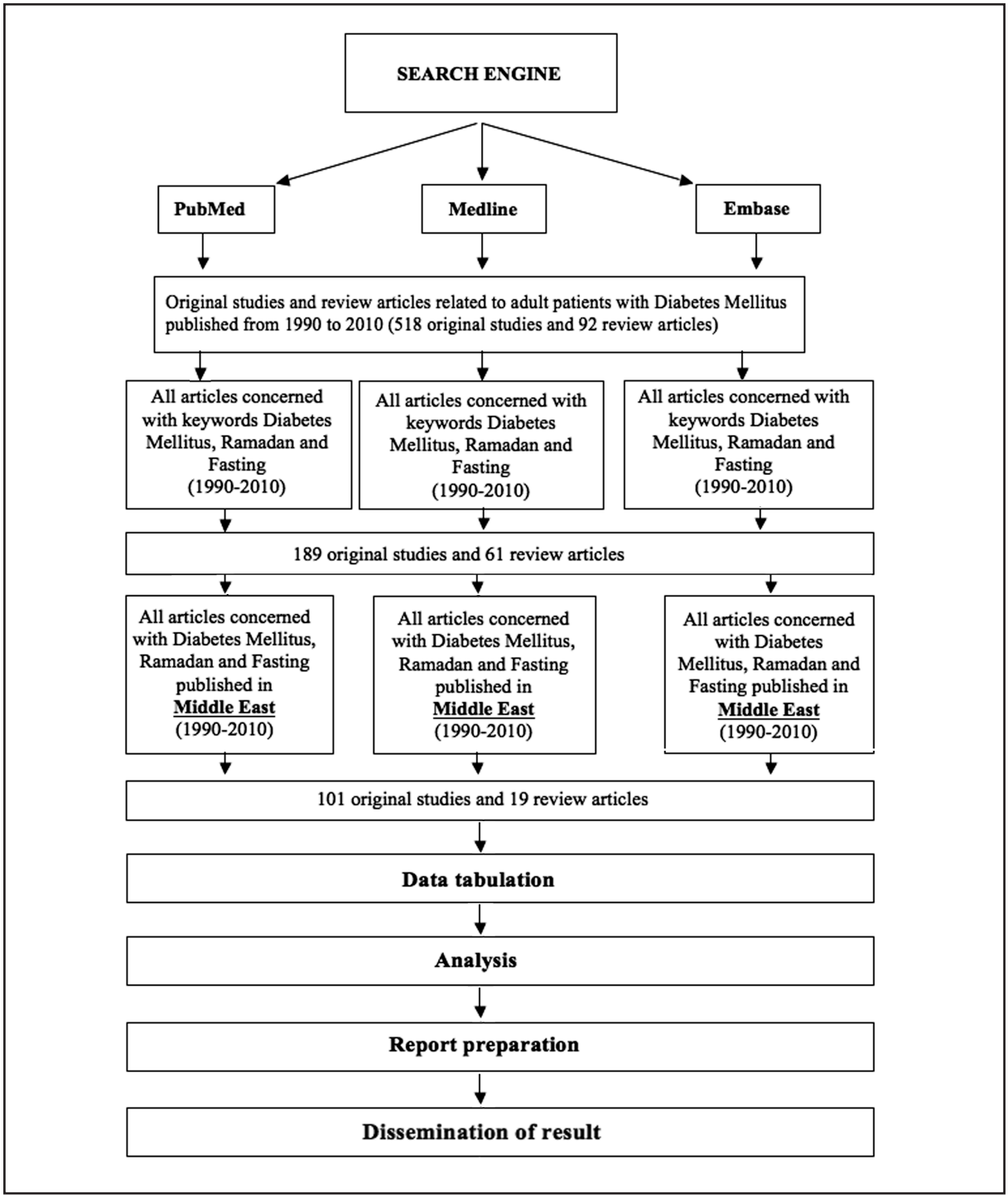
Hypoglycaemia

A prospective study showed that there was an increase in glucose level during the Ramadan compared to pre-Ramadan value and after Ramadan there was statistically significant decrease of glucose level [11]. The effect of fasting during Ramadan on rates of hypoglycaemia in patients with diabetes is not known with certainty. The largest dataset is the EPIDIAR study [8], which showed that fasting during Ramadan increased the risk of severe hypoglycaemia 4.7 fold in patients with type I diabetes and 7.5 fold in patients with type II diabetes. Rates of hypoglycaemia are several times lower in patients with type II compared with type I diabetes [8], with rates being lower in patients with type II diabetes treated with oral agents [12,13].

Hyperglycaemia

Control of glycaemia in patients with diabetes who fasted during Ramadan has been reported to deteriorate, improve or show no changes [14]. The extensive EPIDIAR study showed a fivefold increase in the incidence of severe hyperglycaemia during Ramadan in type II diabetes, and a threefold

Figure 1. Flow chart of the search strategy and selection criteria of the comprehensive literature.



increase in the incidence of severe hyperglycaemia in type I diabetes patients [8].

Diabetic ketoacidosis

Fasting during Ramadan for patients with diabetes, especially with type I, are at higher risk of developing ketoacidosis, particularly if they are grossly hyperglycaemic during pre-Ramadan period [8].

Dehydration and thrombosis

The main cause of dehydration during Ramadan fasting is the limitation of fluid intake, especially if it is prolonged. It becomes severe in hot and humid climates and among individuals who perform hard physical labor [1]. Orthostatic hypotension may develop, especially in patients with pre existing autonomic neuropathy [1, 15].

There are few guidelines concerning what type

of insulin to use, or how and when to adjust the dosage to minimize complications in patients with type I diabetes who wish to fast during Ramadan. Five clinical trials that were relevant to type I diabetes and fasting were identified. Four trials had a prospective, open-label design [16-20]. Some of these trials examined the general feasibility of fasting in patients with type I diabetes, whereas others specifically addressed fasting during Ramadan, suggesting possible insulin regimens for use during the period of fasting and discussing the advantages and disadvantages of various insulin regimens and type of insulin [19].

There are two questions that need to be answered. Firstly, when should a physician advise against fasting? Secondly, what is the optimal therapeutic regimen? Patients with type I and type II diabetes who are allowed, or choose, to fast should be given specific information on the risks associated to fasting and recommendations about therapeutic changes. They should be warned against skipping meals, taking medication irregularly or night time gorging [2,19].

Life style modifications

Life style should be re-enforced before and during Ramadan. Lack of careful attention to diet during the non-fasting night time period with excessive gorging, or compensatory eating of carbohydrates and fatty foods, contributes to poor glycaemic control and weight gain. Ramadan focused education in diabetes can empower patients to change their lifestyle during the festive period for Muslims to minimize the risk of hypoglycaemic events and prevent weight gain, which is a potential benefit for metabolic control [21].

Discussion

It should be stressed that fasting among people with type 1 diabetes, and those with type 2 diabetes with inadequately managed blood glucose levels, is associated with multiple risks. Fasting during Ramadan has been uniformly discouraged by the medical profession for people with diabetes.

Assessment before Ramadan

Expert opinion recommends that, if a patient has made it clear that they wish to fast during Ramadan, their primary physicians and/or diabetes care specialists should assess whether they increase their health risk by doing so [1,15]. Box 1 outlines how patients planning to fast during Ramadan may be categorized as at high, moderate, or low risk of adverse events. Patients classed as high risk are advised not to fast as this can lead to worsening diabetes control, resulting in, for example, severe hypoglycaemia and diabetes ketoacidosis. Patients at moderate risk can reduce their level of risk if they see a healthcare professional several months before Ramadan and make necessary changes to their diabetes treatment. Those at low risk can fast

Box 1. Expert recommendations for risk stratification in patients with type 1 or type 2 diabetes who fast during Ramadan [1,15,21].

Patients at high risk

- Those with severe and recurrent episodes of hypoglycaemia and unawareness
- Those with poor glycaemia control
- Those with ketoacidosis in the three months before Ramadan
- Those who experience hyperosmolar hyperglycaemic coma within the three months before Ramadan
- Those with acute illness
- Those who perform intense physical labour
- Pregnant women
- Those with co-morbidities such as advanced macro-vascular complications, renal disease on dialysis, cognitive dysfunction, uncontrolled epilepsy (particularly precipitated by hypoglycaemia)

Moderate risk

- Well controlled patients treated with short acting insulin secretogogue, sulphonylurea, insulin, or taking a combination of oral or oral plus insulin treatment

Low risk

- Well controlled patients treated with diet alone, monotherapy with metformin, dipeptidyl peptidase-4 inhibitors, or thiazolidinediones who are otherwise healthy

without healthcare advice. Patients who choose to fast, despite advice not to do so, need support to help them fast as safely as possible.

Ramadan focused education: In a large observational study, patients who fasted during Ramadan without attending a structured education session had a fourfold increase in hypoglycaemic events, whereas those who attended an education programme focusing on Ramadan had a significant decrease in hypoglycaemic events [22]. It is therefore recommended that Muslim patients with diabetes attend some form of structured education intervention to increase their chances of being well when fasting during Ramadan. Patients at high risk of complications, and who plan to fast despite medical advice not to, are also invited to attend structured education programmes to support their self management and decision to fast. Box 2 outlines the suggested content of Ramadan focused education.

Management of patients with type I diabetes

It is recommended that treatment regimens aimed at intensive glycaemia management should be used in patients with diabetes. The DCCT (Diabetes Control and Complications Trial) and its follow-up, the EDIC (Epidemiology for Diabetes Interventions and Complications) study, have shown that intensive glycaemia management is protective against micro-vascular complications, and that the benefits are long lasting [26,27]. Glycaemia control at near-normal levels requires the use of multiple daily insulin injections (three or more) or the use of continuous subcutaneous insulin infusion through pump therapy. Close monitoring and frequent insulin dose adjustments are essential[1]. Patients will need to use two daily injections of NPH (Neutral Protamine Hagedorn) as intermediate-acting insulin, administered before the predawn and sunset meals, in combination with short-acting insulin to cover food intake at the associated meals [15]. However, there is an increased risk of hypoglycaemia around midday due to peaking of the early morning insulin dose [1,15]. Using a long-acting insulin ultralente is an option with twice-daily injections at ~12h

Box 2. Four key areas in Ramadan focused education [22,29].

Meal planning and dietary advice

- The diet during Ramadan should be a healthy balanced diet
- Slow energy release foods (such as wheat, semolina, beans, rice) should be taken before and after fasting, whereas foods high in saturated fat should be minimized [22]
- Advise patients to use only a small amount of monounsaturated oils in cooking
- Before and after fasting include high fibre foods such as wholegrain cereals, granary bread, brown rice; beans and pulses; fruit, vegetables, and salads

Exercise

- Regular light and moderate exercise is safe in type 2 diabetes patients [23]
- Rigorous exercise is not recommended as the risk of hypoglycaemia may be increased, particularly in patients taking sulphonylureas or insulin
- Encourage patients to continue their usual physical activity, especially during non-fasting periods
- Tarawaih prayers (a series of prayers after the sunset meal) should be considered as part of the daily exercise regimen as they involve standing, bowing, prostrating, and sitting

Blood glucose monitoring

- Blood glucose monitoring does not constitute the interruption of fasting [24]
- All patients who fast should be provided with the means to monitor their blood Glucose [25]
- Capillary blood glucose testing should be done when:
  - The patient suspects they have symptoms of hypoglycaemia (subjective to the individual). Patients should be advised to break their fast if hypoglycaemia is confirmed on blood glucose testing
  - The patient is unwell (e.g. has a fever) Testing at other times may be useful only if patients are able and willing to adjust their diabetes treatment regimens, such as insulin dosage titration

Recognizing and managing complications

- Patients should be aware of the warning symptoms of dehydration, hypoglycaemia, and hyperglycaemia and should stop the fast as soon as any complications or acute illness occur

Table 1. Recommended changes to treatment regimens in patients with type 2 diabetes who fast during Ramadan.

Before Ramadan	During Ramadan
Patients on diet and exercise control	No change needed (modify time and intensity of exercise), ensure adequate fluid intake
Patients on oral hypoglycemic agents	Ensure adequate fluid intake
Biguanide, metformin 500 mg three times a day, or sustained release metformin (glucophage R	Metformin, 1,000 mg at the sunset meal (Iftar), 500 mg at the predawn meal (Suhur)
Thiazolidinediones or pioglitazone once daily	No change needed
Sulfonylureas once a day, e.g., glimepiride 4 mg daily, gliclazide MR 60 mg daily	Dose should be given before the sunset meal (Iftar); adjust the dose based on the glycemic control and the risk of hypoglycemia
Sulfonylureas twice a day, e.g., glibenclamide 5 mg or gliclazide 80 mg, twice a day (morning and evening)	Use half the usual morning dose at the predawn meal (Suhur) and the full dose at the sunset meal (Iftar), e.g., glibenclamide 2.5 mg or gliclazide 40 mg in the morning, glibenclamide 5 mg or gliclazide 80 mg in evening
Patients on insulin	Ensure adequate fluid intake
70/30 premixed insulin twice daily, e.g., 30 units in morning and 20 units in evening	Use the usual morning dose at the sunset meal (Iftar) and half the usual evening dose at predawn (Suhur), e.g., 70/30 premixed insulin, 30 units in evening and 10 units in morning; also consider changing to glargine or detemir plus lispro or as part

intervals to mimic basal insulin, and a short acting insulin added before the two meals. Yet, ultralente cannot be considered as a truly basal insulin, since it has a broad peak of action at ~8-14h causing protracted hypoglycaemia [1,15,23,28]. Another option would be use of long-acting insulin analogue, glargine, once daily, or another insulin analogue, detemir, twice daily [19,15,28].

Management of patients with type II diabetes

In type 2 diabetic patients who are well controlled with diet alone, the risk associated with fasting is quite low. However, there is still a potential risk for occurrence of postprandial hyperglycaemia after the pre-dawn and sunset meals if patients overindulge in eating [15].

The choice of oral agents should be individualized.

Metformin: Patients treated with metformin alone may safely fast because the possibility of hypoglycaemia is minimal. However, it is suggested that the timing of the doses should be modified [1,15].

Glitazones: Patients on these drugs have a low risk of hypoglycaemia. Usually no change in dose is required [15].

Sulfonylureas: This group of drugs is not suitable for use during fasting because of the inherent risk of hypoglycaemia. Therefore, their use is individualized and should be utilized with caution. The use of chlorpropamide is absolutely un-recommended during Ramadan because of the high possibility of prolonged and unpredicted hypoglycaemia [1,15].

Another category of therapy is represented by short-acting insulin secretagogues: this group of

drugs (repaglinide and nateglinide) are useful because of their short duration of action [1].

The recommended changes to treatment regimens in patients with type 2 diabetes who fast during Ramadan are mentioned in Table 1 [1,15,20].

Conclusions

Fasting during Ramadan for patients with diabetes carries the risk of various complications. In general, patients with type 1 diabetes should be strongly advised not to fast. Patients with type 1 diabetes who have a history of recurrent hypoglycaemia, or hypoglycaemia unawareness, or who are generally poorly controlled, are at very high risk for developing severe hypoglycaemia. On the other hand, an excessive reduction in the insulin dosage in these patients (to prevent hypoglycaemia) may place them at risk for hyperglycaemia and diabetic ketoacidosis. Hypo- and hyperglycaemia may also occur in patients with type 2 diabetes but generally less frequently and with less severe consequences compared to patients with type 1 diabetes. A patients' decision to fast should be made after ample discussion with his or her physician concerning the risks involved. Patients who insist on fasting should undergo pre-Ramadan assessment and receive appropriate education and advice related to physical activity, as well as about dosage and timing of medications. The management plan must be highly individualized. Close follow-up is essential to reduce the risk of developing complications.

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