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Fasting of diabetic patients during Ramadan, challenges and resolves: paper review

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Abstract

The health workers, especially physicians, confront a lot of inquiries regarding ability of diabetic Muslim patients for fasting during Ramadan month and best management method to complete this hallowing month with good glycemc control with minimum risk of hypoglycemia. To reach this purpose we need effective cooperation between patients and local health centers. In this article review we try to discuss some medical articles that deals with important health problems that can affect diabetic patients during Ramadan and their resolving means. The diabetic patient who wants to fast Ramadan should be educated about importance of predawn meal and risk of vigorous exercise during fasting period. The iftar best to contain whole wheat flour chapattis, vegetables, and a meat dish.

Salads increase the fiber intake. A glass of milk or fruit at bedtime will maintain normoglycaemia till suhoor. There are certain diabetic patients with special risk as in elderly, pregnant and those with comorbidities, require careful assessment before make decision of fasting during Ramadan. The management of diabetes mellitus (DM) pre and during Ramadan need careful supervision and changing of the time, type and dose of treatment may be needed also. The diabetic patient should be educated for hypoglycemic features(e. g head ache, tremor sweating, anxiety, nervousness, hunger and palpitation) specially in Ramadan and suitable diet to correct hypoglycemia should be available always with patients - Insulin, sulphonylureas and meglitinides these antidiabetic agents have high risk of hypoglycemia, so need frequent checking of blood sugar or replace them with other gents that have rare risk of hypoglycemia like metformin, Di-peptidyl peptidase-4 inhibitor and thiazolidinediones (TZD).

Keywords: Ramadan, Fasting, Diabetes, Hypoglycemia

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One of the Islamic rules is the fasting of Ramadan of each year (hallowing month for Muslims). This requires no food or fluids from sunup to sundown, so for diabetic patients who fast this period there are many risks that should be managed properly. The pre-Ramadan education of diabetic patients about features of hypoglycemia and good blood sugar control is very effective to maintain good health during Ramadan. The Ramadan

Education and Awareness in Diabetes (READ) study that demonstrated a significant decrease in the number of hypoglycaemic events in a group of patients with type-2 DM that received diabetes education (from nine events pre-Ramadan to just five during Ramadan) compared with an increase (from nine to 36 events) in a control group that did not receive the educational advice ($p < 0.001$) [1].

The education of fasting diabetic patients should include much information about suitable diet regimens, anti-diabetic drugs, possible complications and correct times and method for measuring of blood sugar by patient himself.

The self-measuring of capillary blood sugar (by a glucometer) is important and essential for high-risk patient (Fig 1). This test done multiple time in the day for high-risk group (Fig 2) and if any feature of hypoglycemia occurs or if blood glucose is <70 mg/dL (3.9 mmol/L) or >300 mg/dL (16.7 mmol/L) the patients should break the fast also they should not fast if feel unwell [2]. Low risk patients also need to perform self-measuring of blood sugar at the following times: pre-suhoor, midday, pre-iftar and whenever symptoms of hypoglycaemia or acute illness occur [2].



Figure 1.

The glucometer



Figure 2.

Recommended timings to check blood glucose levels during Ramadan fasting.

According to Ramadan and Diabetes Management, paper edited at June 4, 2016 by Dr. Sushama Ghag (Dietitian working at Aster Hospital Mankhool), there are three risk groups regarding ability for fasting of diabetic patients during Ramadan :

1-High risk group include healthy individual with Hba1c lower range than 7.0% and on oral medications. May choose to fast but observe the body changes.

2-Moderate risk group include healthy individual with Hba1c lower range at 8.0% and treated with oral medications. May choose to fast but always take precautions. 3-High risk group include individuals with the complications with uncontrolled blood sugar. A person with type 1 diabetes, severe hypo or hyperglycemia symptoms, acute illness, intense physical labor, pregnancy, renal conditions, on dialysis. By this paper the patients in high-risk group are not allowed to fast.

Other studies mention that the patients with type 1 DM who have any of the following conditions must not fast [3, 4].

-History of recurrent hypoglycaemia .

-Hypoglycaemia unawareness .

-Poor diabetes control .

-Brittle diabetes .

-Non-compliance with medical treatment .

-Patients who are 'unwilling' or 'unable' to monitor and manage their blood glucose levels .

Lines of management :

Diet control

As in other time, during Ramadan the diet is important and, in some patients, the alone method of DM treatment. The difference will be the period of continuous fasting and numbers of meals that usually reduced during Ramadan.

The Diabetes and diet in Ramadan study is suggested that during Ramadan similar general dietary guidelines should be followed as those throughout the year [5]. The pre-dawn meal should be taken as late as possible, before the start of the fast and should have a high proportion of carbohydrates with fibers. The traditional sugar drinks and foods rich in fat taken at iftar should be avoided. The evening meal or dinner should be consumed as early as possible at iftar and contain whole wheat flour chapattis, vegetables, and a meat dish. Salads increase the fiber intake. A glass of milk or fruit at bedtime will maintain normoglycaemia till suhur.

The diabetic patient should be encouraged also for drinking a lot of sugar free fluid during non-fasting period of the day to avoid hyperviscosity state.

*Regarding pharmacological treatment of DM during Ramadan many research deal with this subject, one of these is Diabetes and Ramadan: Practical guidelines [6]. It shows tow figures summarize the required changes in insulin and non-insulin anti diabetic agents according to glycemic state during days of Ramadan (Fig 3 and 4).

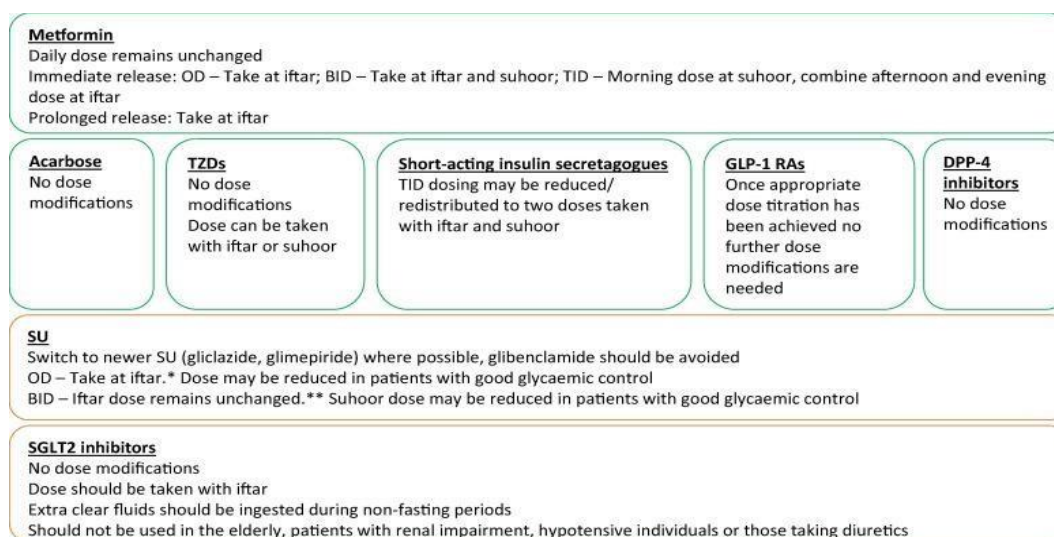


Figure 3.

Non-insulin dose modifications for patients with T2DM

SU (sulphonylurea) combination therapy OD – take at iftar and consider reducing the * dose by 50%; **SU combination therapy BID – omit morning dose and take normal dose at iftar. BID, twice daily; DPP-4, dipeptidyl peptidase-4 inhibitor; GLP-1 RAs, glucagon like protein-1 receptor agonists; OD

once daily; SGLT2, sodium glucose co-transport 2; SU, sulphonylurea; TID, three times a day; TZD, thiazolidinedione; T2DM, type 2 diabetes mellitus.

Insulin therapy
Switch to insulin analogues where possible

- **Long- or intermediate-acting basal insulin:**
 - OD – NPH*/detemir/glargine/degludec. Take at iftar. Reduce dose by 15–30%
 - BID – NPH/detemir/glargine. Take usual morning dose at iftar. Reduce evening dose by 50% and take at suhoor
- **Rapid- or short-acting prandial/bolus insulin:**
 - Take normal dose at iftar. Omit lunch-time dose. Reduce suhoor dose by 25–50%
- **Premixed insulin:**
 - OD – Take normal dose at iftar
 - BID – Take usual morning dose at iftar. Reduce evening dose by 25–50% and take at suhoor
 - TID – Omit afternoon dose. Adjust iftar and suhoor doses

Dose titration should be performed every three days and dose adjustments made according to BG levels

Fasting/Pre-iftar/Pre-suhoor BG	Pre-iftar**	Post-iftar**/Post-suhoor***	
	Basal insulin	Short-acting insulin	Premixed insulin
< 70 mg/dL (3.9 mmol/L) or symptoms	Reduce by 4 units	Reduce by 4 units	Reduce by 4 units
70–90 mg/dL (3.9–5.0 mmol/L)	Reduce by 2 units	Reduce by 2 units	Reduce by 2 units
90–126 mg/dL (5.0–7.0 mmol/L)	No change required	No change required	No change required
126–200 mg/dL (7.0–11.1 mmol/L)	Increase by 2 units	Increase by 2 units	Increase by 2 units
> 200 mg/dL (11.1 mmol/L)	Increase by 4 units	Increase by 4 units	Increase by 4 units

- **Insulin pump:**
 - Basal rate – Reduce dose by 20–40% in the last 3–4 h of fasting. Increase dose by 0–30% early after iftar
 - Bolus rate – Normal carbohydrate counting and insulin sensitivity principles apply

Figure 4.

Insulin dose modifications for patients with diabetes. *Alternatively, reduced NPH dose can be taken at suhoor or at night; **adjust the insulin dose taken before suhoor; ***adjust the insulin dose taken before iftar. BG, blood glucose; BID, twice daily; NPH, neutral protamine Hagedorn; OD, once daily; TID, three times a day.

So regarding Metformin and α -glucosidase inhibitors (acarbose) generally the occurrence of hypoglycemia is rare and no need for dose modification but the time of drug intake is changed during Ramadan. Other antidiabetic group is Thiazolidinediones (TZD): the medical data about pioglitazone use during Ramadan is limited, there is study that compare between two groups first is treated with pioglitazone and the other with placebo. In the first group the glycemic control improved significantly during the early, mid- and post Ramadan periods. There was no difference in the incidence of hypoglycemic attacks, but there is significant increase in weight of 3.02 kg ($p = 0.001$) was observed in the pioglitazone group compared with a non-significant loss in weight (-0.46 kg) in the placebo group [7].

There is no need for modification of TZD during Ramadan and doses can be taken with iftar or suhoor (Fig. 3)

Dipeptidyl peptidase 4(DPP-4) inhibitors : such as alogliptin, saxagliptin, sitagliptin, and vildagliptin, this group relatively new hypoglycemic agent and in general with low risk of hypoglycemia, but can increase hypoglycemic risk of sulphonylureas. There is prospective study (involve 2789 patients with type 2 diabetes) was showed that the hypoglycemia less with use of vildagliptin in comparison to glimepiride [8]. The VECTOR study, which include 72 type 2 diabetic patients, mention that there are no attacks of hypoglycemia with vildagliptin when compared with gliclazide in the setting of combination therapy with metformin during Ramadan [9].

Other study is VIRTUE study, which involves 1300 type 2 diabetic patients who fasting during Ramadan, this study gives similar result and showed that vildagliptin has significantly fewer hypoglycemic attacks than with sulfonylurea treatment (5.4 versus 19.8%, respectively; $P < 0.001$) [10].

Sulphonylureas : such as glibenclamide, glibornuride, gliclazide, glipizide and glimepiride, these are group of widely used drugs for treatment of type 2 diabetes mellitus. They stimulate secretion of insulin from B-cell of the pancreas. Sulphonylureas should be used with careful monitoring during fasting because of significant risk of hypoglycemia. The hypoglycemic risk is different between the drugs of this group, where the risk is less with gliclazide, glimepiride, and glipizide [11,12] .

So, during fasting the glibenclamide should be avoided and if sulphonylureas are needed, newer generations (like glemipiride and gliclazide) are used as mention above in Fig. 3

Meglitinides such as repaglinide, nateglinide and mitiglinide: these are short acting glucose lowering drugs that act by stimulation of insulin secretion.

There are some studies that indicate low risk of hypoglycemia with use of this drugs during Ramadan, one of these studies is small prospective study their result appear that repaglinide t.i.d. plus single-dose insulin glargine regimen was safe for low-risk type 2 diabetic patients during fasting [13]. However the risk of hypoglycemia still present but seems to be less than that with sulphonylureas.

Glucagon-like peptide-1 receptor agonists (GLP-1 receptor agonists) or incretin mimetics: such as exenatide, liraglutide, lixisenatide and semaglutide. These drugs are used for the treatment of type 2 diabetes and characterized by having lower risk of hypoglycemia than that with sulfonylureas or meglitinides [14].

When GLP-1 receptor agonists are used alone for treatment of diabetes during Ramadan, the dose agistment is not needed and there is randomized control trial that compares between liraglutide and sulphonylureas as they used in combination therapy with metformin for treatment of 99 patients with type 2 diabetes. This study showed that the hypoglycemic

events is lower with liraglutide and this drug is well tolerated and may effective when used in combination with metformin during Ramadan [15].

Insulins: There are three main groups of insulins .

*Fast-acting insulin: this include

-Rapid Acting Insulin Analogs (Insulin Aspart, insulin Lyspro, Insulin Glulisine)

-Regular Human Insulin

*Intermediate-acting

-NPH Human Insulin (Neutral Protamine Hagedorn Insulin)

-Pre-Mixed Insulin (which is NPH pre-mixed with either regular human insulin or a rapid-acting insulin analog)

*Long-acting insulin: (Insulin Glargine, Insulin Detemir, Insulin Degludec)

Type of Insulin	Onset	Peak	Duration	Appearance
Fast-acting				
Regular	½-1 hr.	2-4 hr.	6-8 hr.	clear
Lyspro/ Aspart/ Glulisine	<15 min.	1-2 hr.	4-6 hr.	clear
Intermediate-acting				
NPH	1-2 hr.	6-10 hr.	12+ hr.	cloudy
Long-acting				
Detemir	1 hr.	Flat, Max effect in 5 hrs.	12-24 hr.	clear
Glargine	1.5 hr.	Flat, Max effect in 5 hrs.	24 hr.	clear

Table 1.

Show characteristics of different types of insulin [16]

Rapid-acting insulin analogs are better than regular insulin for treatment of diabetes in fasting patients during Ramadan as they associated with a lower incidence of hypoglycemia and minimal postprandial hyperglycemia [17]. This type of insulin characterized by faster onset, shorter peak and shorter duration of action. They are used before meal and in Lyspro and Glulisine can be injected even after starting of eating (giving meal flexibility).

According to Figure 4, there are advisable modifications of insulin regimens during fasting of Ramadan :

-Patients on single dose of (NPH or detemir or glargine or degludec), take their dose at iftar and reduce it by 15-30% if possible

-In patients who are treated with (NPH or detemir or glargine) twice daily, the usual morning dose is taken at iftar and evening dose is reduced by 50% and taken at suhoor.

-Regarding rapid or short acting prandial/bolus insulin, patient can take normal dose at iftar and omit the dose at lunch time. The suhoor dose is reduced by 25-50% -Patients on premixed insulin who use single dose, take it as usual and in those on two doses daily, the usual morning dose is taken at iftar and evening dose is reduced by 25-50% and taken at suhoor. Patients on three doses daily, omit afternoon dose and take two doses one at iftar and the other at suhoor with adjustment of these doses according to blood sugar.

In all these types of insulin regimens, the dose should be titrated every 3 days and adjustments made according to blood sugar results .

Although it still not widely used, some diabetic patients are treated with insulin pump and for fasting patients during Ramadan, the modification of basal rate include reduction of the dose by 20-40% in the last 3-4 hours of fasting and increasing of the dose by 0-30% early after iftar. For the bolus rate, normal carbohydrate counting, and insulin sensitivity principles apply.

The risk of hypoglycemia

For patients with type 1 diabetes, fasting increases the risk of hypoglycemia 4.7 times, and the risk is 7.5 times higher for patients with type 2 diabetes [18]. However, the incidence of hypoglycemia during fasting of Ramadan cannot be estimated perfectly as there are many events of mild to moderate hypoglycemia corrected by the patients without medical help in both type-1 and type-2 diabetes mellitus. The main predisposing factors are length of fasting period, missing of suhoor meal, improper monitoring of blood sugar level and failure of suitable modification of timing and dose of anti-diabetic drugs..

Fasting of diabetic pregnant

The permission for fasting of Muslim pregnant women with diabetes mellitus need medical and religious opinions and even with many advices to avoid the fasting if there is significant risk of harm or if they was near term, many of them insist on fasting in Ramadan.

Treatment of DM during pregnancy is achieved by diet control alone or by diet control with insulin therapy.

Metformin is another anti-diabetic agent that can be used with diet therapy for treatment of DM during pregnancy in certain situations.

The strict blood sugar control is indicated for management of DM in pregnancy, this put the pregnant and her baby at higher risk of hypoglycemia if she is fasting. So careful and more frequent monitoring of blood sugar with early detection of any event of hypoglycemia is mandatory.

Recommendations

The diabetic patient who want to fast Ramadan should be educated about importance of predrawn meal and risk of vigorous exercise during fasting period -The iftar best to contain whole wheat flour chapattis, vegetables and a meat dish. Salads increase the fiber intake. A glass of milk or fruit at bedtime will maintain normoglycaemia till suhoor. -There are certain diabetic patients with special risk as in elderly, pregnant and those with comorbidities, require careful assessment before make decision of fasting during Ramadan.

The management of diabetes mellitus (DM) pre and during Ramadan need careful supervision and changing of the time, type and dose of treatment may be needed also. -The diabetic patient should be educated for hypoglycemic features(e.g head ache, tremor sweating, anxiety, nervousness, hunger and palpitation) specially in Ramadan and suitable diet to correct hypoglycemia should be available always with patients - Insulin, sulphonylureas and meglitinides these antidiabetic agents have high risk of hypoglycemia, so need frequent checking of blood sugar or replace them with other gents that have rare risk of hypoglycemia like metformin, Di-peptidyl peptidase-4 inhibitor and thiazolidinediones (TZD).

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Ethical Approval

The study was approved by the Ethical Committee.

Conflicts of Interest

The author declare that I have no competing interests.

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