Managing diabetes in
Ramadan

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Objectives

- To review changes in metabolism of carbohydrates during fasting of Ramadan
- To present the evidence-based management of diabetic patients during Ramadan
- To discuss practical management of diabetic cases during Ramadan
Introduction

- There are over 1.6 billion Muslims world-wide, constituting 23% of the total global population.

- Observance of Ramadan requires fasting from dawn to sunset, abstaining from eating and drinking during daylight hours, most Muslims will consume two meals each day.

- The timing of Ramadan follows the lunar calendar, therefore the length of the fast varies depending on the time of year and the geographical location but is usually between 10-20 hours.
Differences of fasting in Ramadan and experimental fasting

1. Intermittent in Ramadan
2. Fasting 11-18 hours daily
3. Avoidance of liquid intake
4. Various effects of temperature in each region
5. Difference in food habits in various regions
6. Change in sleep pattern
7. Difference in aim of fasting and moral issues
Up to 79% of Muslims with diabetes fast for at least 15 days during Ramadan

Introduction

• Globally it is estimated that 50 million Muslims with T2DM fast during Ramadan
• However, the proportion of those with T2DM who observe Ramadan varies considerably between 58% to 90% amongst different Islamic countries

Introduction

• Many Muslims, even those who could seek exemption, have an intense desire to participate in fasting during Ramadan.

• Most of the guidance available for the management of diabetes during Ramadan represents expert opinion rather than medical evidence.

• Generating optimized Ramadan-specific treatment regimens for each patient is essential if a physician is to offer the best possible care.
Changes in Carbohydrates Metabolism During Fasting of Ramadan
Effects of fasting on glucose homeostasis in healthy individuals

A. Physiology of feeding in healthy individuals

Liver → Glucose → Muscle

Gluconeogenesis: Inhibits
Pancreas: Stimulates
Insulin secretion: ↑ Glucose

B. Physiology of fasting in healthy individuals

Liver → Glucose → Muscle

Gluconeogenesis: Stimulates
Glycogen stores depleted: Inhibits
Insulin secretion: ↓ Glucose

Food
Fasting state

- In a healthy individual, fasting causes the release of glucose from glycogen stores (glycogenolysis) and the formation of glucose from non-carbohydrate substrates (gluconeogenesis).
Fasting state

- Liver glycogen can provide enough glucose for the brain and peripheral tissues for around 12 hours.
- When glycogen stores are depleted and levels of insulin are low, fatty acids are released from adipocytes and oxidised to generate ketones, which can be used as fuel by many organs, preserving glucose for the brain and erythrocytes.
<table>
<thead>
<tr>
<th>Tissue</th>
<th>Post Absorptive Period</th>
<th>Early Starvation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Liver</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Production of glucose by glycogenolysis</td>
<td>5 g / h</td>
<td>2 g / h</td>
</tr>
<tr>
<td>Production of ketone bodies</td>
<td>1 g / h</td>
<td>3 g / h</td>
</tr>
<tr>
<td><strong>Muscle</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amino acid release</td>
<td>1.5 g / h</td>
<td>2.5 g / h</td>
</tr>
<tr>
<td><strong>Adipose tissue</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatty acid release</td>
<td>7 g / h</td>
<td>14 g / h</td>
</tr>
</tbody>
</table>
Carbohydrate metabolism in healthy persons

- Most of the studies show slight decrease in serum glucose (60 mg/dl to 70 mg/dl) occurs in normal adults.
- Changes in serum glucose may occur in individuals depending upon food habits and individual differences in metabolism and energy regulation.
Figure 5. Mean continuous glucose monitoring (CGM) profiles from healthy subjects before and during Ramadan; there is a remarkable stability of blood glucose during fasting hours followed by a minimal rise in blood glucose at iftar*

Fasting in Ramadan

- During Ramadan, each fasting period is often longer than 12 hours, **most subjects who take their first meal at dawn are in a state of glycogen depletion by late afternoon, at which point ketogenesis occurs**
Pathophysiology of fasting in patients with diabetes

Gluconeogenesis and ketogenesis (T1DM)

Stimulates

Pancreas

Glycogen stores depleted
Excessive breakdown

Inhibits

Insulin secretion
decreased or absent/
insulin resistance

Glucose

* * *
Fasting in Type 1

• During the fast, patients with T1DM may **fail to secrete adequate levels of glucagon** in response to hypoglycaemia, leading to further decreases in blood glucose levels

• In addition, as a result of **autonomic neuropathy**, some patients with DM may have a defective adrenaline response and therefore an inadequate response to hypoglycaemia.
Figure 7. Mean continuous glucose monitoring (CGM) profiles from patients with diabetes before and during Ramadan. A rapid rise in blood glucose is seen at iftar time.

Importance of sahur

• During longer fasting days of >16 h, which follow a rather heavy meal taken before dawn (Sahur), the stores of glycogen, along with some degree of gluconeogenesis, maintain serum glucose levels within normal limits.

• Since gluconeogenesis becomes the only source of glucose after 16–24 h of fasting, it is recommended that observers of fasts do not skip Sahur, their predawn meal, because of the possibility of extended gluconeogenesis.
Changing in lifestyle during Ramadan

- Dietary Habits
- Daily Physical Activity
- Sleeping Pattern
- Glycemic Control
- Lipid Profile
- Weight & Dietary Intakes
Major risks associated with fasting in patients with diabetes

Hypoglycemia

Hyperglycemia

Diabetic ketoacidosis

Dehydration and thrombosis

Diabetes Care 2004; 28: 2305
Al-Arouj et al. Diabetes Care 2010; 33: 1895
EPIDIAR study: mean numbers of severe glycemic events/month during Ramadan compared with before Ramadan

Evidence-Based Management of Diabetes During Ramadan
Diabetes and Ramadan: Practical Guidelines

International Diabetes Federation (IDF), in collaboration with the Diabetes and Ramadan (DAR) International Alliance

April 2016
• **Education** as a cornerstone for Ramadan diabetes management
Ramadan-focused diabetes education

- Ramadan-focused diabetes education is an extension of structured diabetes education aiming to give patients the knowledge to make informed decisions regarding their behavior and enabling them to effectively self-manage their condition.\(^1\)
  - enables patients with diabetes to maintain and improve glycemic control during and after fasting.\(^1\)
  - raises awareness of the risks associated with diabetes and fasting, and provides strategies to minimize them.\(^2\)

- Education should be simple, engaging, and delivered with cultural sensitivity by well informed individuals.\(^2\)

2) IDF Diabetes and Ramadan guideline 2016; p:64.
Targets of Ramadan-focused diabetes education

Health Care Professionals

General Public

Patients with Diabetes
Key components of a Ramadan-focused educational program

- Risk quantification
- Blood glucose monitoring
- Fluids and dietary advice
- Exercise advice
- Medication adjustments
- When to break the fast

IDF Diabetes and Ramadan guideline 2016; p:66
Key components of a Ramadan-focused educational program

Risk Quantification

• **Medical assessment**: 6-8 weeks before Ramadan

• **Risk quantification**: The type of diabetes, current diabetes medication, individual social and work circumstances, individual hypoglycemic risk, self management capabilities and the presence of any complications and/or co-morbidities

• **Risk Stratifications**

• **Providing advices**: appropriate knowledge to minimize the risks \(^{[1,2,3]}\)
Risk Quantification:

Factors for risk quantification

- Type of diabetes
- Patient medications
- Individual hypoglycaemic risk
- Presence of complications and/or comorbidities
- Individual social and work circumstances
- Previous Ramadan experience

IDF Diabetes and Ramadan guideline 2016; p:44
Category Red:
Very High Risk

If patients insist on fasting then they should:
- Receive structured education
- Be followed by a qualified diabetes team
- Check their blood glucose regularly (SMBG)
- Adjust medication dose as per recommendations
- Be prepared to break the fast in case of hypo- or hyperglycaemia
- Be prepared to stop the fast in case of frequent hypo- or hyperglycaemia or worsening of other related medical conditions

One or more of the following:
- Severe hypoglycaemia prior to Ramadan
- DKA within the 3 months prior to Ramadan
- Hyperosmolar hyperglycaemic state within the 3 months prior to Ramadan
- History of recurrent hypoglycaemia
- History of hypoglycaemia
- Poorly controlled T1DM
- Acute illness
- Pregnancy in pre-existing diabetes treated with insulin or oral medication
- Chronic dialysis or CKD
- Advanced macrovascular disease
- Old age with ill health

Category 1:
very high risk
Listen to medical advice
MUST NOT fast

IDF Diabetes and Ramadan guideline 2016,p:47
If patients insist on fasting then they should:
- Receive structured education
- Be followed by a qualified diabetes team
- Check their blood glucose regularly (SMBG)
- Adjust medication dose as per recommendations
- Be prepared to break the fast in case of hypo- or hyperglycaemia
- Be prepared to stop the fast in case of frequent hypo- or hyperglycaemia or worsening of other related medical conditions

One or more of the following:
- T2DM with sustained poor glycaemic control
- Well-controlled T1DM
- Well-controlled T2DM on insulin or oral agents
- Pregnant T2DM or GDM controlled on metformin
- CKD stage 3
- Stable macrovascular complications
- Patients with comorbid conditions and additional risk factors
- People with diabetes performing intense physical labour
- Treatment with drugs that may affect cognitive function

**Category 2:**

**high risk**

**Listen to medical advice**

**Should NOT fast**

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- IDF Diabetes and Ramedan guideline 2016, p:47
Category Green: Moderate/low risk

Well-controlled T2DM treated with one of the following:
- Lifestyle therapy
- Metformin
- Acarbose
- Thiazolidinediones
- Second-generation SUs
- Incretin-based therapy
- SGLT2 inhibitors
- Basal insulin

Category 3: moderate/low risk
Listen to medical advice
Decision to use licence not to fast based on discretion of medical opinion and ability of the individual to tolerate fast

IDF Diabetes and Ramedan guideline 2016,p:47
Key components of a Ramadan-focused educational program

Blood glucose monitoring

Pricking the skin for blood glucose testing does not invalidate the Ramadan fast.\[1\]

• Having the skills to do SMBG can empower patients with diabetes to effectively self-manage their disease.\[2\]

• The frequency of SMBG depends on many factors including the type of diabetes and current medications but should be carried out regularly by all:
  – moderate or low risk: once or twice a day
  – high or very high risk: several times a day

• Patients should check blood glucose levels whenever they experience symptoms of hypoglycemia.\[2\]
Recommended timings to check blood glucose levels during Ramadan fasting

1. Pre-dawn meal (suhoor)
2. Morning
3. Midday
4. Mid-afternoon
5. Pre-sunset meal (iftar)
6. 2-hours after iftar
7. At any time when there are symptoms of hypoglycaemia/hyperglycaemia or feeling unwell

IDF, Diabetes and Ramadan: Practical Guidelines, April 2016
Key components of a Ramadan-focused educational program

**Fluids and dietary advice**

- Divide daily calories between Suhoor and Iftar, plus 1–2 snacks if necessary
- Ensure meals are well balanced
  - 45–50% carbohydrate
  - 20–30% protein
  - <35% fat (*preferably mono- and polyunsaturated*)
- Include low glycemic index, high fiber foods that release energy slowly before and after fasting (*granary bread, beans, rice,...*)
- Keep hydrated between sunset and sunrise by drinking water or other non-sweetened beverages
- Minimize foods that are high in saturated fats (*ghee, samosas, pakoras,...*)
- Use small amounts of oil when cooking (*olive, rapeseed*)
- Include plenty of fruit, vegetables and salads
- Avoid caffeinated and sweetened drinks
- Avoid sugary desserts
Key components of a Ramadan-focused educational program

Exercise

- Maintain normal level of physical activity
- Beware that excessive physical activity may increase risk of hypoglycemia (*especially before Iftar*)
Individualization of treatment options

• Pre-Ramadan patient assessment

• Medication adjustment during Ramadan

• Post-Ramadan follow-up
The safety and effectiveness of non-insulin glucose lowering agents in the treatment of people with Type 2 Diabetes who observe Ramadan: A systematic review and meta-analysis

Diabetes Obes Metab. 2015 Jul;17(7):639-48

Strategies to Make Ramadan Fasting Safer in Type 2 Diabetics

A Systematic Review and Network Meta-analysis of Randomized Controlled Trials and Observational Studies

Medicine Volume 95, Number 2, January 2016
The safety and effectiveness of non-insulin glucose lowering agents in the treatment of people with Type 2 Diabetes who observe Ramadan: A systematic review and meta-analysis

- To determine which non-insulin glucose lowering treatment regimens are most appropriate in people with type 2 diabetes who choose to fast during Ramadan

- Sixteen studies included; nine RCTs (2,927 participants) and seven observational studies (1,775 participants)

Diabetes Obes Metab. 2015 Jul;17(7):639-48
Outcomes

- Number of participants having one or more hypoglycemic episodes during Ramadan
- Number of participants having one or more severe hypoglycemia episodes during Ramadan
- HbA1c change post Ramadan
- Weight change post Ramadan
<table>
<thead>
<tr>
<th>Study ID</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Devendra 2009</td>
<td>0.13 (0.03, 0.49)</td>
</tr>
<tr>
<td>Hassanein 2011</td>
<td>0.05 (0.00, 0.79)</td>
</tr>
<tr>
<td>Al-Arouj 2013</td>
<td>0.27 (0.19, 0.39)</td>
</tr>
<tr>
<td>Halimi 2013</td>
<td>0.92 (0.63, 1.34)</td>
</tr>
<tr>
<td>Shete 2013</td>
<td>0.15 (0.01, 3.12)</td>
</tr>
<tr>
<td><strong>Subtotal (I-squared = 86.7%, p = 0.000)</strong></td>
<td><strong>0.28 (0.10, 0.75)</strong></td>
</tr>
</tbody>
</table>

**RCTs: Vildagliptin vs. Sulphonylurea**

<table>
<thead>
<tr>
<th>Study ID</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hassanein 2014</td>
<td>0.71 (0.39, 1.28)</td>
</tr>
<tr>
<td>Malha 2014</td>
<td>0.81 (0.30, 2.23)</td>
</tr>
<tr>
<td><strong>Subtotal (I-squared = 0.0%, p = 0.814)</strong></td>
<td><strong>0.73 (0.44, 1.23)</strong></td>
</tr>
</tbody>
</table>

**RCTs: Sitagliptin vs. Sulphonylurea**

<table>
<thead>
<tr>
<th>Study ID</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Al-Sifni 2011</td>
<td>0.47 (0.34, 0.67)</td>
</tr>
<tr>
<td>Aravind 2012</td>
<td>0.49 (0.29, 0.83)</td>
</tr>
<tr>
<td><strong>Subtotal (I-squared = 0.0%, p = 0.891)</strong></td>
<td><strong>0.48 (0.36, 0.64)</strong></td>
</tr>
</tbody>
</table>

**NOTE**: Weights are from random effects analysis.
Key messages

• This systematic review and meta-analysis suggests that DPP-4 inhibitors and possibly GLP-1 receptor agonists could be used during Ramadan over sulfonylureas for fewer hypoglycemic episodes and a greater reduction in weight and possibly HbA1c.

• The results should be interpreted with caution however given the variable quality of the studies included.
Pharmacological management of people with T2DM

- Metformin
- Acarbose
- TZDs
- Short-acting insulin secretagogues
- Sulfonylureas
- SGLT2 inhibitors
- DPP4 inhibitors
- GLP-1 Ras
- Insulin treatment for T2DM
Pharmacological management of people with T2DM

- Metformin
- Acarbose
- TZDs
- Short-acting insulin secretagogues
- Sulfonylureas
- SGLT2 inhibitors
- DPP4 inhibitors
- GLP-1 Ras
- Insulin treatment for T2DM
Figure 2. Ramadan fasting dose adjustments for metformin in people with T2DM

Changes to metformin dosing during Ramadan

- **Once-daily dosing**
  - No dose modification usually required
  - Take at iftar

- **Twice-daily dosing**
  - No dose modification usually required
  - Take at iftar and suhoor

- **Three times daily dosing**
  - Morning dose to be taken before suhoor
  - Combine afternoon dose with dose taken at iftar

- **Prolonged-release metformin**
  - No dose modification usually required
  - Take at iftar
Pharmacological management of people with T2DM

- Metformin
- Acarbose
- TZDs
- Short-acting insulin secretagogues
- Sulfonylureas
- SGLT2 inhibitors
- DPP4 inhibitors
- GLP-1 Ras
- Insulin treatment for T2DM
While no RCTs have been conducted on ACARBOSE in fasting patients with diabetes, NO DOSE MODIFICATION is considered necessary as the risk of hypoglycaemia is low.
Pharmacological management of people

- Metformin
- Acarbose
- TZDs
- Short-acting insulin secretagogues
- Sulfunylureas
- SGLT2 inhibitors
- DPP4 inhibitors
- GLP-1 Ras
- Insulin treatment for T2DM
### Table 1. Studies evaluating TZD treatment in people with T2DM during Ramadan

<table>
<thead>
<tr>
<th>Study drug</th>
<th>Authors</th>
<th>Study details</th>
<th>Hypoglycaemia</th>
<th>Glycaemic control</th>
<th>Additional observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pioglitazone</td>
<td>Vasan et al, 2006 [6]</td>
<td>n=86 &lt;br&gt;&lt;br&gt;<em>Study type:</em> Double-blind, randomised, controlled trial &lt;br&gt;<em>Country:</em> India &lt;br&gt;<em>Additional medication(s):</em> Oral anti-hyperglycaemic agents &lt;br&gt;<em>Comparator:</em> Placebo</td>
<td>Events: Pioglitazone &gt; placebo &lt;br&gt;39 vs 32 (p=0.21)</td>
<td>Fructosamine levels: Pioglitazone &lt; placebo &lt;br&gt;Early Ramadan: (p=0.003) &lt;br&gt;Mid-Ramadan: (p=0.01) &lt;br&gt;Post-Ramadan: (p=0.04)</td>
<td>Body weight: Pioglitazone: ( \uparrow 3.02 \text{ kg} ) (p=0.001) &lt;br&gt;Placebo: ( \downarrow 0.46 \text{ kg} ) (p=0.37)</td>
</tr>
</tbody>
</table>

n, number of patients included in study

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Due to the low risk of hypoglycaemia with PIOGLITAZONE, NO DOSE MODIFICATION is required during Ramadan and doses can be taken with iftar or suhoor
Pharmacological management of people with T2DM

• Metformin
• Acarbose
• TZDs
  • Short-acting insulin secretagogues
• Sulfunylureas
• SGLT2 inhibitors
• DPP4 inhibitors
• GLP-1 Ras
• Insulin treatment for T2DM
Short-acting insulin secretagogues

• In two small observational studies, no hypoglycemic events were reported in patients treated with repaglinide during Ramadan, while a third demonstrated no difference in hypoglycemia when compared with insulin glargine or glimepiride, a sulphonylurea (SU) therapy.

• In two randomized parallel-group trials, a low incidence of hypoglycemic events was associated with repaglinide treatment during Ramadan, occurring in similar proportions of patients treated with glibenclamide and glimepiride.
• The short duration of action of these agents make them appealing for use during Ramadan as they can be taken before iftar and suhoor and carry a low risk of hypoglycemia

The daily dose of SHORT-ACTING INSULIN SECRETAGOGUES (based on a three-meal dosing) may be REDUCED or REDISTRIBUTED to two doses during Ramadan according to meal size
Pharmacological management of people with T2DM

- Metformin
- Acarbose
- TZDs
- Short-acting insulin secretagogues
- Sulfonylureas
- SGLT2 inhibitors
- DPP4 inhibitors
- GLP-1 Ras
- Insulin treatment for T2DM
Sulfonylureas

- SUs are widely used as second-line treatment for T2DM after metformin and so there is a wealth of evidence and experience with this low cost efficacious drug class.
In a multinational observational study of 1,378 patients with T2DM treated with SUs, approximately one fifth of patients experienced a symptomatic hypoglycemic event during Ramadan.

<table>
<thead>
<tr>
<th>Study drug</th>
<th>Authors</th>
<th>Study details</th>
<th>Hypoglycaemia</th>
<th>Glycaemic control</th>
<th>Additional observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥1 SUs</td>
<td>Aravind et al, 2011 [12]</td>
<td>n=1,378&lt;br&gt;Study type: Observational&lt;br&gt;Countries: India, Israel, Malaysia, UAE, Saudi Arabia&lt;br&gt;Additional medication(s): Metformin (not all patients)&lt;br&gt;Comparators: NR</td>
<td>Symptomatic patients: Gliclazide&lt;br&gt;Severe events: Gliclazide</td>
<td>NR</td>
<td>14.0% vs 16.8% vs 25.6%</td>
</tr>
</tbody>
</table>
Sulfonylureas

- More recent SUs such as **glimepiride**, **glipizide** and **gliclazide** are therefore preferred over conventional SUs, such as glibenclamide, because of their more favorable safety profile in terms of hypoglycemia.

- To date, no trials have been conducted looking at the modified-release formulation of gliclazide during Ramadan.
Figure 3. Ramadan fasting dose adjustments for SUs in people with T2DM

Changes to SU dosing during Ramadan

**Once-daily dosing**
- Take at iftar
- In patients with well-controlled BG levels the dose may be reduced

**Twice-daily dosing**
- Iftar dose remains the same
- In patients with well-controlled BG levels, the suhoor dose should be reduced

**Older drugs in the class**
- Older drugs (e.g. glibenclamide) carry a higher risk of hypoglycaemia and should be avoided
- Second-generation SUs (glicazide, glimepiride) should be used in preference
Pharmacological management of people with T2DM

- Metformin
- Acarbose
- TZDs
- Short-acting insulin secretagogues
- Sulfonylureas
- SGLT2 inhibitors
- DPP4 inhibitors
- GLP-1 Ras
- Insulin treatment for T2DM
Table 4. Studies evaluating SGLT2 inhibitor treatment in people with T2DM during Ramadan

<table>
<thead>
<tr>
<th>Study drug</th>
<th>Authors</th>
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<th>Glycaemic control</th>
<th>Additional observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dapagliflozin</td>
<td>Wan Juani et al, 2016 [21]</td>
<td>n=110</td>
<td>Events: Dapagliflozin &lt;SU 6.9% vs 28.8% (p=0.002)</td>
<td>No significant differences in HbA1c, fasting BG, or fructosamine levels were observed between the groups</td>
<td>Postural hypotension: Dapagliflozin &gt;SU 13.8% vs 5.8% (p=0.210) UTIs: Dapagliflozin &gt;SU 10.3% vs 3.8% (p=0.277)</td>
</tr>
</tbody>
</table>
SGLT2 inhibitors

• Further studies are warranted in order to prove the efficacy and safety of SGLT2 inhibitors during Ramadan
• Those that are deemed more at risk of complications such as the elderly, patients with renal impairment, hypotensive individuals, those at risk of dehydration or those taking diuretics should not be treated with SGLT2 inhibitors

SGLT2 inhibitors can be used with CAUTION in SOME patients. During Ramadan NO DOSE ADJUSTMENT is required and it is advised that the dose be taken with iftar
Pharmacological management of people with T2DM

- Metformin
- Acarbose
- TZDs
- Short-acting insulin secretagogues
- Sulfonylureas
- SGLT2 inhibitors
- DPP4 inhibitors
- GLP-1 Ras
- Insulin treatment for T2DM
DPP4 inhibitors

• Four RCTs and five observational studies have examined the efficacy and safety of DPP-4 inhibitor treatment during Ramadan.

• Specifically, the four RCTs examined the effects of switching from SU therapy to either vildagliptin or sitagliptin prior to Ramadan compared with continuing on SU.

• The largest of these studies compared the incidence of self-reported hypoglycaemic events in 1,066 patients with T2DM treated with sitagliptin or SUs during Ramadan.

• Overall, the risk of hypoglycemia significantly decreased on the sitagliptin-based regimen compared to continuing with SU treatment (relative risk ratio [95% CI] = 0.51[0.34, 0.75]; p<0.001)
DPP4 inhibitors

• The results of the studies described above indicate that vildagliptin is effective in improving glycemic control and that both vildagliptin and sitagliptin are associated with low rates of hypoglycemia during fasting, making them attractive treatment options during Ramadan.

• These drugs do not require any treatment modifications during Ramadan
Pharmacological management

• Metformin
• Acarbose
• TZDs
• Short-acting insulin secretagogues
• Sulfonylureas
• SGLT2 inhibitors
• DPP4 inhibitors
• GLP-1 Ras
• Insulin treatment for T2DM
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<th>Glycaemic control</th>
<th>Additional observations</th>
</tr>
</thead>
</table>
| **Liraglutide** | Azar et al, 2015 [34] | n=343  
*Study type*: Open-label, randomised, controlled trial  
*Countries*: Algeria, India, Israel, Lebanon, Malaysia, South Africa, UAE  
*Additional medication(s)*: Metformin  
*Comparator*: SU | Symptomatic events during Ramadan: Liraglutide<SU (p=0.0009)  
Symptomatic events from BL to end of Ramadan: Liraglutide<SU (p<0.0001) | Fructosamine ↓ during Ramadan: Liraglutide similar to SU (despite better glycaemic control in liraglutide group at start of Ramadan)  
Fructosamine ↓ from BL to end of Ramadan: Liraglutide<SU (p<0.05)  
HbA1c (%) ↓ from BL to end of Ramadan: Liraglutide>SU (p<0.0001) | Body weight ↓ during Ramadan: Liraglutide>SU (p=0.0091)  
Body weight ↓: from BL to end of Ramadan: Liraglutide>SU (p<0.0001) |
Table 6. Studies evaluating GLP-1 RA treatment in people with T2DM during Ramadan

<table>
<thead>
<tr>
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<th>Study details</th>
<th>Hypoglycaemia</th>
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<tbody>
<tr>
<td></td>
<td>Brady et al, 2014 [35]</td>
<td>n=99&lt;br&gt;Study type: Open-label, randomised, controlled trial&lt;br&gt;Country: UK&lt;br&gt;Additional medication(s): Metformin&lt;br&gt;Comparator: SU (gliclazide, glipizide or glibenclamide)</td>
<td>Self-recorded episodes of BG ≤3.9 mmol/L:&lt;br&gt;Liraglutide&lt;SU (p&lt;0.0001)&lt;br&gt;No severe episodes</td>
<td>Change in HbA1c:&lt;br&gt;3 weeks post-Ramadan:&lt;br&gt;Liraglutide&gt;SU&lt;br&gt;↓0.54% vs ↓0.27% (p=0.03)&lt;br&gt;12 weeks post-Ramadan:&lt;br&gt;Liraglutide&gt;SU&lt;br&gt;↓0.32% vs ↑0.02% (p=0.05)</td>
<td>Body weight:&lt;br&gt;3 weeks post-Ramadan:&lt;br&gt;Liraglutide&gt;SU&lt;br&gt;↓2.23 kg vs ↓0.42 kg (p=0.02)&lt;br&gt;12 weeks post-Ramadan:&lt;br&gt;Liraglutide&gt;SU&lt;br&gt;↓2.57 kg vs ↑0.25 kg (p=0.002)</td>
</tr>
</tbody>
</table>
GLP-1 Ras

• These studies demonstrate that liraglutide is safe as an add-on treatment to metformin and can be effective in reducing weight and HbA1c levels during Ramadan.

• Data on exenatide is limited to one study but the short duration of action and dosing of exenatide suggest that, like liraglutide, the risk of hypoglycemia during Ramadan is low.

As long as GLP-1 RAs have been appropriately DOSE-TITRATED prior to Ramadan (6 weeks before), NO FURTHER TREATMENT MODIFICATIONS are required.
Pharmacological management of people with T2DM

- Metformin
- Acarbose
- TZDs
- Short-acting insulin secretagogues
- Sulfonylureas
- SGLT2 inhibitors
- DPP4 inhibitors
- GLP-1 Ras
- **Insulin treatment for T2DM**
Insulin treatment for T2DM

• Insulin use during prolonged fasting carries an increased risk of hypoglycemia, particularly for those with T1DM but also for those with T2DM.

• The use of insulin analogues is recommended over regular human insulin due to a number of advantages that include less hypoglycemia.

• Although a number of small randomized trials and observational studies have been conducted to assess some insulin regimens during Ramadan, large RCT data in this area are lacking.
There are limited data available regarding the optimal insulin type or regimen for patients with T2DM during Ramadan but results from the studies described above indicate it may be safe to fast while on insulin, however treatment must be appropriately individualized.
Figure 4. Ramadan fasting dose adjustments for long- or short-acting insulins in people with T2DM

Changes to long- and short-acting insulin dosing during Ramadan

Long/intermediate-acting (basal) insulin

NPH/determir/glargine/degludec once-daily
Reduce dose by 15–30%
Take at iftar

NPH/determir/glargine twice-daily
Take usual morning dose at iftar
Reduce evening dose by 50% and take at suhoor

Short-acting insulin

Normal dose at iftar
Omit lunch-time dose
Reduce suhoor dose by 25–50%
Figure 5. Ramadan fasting dose adjustments for premixed insulin in people with T2DM

Changes to premixed insulin dosing during Ramadan

**Once-daily dosing**
- Take normal dose at iftar

**Twice-daily dosing**
- Take normal dose at iftar
- Reduce suhoor dose by 25–50%

**Three times daily dosing**
- Omit afternoon dose
- Adjust iftar and suhoor doses
- Carry out dose-titration every 3 days (see below)
Individualization of treatment options

- Pre-Ramadan patient assessment
- Medication adjustment during Ramadan
- Post-Ramadan follow-up
Post-Ramadan follow-up

• Patients with diabetes should be made aware of the risks of overindulgence during this time

• A post-Ramadan follow-up meeting with HCPs is advisable in order to discuss medication and regimen readjustments and assess how the patient handled the fasting

• It should be stressed to the patient that a safe fast one year does not automatically make them a low risk for the next year due to the progressive
Recommendations for prevention of hypoglycaemia during Ramadan

- Blood glucose monitoring
- Record blood glucose to determine pattern of hypoglycaemia
- Medication adjustment (1-2 month before)
- Avoid skipping Sahur meals
- Avoid strenuous physical activity during fasting
- Breaking fast if there is hypoglycaemia
Key components of a Ramadan-focused educational program

When to break the fast?

**Figure 3. When to break the fast**

All patients should break their fast if:
- Blood glucose <70 mg/dL (3.9 mmol/L)
- re-check within 1 h if blood glucose 70–90 mg/dL (3.9–5.0 mmol/L)
- Blood glucose >300 mg/dL (16.6 mmol/L)*
- Symptoms of hypoglycaemia, hyperglycaemia, dehydration or acute illness occur

### Hypoglycaemia
- Trembling
- Sweating/chills
- Palpitations
- Hunger
- Altered mental status
- Confusion
- Headache

### Hyperglycaemia
- Extreme thirst
- Hunger
- Frequent urination
- Fatigue
- Confusion
- Nausea/vomiting
- Abdominal pain

*Consider individualisation of care.*
Conclusion

• Diabetics with complications and those who are high risk should not fast
• Diabetics must visit the physician at least one month prior to Ramadan
• Only those with appropriate diets and physical activity, having controlled diabetes could fast during Ramadan
• Patient education must be conducted before entering Ramadan
• Management of diabetics in Ramadan is a good example of “Patient Centered Care (PCC)”.  
• Appropriate self management is the key to Ramadan fasting for diabetics.