

Review Article

Insulin therapy in ramadan

Sarita Bajaj¹, Ankit Singh¹

Ramadan is one of the five main pillars of islam . A significant proportion of muslim patients with diabetes fast in Ramadan are either already on insulin or may be started (naïve), presenting a challenge for the management to the healthcare providers as these patients have a very high risk of developing complications because of marked variability in meal and fluid intake during Ramadan. The Ramadan fast usually consist of a fasting period which can extend upto 9-12 hours. Once the fast is broken, it is followed by a heavy carbohydrate and fat rich evening meals. Excessive decrease of insulin dose during fasting can precipitate hyperglycemia and DKA and relatively higher dose can lead to hypoglycemia. However, fasting during Ramadan for patients with diabetes mellitus is feasible, provided there is good pre-Ramadan glycemic control, proper education regarding fast during Ramadan and a good coordination between the healthcare provider and the patients is maintained throughout the fasting period and also subsequently. Monitoring of blood glucose for dose adjustment and prevention of glycemia excursions are dealt with. Insulin regimens should be tailored to meet individuals needs of a patients in Ramadan. This chapter emphasizes on the importance of prerequisite of insulin, type of insulin, its strategies during Ramadan.

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Key words : Ramadan, Insulin, Euglycemia.

Much of what is recommended regarding the use of insulin during Ramadan is based on expert opinion, and few randomized controlled studies have investigated best treatment regimens during Ramadan in patients with diabetes to ensure safe and effective usage of insulin. All this guidance is based upon an understanding of the basic pharmacology of various insulins, and ensuring that prescribed insulin therapy correlate with the dietary regimes followed in Ramadan^{1,2}. Patients should be stratified into their risk of hypoglycemia and/or the presence of complications prior to the beginning of fasting. Patients at high risk of hypoglycemia and with multiple diabetic complications should be advised against prolonged fasting

Recently published South Asian consensus guidelines on use of insulin during Ramadan offer a definite approach to this subject. They suggest simple changes in dosage of insulin during this month. These guidelines support the use of rapid acting, premixed and basal analogues in view of the lesser risk of hypoglycemia associated with them. Examples of dose adjustment are also given³.

This review consist of essential information from these articles, while emphasizing the need for active involvement of patients in decision-making and management.

Recommendations for Insulin Therapy during Ramadan :

(I) Following recommendations can be made for

¹Department of Medicine, MLN Medical College, Allahabad, Uttar Pradesh 211002

- Proper glycemic control is a challenge during Ramadan.
- Glycemic variability with complications to be prevented.
- Proper education about fasting, diet, regular CBG monitoring with insulin dose adjustment is needed.
- Insulin regimen should be tailored to meet individual's need.

adolescents who are in good health and who wish to fast :

Individualization

Management plan must be individualized for each patient according to the need.

Diabetic education during Ramadan

The role of structured education for patients is well established in the management of diabetes. This should be extended to Ramadan-focused diabetes education. Patients should receive education regarding the following:

- (1) Self-monitoring of blood glucose at home.
- (2) Focus on the causation, early recognition, and emergency management of hypoglycemia, hyperglycemia, dehydration, and impending diabetic ketoacidosis.
- (3) Meal planning and dietary advice.
- (4) Timing and intensity of physical activity.
- (5) Compliance to medications.

Pre-Ramadan medical assessment

- (1) Preferably undertaken 1–2 months before the fasting month starts.
- (2) Physical status, glycemic status, and appropriate blood studies.
- (3) Look for any acute and chronic complications and

individual risk stratification to identify those not fit to fast.

Diet and nutrition

(1) Ingestion of large amount of foods rich in carbohydrate and fat during Iftar should be avoided.

(2) Meal at Sehri should contain complex carbohydrate, as this will delay digestion and absorption (slow digesting foods). This should be taken as late as possible.

(3) Inclusion of fruits, vegetables, lentils, yogurt, cereal (eg, puffed rice).

(4) Fluid should be taken liberally during non fasting hours

Exercise and physical activity

(1) Normal level of physical activity should be maintained.

(2) Rigorous exercise during fasting hours should be avoided.

Checking glycemic status

(1) Under Al Shariaa and Al Fatwa law, neither blood testing nor administration of insulin is forbidden and neither is considered to invalidate the fasting state. Patients should be encouraged to do frequent home monitoring.

(2) Urine should be checked for ketone if blood glucose is high (>270mg/dL).

Breaking the fast

(1) Patient should break fasting if blood glucose levels are low (<70mg/dL) or patient experiences signs/symptoms of hypoglycemia and if blood glucose level is >300mg/dL.

(2) Patient should avoid fasting on sick days.

(II) Type 1 Diabetes, With Stable Control

The ideal insulin regimen for type 1 diabetes is a basal-bolus regime with a regulated diet plan. Such a regimen provides safe and effective glycemic control, while assuming a regular 3+3 meal pattern (3 major meals and 3 snacks) and a fixed physical activity profile.

During Ramadan, however, the basal bolus regimen is not possible. Persons with type 1 diabetes, who enjoy stable control, without significant complications or comorbidity, and wish to fast, will require modification in insulin regimens (Table 1).

Such persons may benefit from a modified basal plus regime. Persons with type 2 diabetes, on basal bolus or split mix therapy, will need similar modification in therapy³.

Modern insulin analogues are reported to be effective at achieving glycemic control, with lower hypoglycemia risks⁴⁻⁶. Insulin detemir or glargine has demonstrated a significant decline in mean plasma glucose with minimal episodes of mild hypoglycemia. Similar results are seen with insulin glulisine, lispro, or aspart used instead of regular insulin in combination with intermediate-acting insulin injected twice a day. Compared with those who did not fast during Ramadan, patients with type 1 diabetes on in-

Table 1 — *Modification of Intensive Insulin therapy during Ramadan*

Modification of basal-bolus therapy :		
Bolus dose	Morning dose	Transfer full dose at iftar
	Evening dose	Transfer 1/2 dose at suhur
	Lunch dose	Omit the dose
Basal portion	If patient is on NPH	50% dose at suhur
	If patient is on basal analog	Same dose at bedtime
Modification of split insulin therapy :		
Split with three time short acting and NPH at dinner	Morning short acting	transfer full dose at iftar
	Lunch short acting	Omit dose
	Dinner short	transfer 1/2 dose at suhur
	Intermediate acting	Keep same dose at suhur
Split short acting and NPH twice daily	Morning short acting	transfer full dose at iftar
	Morning intermediate	transfer full dose at iftar
	Dinner short acting	transfer 1/2 dose at suhur
	Dinner intermediate	transfer 1/2 dose at suhur

sulin pump therapy who fasted showed a slight improvement in A1C without increasing the risk of hypoglycaemia^{7,8}.

The ultra-long acting insulin degludec aspart (I Deg Asp) has been studied as part of a three-dose regime in adult type 1 diabetes^{9,10}. This entails use of I Deg Asp with one major meal, and insulin aspart with the other two meals, daily. This may be modified in Ramadan to a twice daily I Deg Asp regime, as has been reported in type 2 diabetes¹⁰. Such a shift should be done a few weeks prior to the start of Ramadan, so that dose titration can be done safely. A shift from biphasic aspart (BI Asp) to I Deg Asp will require a 10-20% reduction of dosage.

(III) Type 1 Diabetes with Unstable Control

Persons with type 1 diabetes, who experience unstable control, brittle diabetes, frequent hypoglycaemia, hypoglycaemia unawareness, or have significant chronic complications or acute/ chronic comorbidity, should be dissuaded from observing the Ramadan fast. The appropriate religious exemptions should be explained to them with empathy.

(IV) Type 2 Diabetes, With Stable Control

Various insulin regimens are available for use in type 2 diabetes. The choice of insulin regimens and preparation depends upon a multitude of objective and subjective parameters, including the person's gluco-phenotype, dietary and physical activity patterns risk of hypoglycaemia and personal preferences. As all these factors change during Ramadan, modification of insulin regimens may be needed (Table 2).

Use of a rapid acting insulin analogue instead of regular human insulin before meals in patients with type 2 diabetes who fast during Ramadan is associated with less hypoglycemia and less post prandial glucose excursions.

While switching from human premix to analogue premix insulin, the dose of analogue insulin at pre-Iftar should be 20 to 30% lower than the morning human insulin dose pre-Ramadan. Pre-Suhur dose should be roughly half of the evening dose pre-Ramadan. Further dose ad-

Table 2 — Management of patients with type 2 diabetes mellitus

Diatebes treatment	Recommended Regimen during Ramadan
Once daily long-acting basal insulin (glargine, detemir)	Reduce dose by 10% to 30% Take at sunset meal (iftar)
Once daily premixed insulin	Keep the same dose, at sunset meal (iftar)
Twice daily premixed insulin	Keep sunset meal (iftar) dose the same the morning dose is shifted to before iftar cum dinner Reduce the second dose by 20% to 30% and take with re-dawn meal (suhar), the evening dose is reduced by 50% before suhur
Thrice daily premixed insulin	Omit afternoon dose. Thrate preifter and pre-suhur doses
Rapid-acting insulin (aspart, lispro, glulisine)	Start with the samemeal dose, butmay need to increase sunset meal (iftar) dose by 10% to 20% to avoid hyperglycaemia Same meal dose for pre-dawn meal (suhur) If morning hypoglycaemia occurs, reduce pre-dawn meal (suhur) dose by 10% to 20% or omit it completely if needed
Insulin pump	Basal rate reduced by 20% Meal doses per above (rapid-acting insulin)

are used for nutrition by the body¹².

Patients with insulin deficiency especially Type 1 diabetes, may have excessive glycogenolysis, gluconeogenesis and ketogenesis. All of this may lead to hyperglycaemia and ketoacidosis that may be life-threatening. Therefore, insulin is as necessary during Ramadan fasting, as it is during other times of the year, for persons who require this drug. Fasting or starvation does not imply lack of insulin requirement.

Examples of insulin dose modification during Ramadan :		
Insulin regime	Pre-Ramadan dose (unit)	Starting dose during Ramadan (units)
Basal; o.d	10	8
Basal; b.d	10 AM-10PM	5 AM-10 PM
Premixed; o.d am	10 (AM)	- 6 units (AM)
Premixed; o.d PM	10 (PM)	10 (PM)
Premixed; b.d 70/30	20-10	20-May
Split mix		
Basal - bolus	R6-R6-R6-B10	R3-RoR9-10
R=rapid ; B=basal ; PM=post-sunset ; AM=pre-dawn		

justment is decided as per glucose monitoring trends.

No consensus statement has been released so far regarding the use of insulin degludec and I Deg Asp in Ramadan. However, the unique time-action profile of these drugs supports their use during fasting. If used as basal therapy, the dose of insulin degludec should be reduced by 10-20% during Ramadan. If taken as part of basal bolus therapy, the same rules will follow, as described in the section on type 1 diabetes. If utilized as a twice daily regime during Ramadan, the I Deg Asp co-formulation can be used in a manner similar to that suggested for premixed insulins.

Counselling :

The need for Ramadan- focused diabetes education has been discussed in detail by Hassanein¹¹. Three points, however, need to be reinforced here.

The Need for Insulin :

In normal healthy individuals eating stimulates the secretion of insulin from the islet cells of the pancreas. This in turn results in glycogenesis and storage of glucose as glycogen in liver and muscle. On the contrary, during fasting, secretion of insulin is reduced while counter-regulatory hormones glucagon and catecholamines are increased. This leads to glycogenolysis and gluconeogenesis. The low levels of insulin in circulation also lead to increased fatty acid release and oxidation that generates ketones which

Safety First :

Fasting is obligatory upon each sane, responsible and healthy Muslim. Certain individuals, however, are exempt from fasting: children under the age of puberty, those with learning difficulties (those unable to understand the nature and purpose of the fast), the old and frail, the acutely unwell, those with chronic illnesses in whom fasting may be detrimental to health, and those travelling a distance greater than 50 miles in single journey^{3,12}.

At times, unexpected life-threatening, limb- threatening or organ- threatening complications may occur during Ramadan. Such a complication may require intensive insulin therapy, which may not be concordant with the dietary restrictions imposed by Ramadan. In such a case, the fast may be broken, without religious demerit. Mere self-monitoring of blood glucose, venous blood sampling, or any diagnostic procedure which does not involve oral intake, does not constitute break in fasting, and is not prohibited by religion.

Hypoglycemia Awareness :

Person on insulin or other glucose-lowering therapy must be aware of the symptoms and signs of hypoglycemia, and how to prevent and manage them. This information is especially relevant during Ramadan, and must be shared with family members and colleagues as well. Difficulty in concentrating, meditating or praying may be a subtle symptom of neuroglycopenia¹³, and should not be ignored. Blood glucose should be monitored immediately on occurrence of any unusual symptom. People with diabetes and hypoglycemia unawareness should not fast as they are at higher risk of severe hypoglycemia.

Important points to be considered for Safe Insulin Use in Ramadan

- (1) Select appropriate insulin regimens and preparations prior to Ramadan. Visit your doctor a month before the advent of Ramadan.

- (2) Take a small snack three hours after iftar, followed by Suhur just before sunrise
- (3) Avoid heavy exercise and unaccustomed physical activity.
- (4) Regular blood glucose monitoring
- (5) Take symptoms suggestive of hypoglycaemia seriously and reduce insulin doses in case of doubt
- (6) Follow physician's advice in the spirit of shared decision making

Conclusion :

Fasting should be encouraged but with medical supervision. More counseling for patients and more training for healthcare providers should be done, to strengthen the patient-physician relationship. Insulin regimens should be tailored to meet individual needs of a patient in Ramadan. Counseling must be provided at all levels of insulin therapy. Care should be taken to avoid hypoglycemia throughout, with special emphasis to iatrogenic hypoglycemia. Regular monitoring of glucose would help in titrating insulin dose accurately. The aim of insulin therapy is to prevent hypoglycemia when fasting and to control postmeal hyperglycemia.

REFERENCES

- 1 Jaleel MA, Fathima FN, Jaleel BN — Nutrition, energy intake-output, exercise, and fluid homeostasis during fasting in Ramadan. *J Med Nutr Nutraceut* 2013; **2**: 63-8
- 2 Hassanein M, Belhadj M, Abdallah K, Bhattacharya AD, Singh AK, Tayeb K, *et al* — Management of Type 2 diabetes in Ramadan: Lowratio premix insulin working group practical advice. *Indian J Endocr Metab* 2014; **18**: 794-9
- 3 Pathan M, Sahay RK, Zargar AH, Raza SA, Azad Khan A K, Ganie MA, *et al* — South Asian Consensus Guideline: Use of insulin in diabetes during Ramadan. *Indian J Endocr Metab* 2012; **16**: 499-502
- 4 Siebenhofer A, Plank J, Berghold A, Jeitler K, Horvath K, Narath M, *et al* — Short acting insulin analogues versus regular human insulin in patients with diabetes mellitus. *Cochrane Database Syst Rev* 2006: CD003287.
- 5 Horvath K, Jeitler K, Berghold A, Ebrahim SH, Gratzner TW, Plank J, *et al* — Long-acting insulin analogues versus NPH insulin (human isophane insulin) for type 2 diabetes mellitus. *Cochrane Database Syst Rev* 2007 CD005613.
- 6 Ahmed I. Ramadan: type 2 diabetes and risk of hypoglycaemia. *Int J Clin Pract* 2013; **67**: 933-4. doi: 10.1111/ijcp.12259.
- 7 Kadir A, Al-Nakhi A, El-Ghazali S, Jabbar A, Al Arouj M, Akram J, *et al* — Treatment of type 1 diabetes with insulin lispro during Ramadan. *Diabetes Metab* 2001; **27**: 482-6.
- 8 Kassem HS, Zantout MS, Azar ST — Insulin therapy during Ramadan fast for Type 1 diabetes patients. *J Endocrinol Invest* 2005; **28**: 802-5.
- 9 Davies MJ, Gross JL, Ono Y, Sasaki T, Bantwal G, Gall MA — Efficacy and safety of insulin degludec given as part of basal-bolus treatment with mealtime insulin aspart in type 1 diabetes: a 26-week randomized, open-label, treat-to-target non-inferiority trial. *Diabetes Obes Metab* 2014; **16**: 922-930. doi: 10.1111/dom.12298
- 10 Kalra S — Insulin degludec aspart: the first co-formulation of insulin analogues. *Diabetes Ther* 2014; **5**: 65-72. doi: 10.1007/s13300-014-0067.
- 11 Hassanein M — Ramadan focused diabetes education; a much needed approach. *JPMA* 2015; **65**: S76-S78.
- 12 Jaleel MA, Raza SA, Fathima FN, Jaleel BF — Ramadan and diabetes: As-Saum (The fasting). *Indian J Endocr Metab* 2011; **15**: 268-73
- 13 Kalra S, Gupta Y — Culture bound hypoglycemia symptomatology. *J Mid-life Health* 2014; **5**: 98.