

South Asian Guidelines for Management of Endocrine Disorders in Ramadan

South Asian Consensus Guideline: Use of GLP-1 analogue therapy in diabetes during Ramadan

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ABSTRACT

Ramadan is a lunar based month, during which Muslims across the world observe the ritual fast. This provides a challenge not only to the diabetic patient who wishes to observe the fast but also to the health care professional managing his diabetes. The challenge is to use therapies which are effective in maintaining good glycemic control and at the same time have a low propensity to cause hypoglycemia during the several hours of no calorie intake. The GLP-1 analogues are unique agents which are effective in providing glycemic reduction with a very low risk of hypoglycemia and hence find an important place in the management of diabetes during Ramadan. This Consensus Statement describes the pre-Ramadan assessment, planning, prescription and management and monitoring of patients who are on GLP-1 analogues, with or without other antidiabetic therapies.

Key words: DPP4, exanetide, hypoglycemia, insulin, Liraglutide, oral antidiabetic drugs, type 2 diabetes

INTRODUCTION

Ramadan is a lunar-based month, during which Muslims across the world observe the ritual fast. They abstain from eating, drinking, smoking or use of oral medications from predawn to sunset. However, there are no restrictions on the food and fluid intake in the period between sunset and sunrise on the following day.^[1,2] Although such a fast may not cause significant problems in healthy non-diabetic individuals, it may be a challenge for those with diabetes. This is particularly so with certain diabetes therapies that tend to cause hypoglycemia, and also in the presence of any

of the complications of diabetes. Most people observing the fast consume two meals per day, one after sunset and the other one before sunrise.^[3] Some people take a third meal in the form of a late night dinner. In terms of effective glycemic management of such patients, there is a need for therapy which is effective in controlling postprandial hyperglycemia with minimal risk of hypoglycemia during the period of prolonged fast.^[4]

GLP-1 is an incretin hormone secreted from the L cells of the intestine, which has been considered as a new and promising treatment for type 2 diabetes. GLP-1 stimulates endogenous insulin secretion when plasma glucose levels are elevated and decreases glucagon secretion. It also decreases gastric motility, which delays gastric emptying and leads to reduced appetite and food intake.^[5] The combination of these mechanisms makes GLP-1 a potent blood glucose-lowering agent and an attractive pharmacological treatment for type 2 diabetes. Since the GLP-1 molecule is rapidly broken down to inactive molecules by the DPP4 enzyme, analogues of GLP-1 which are resistant to DPP4 mediated

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inactivation and renal clearance have been developed. At present, these include exenatide, a twice daily GLP-1 receptor agonist, and liraglutide, a longer acting GLP-1 analogue which is used once daily.^[6]

GLP-1 analogues have been shown to be effective in improving glycemic control in patients who had insufficient glycemic control on lifestyle changes or with one or two oral antidiabetic medications. The glycemic control so achieved was with much lower risk of hypoglycemia and with an additional benefit of weight loss. In the LEAD trials, treatment with liraglutide also presented a lower risk of hypoglycaemia. This finding was expected, since liraglutide stimulates insulin secretion in a glucose-dependent manner and has no effect on glucagon secretion when plasma glucose is low.^[7-12] GLP-1 analogues are therefore very useful agents for management of diabetes, particularly in the setting of Ramadan. They can be combined with the insulin sensitizers which also have a very low risk of hypoglycemia.

GLP-1 analogues as described above are very attractive agents in the setting of the Ramadan fast. They can be either used as monotherapy or in combination with one or more oral agents. They can also be combined with insulin. Although there is enough evidence regarding the use of these agents, the evidence regarding their use in Ramadan fasting is not available. However they are safe in terms of hypoglycemia and renal and hepatic functional aspect except for their GI side effect. Hence they can be used in Ramadan safely.

INITIAL ASSESSMENT OF DIABETIC PATIENTS WHO WISH TO FAST DURING RAMADAN

Those diabetic patients who intend to perform fasting in Ramadan, should plan at least 3 months before the Ramadan month. Certain factors should be assessed by their physician:

1. Assessment of glycaemic status - Avoid fasting if $HbA_{1c} > 10\%$, frequent hypoglycemia, hypoglycemic unawareness, high fluctuation of blood glucose profile.
2. Assessment of complications and other co-morbid conditions which may be aggravated by prolong fasting, particularly chronic kidney disease, hepatic failure, severe cardiac problems-unstable angina, heart failure, and others.
3. Change of diet and meal plan according to own customs and habit for Ramadan itself, keeping the daily calorie requirement same.
4. Possibility of dehydration and electrolyte imbalance should be looked for.

RECOMMENDED CHANGES TO TREATMENT REGIMEN WITH GLP-1 ANALOGUE IN PATIENTS WITH TYPE 2 DIABETES WHO FAST DURING RAMADAN

Patient on GLP-1 analogue before Ramadan

- There may be any of these three scenarios, as combination therapy or as monotherapy.
- Patient is on once daily dose with liraglutide (0.6 mg, 1.2 mg or 1.8 mg daily).
- Patient is on twice daily dose with exenatide (5 mcg or 10 mcg twice daily).
- Patient is on extended release preparation of exenatide (2 mg once a week).

Patient on GLP-1 analogue during Ramadan

- Ensure adequate fluid intake.

If patient is on monotherapy with GLP-1 analogue

- In case of liraglutide, keep the same dose anytime but preferably during iftaar.
- In case of exenatide, the morning dose should be same at iftaar and the evening dose should be same at sahur.
- The same dose of extended release preparation of exenatide should be continued during Ramadan.

If patient is on combination with oral hypoglycemic agent and GLP-1 analogue

- Keep same dose of liraglutide preferably during iftaar. Keep same dose of metformin. Dose and time schedule of secretagogues should be reduced according to the South Asian treatment guidelines of OHA during Ramadan.
- In case of exenatide, morning dose should be shifted to iftaar as same and evening dose should be shifted to sahur remaining same. OHA dose should be reduced according to South Asian OHA recommendation during Ramadan.

If patient is on combination with basal insulin and GLP-1 analogue

- Keep the same dose of liraglutide preferably during iftaar. Basal insulin dose should be same at bed time. Long acting basal insulin dose should be readjusted by monitoring midday and before iftaar blood glucose

Blood glucose monitoring during Ramadan

Blood glucose level monitoring during fasting is required recognize subclinical hypo and hyperglycemia. Monitoring should be done 2 hours post-sahur and one/two hour pre-iftaar to pick subclinical hypoglycemia. However, as there

is less risk of hypoglycemia with GLP-1 analogues, the need for glucose monitoring is less pressing these patients as compared to those on insulin and oral secretagogues. This makes GLP-1 analogues an attractive choice of therapy in Ramadan.

CONCLUSION

It is possible for people with diabetes to fast safely during Ramadan. But it requires careful planning in order to avoid problems that could be serious and have long-term effect. The GLP-1 analogues in view of their unique properties of having good glycemic efficacy, without causing hypoglycemia, provide a very useful choice for management of diabetes during the Ramadan fasting either as monotherapy or in combination with other antidiabetic drugs. Further evidence regarding their use in this period is awaited.

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