



The Choice of Insulin Type and Regimen for Adolescents with Type 1 Diabetes during Ramadan Fasting: A Continuing Debate

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The intertwined complexity of type 1 diabetes (T1D) and the amplification of its associated symptoms during Ramadan fasting inevitably imposes a challenge in the appropriate apportionment of insulin. Based on clinical experience, different recommendations on adjusting the type, dose, and timing of insulin in adults have been suggested.¹ However, clear evidence-based guidelines on insulin adjustment for children and adolescents with T1D are lacking.

The ongoing challenge for medical practitioners during the holy month is highlighted by Kaplan et al in their study comparing insulin glargine and insulin detemir in adolescents with T1D during Ramadan fasting published in the current issue of *Journal of Diabetes and Endocrine Practice*,² as it explores the multisectoral factors involved in the long-lasting debate regarding which insulin is more suitable by comparing insulin glargine and insulin detemir on the glucose profile in fasting adolescents with T1D. Overall, the study concludes that insulin detemir given twice daily results in less hypoglycemia than once daily insulin glargine, which implies that it may be more suitable.

Several observational studies report favorable safety and efficacy of insulin analogs in relatively well-controlled patients with T1D who fasted with no severe episodes of hypoglycemia.³ Hayakawa et al demonstrated that the risk of hypoglycemia is shown to be reduced through the application of long-acting insulin analogs, glargine and detemir.⁴ Insulin glargine is a synthetic version of human insulin that is Food and Drug Administration approved to treat adults and

children with T1D and adults with type 2 diabetes (T2D) to improve and maintain glycemic control.⁵ In contrast, insulin detemir (Levemir) is a soluble long-acting human insulin analog acylated with a 14-carbon fatty acid. The fatty acid modification allows insulin detemir to reversibly bind to albumin, thereby providing slow absorption and a prolonged metabolic effect (up to 24 hours) with low variability.⁶

Overall, the study of Kaplan et al² emphasizes how prolonged abstinence from drinking and eating during Ramadan increases the risk of hypoglycemia in patients with T1D, a concern that has been raised in previous recommendations.⁷ As highlighted in their results, the duration and proportion of hypoglycemia were by far highest in the late fasting period in both groups, followed by the early fasting period. At the same time, there was barely any hypoglycemia during the post-iftar period. Furthermore, despite medical advice contradicting the act of fasting due to its association with high health risks, adolescents continue to fast due to religious and cultural factors, emphasizing the importance of the appropriate selection of insulin.⁸ Moreover, due to long fasting periods, clinical practitioners may reduce the basal insulin dose to reduce the risk of hypoglycemia.⁹ However, a proper dose of adjustment of the basal insulin has yet to be established, thus creating a gray area in clinical practice.¹⁰ Moreover, this imposes a contradicting limitation as recent studies reveal hyperglycemia levels increase once the patient's fast is broken due to consumption of a lower dose of basal insulin.¹¹

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The amplification of T1D complications during Ramadan causes a substantial strain on the quality of life for adolescents in Muslim communities, which has caused the non-communicable disease to remain an alarming public health issue for the unforeseeable future. In addition to amplifying the global burden of disease, the literature available pertaining to the application of long-acting insulin in adolescents during the holy month is scarce, which has led to greater uncertainties in practice.¹² Further research, including clinical trials, should be conducted to overcome the challenges in the selection of insulin and the minimization of hypoglycemia and hyperglycemia. This can eventually lead to better management and a lower risk of long-term effects. Moreover, certain health disparities such as geographical location are more pronounced during the holy month, and thus, public health intervention should establish inclusive target audiences. In essence, populations residing in geographical locations that entail a more extended fasting period must be taken into consideration to avoid the manifestation of health research inequities

Health economics and access to “safer” insulins can be another barrier to fasting. In some countries around the world, twice-daily insulin regimens are practiced. Patients using this regime are more prone to hyperglycemia with or without ketosis during fasting.¹³ Using these regimens during Ramadan is possible but requires more dose adjustments and monitoring. Another commonly used type of insulin, where newer analogs are not available, is the premixed insulin. This type is given twice daily, thus requiring a fixed intake of carbohydrates to counteract the two peaks of insulin activity. Such a regimen is associated with a higher risk of hypoglycemia.¹⁴

More studies are required to examine the safety and efficacy of *newer insulins* in the younger age group. Although some experience with these insulins in adults with diabetes has been reported, further data are needed in the pediatric population to establish clear guidance around their use. Some of these insulins include more concentrated forms of insulin (insulin glargine 300) and the newer basal insulin degludec with flatter pharmacodynamic profiles.

Insulin degludec is approved for clinical use in the pediatric population, starting from the first year of age. It resulted in a lower frequency of nocturnal hypoglycemia, more flexibility in insulin administration timing, and better quality of life.¹⁵ These advantages might be of utmost importance, especially during fasting. Its safety has been proven in T2D adult patients who experienced fewer episodes of hypoglycemia when switched to this type of insulin during the fasting month of Ramadan.¹⁶ Moreover, the ORION study, a prospective, observational, international multicenter study, evaluated the safety and effectiveness of glargine 300 in insulin-treated adults with T2D before, during, and after Ramadan, in a real-world setting.¹⁷ The study showed that people with T2D treated with glargine 300 who fasted during Ramadan had a low risk of severe/symptomatic hypoglycemia and improved glycemic control. Lastly, clinical practices should adopt closer monitoring and documentation of issues likely to affect adolescents with T1D and improve the man-

agement based on available clinical and experimental evidence.

Authors' Contribution

Equal contribution.

Compliance with Ethical Principles

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Conflict of Interest

None declared.

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