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Original Research Article

Ultra-Rapid Lispro vs. Insulin aspart: A Comparison of Postprandial Glucose Control in T2DM

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Abstract

Background: Effective management of postprandial glucose (PPG) levels is a critical component in controlling type 2 diabetes mellitus (T2DM) and preventing its long-term complications. While rapid-acting insulin analogs like insulin aspart are commonly used, "ultra-rapid lispro (URLi) has emerged as a newer formulation designed to more closely mimic physiological insulin secretion. This study aimed to compare the efficacy and safety of URLi versus insulin aspart in achieving optimal PPG control in patients with T2DM.

Methods: A prospective, open-label, randomized comparative study was conducted at Patna Medical College & Hospital, Patna, Bihar, from January 2025 to June 2025. A total of 100 adult patients with T2DM (HbA1c 7%–9.5%) on basal-bolus insulin regimens were enrolled and randomly assigned into two equal groups: Group A received ultra-rapid lispro, and Group B received insulin aspart before meals. Fasting blood glucose, 2-hour PPG levels, and HbA1c were recorded at baseline and monitored weekly for 8 weeks. Adverse events, particularly hypoglycemia, were also assessed. Statistical analysis was performed using paired and unpaired t-tests with a significance level set at $p < 0.05$.

Results: Group A demonstrated a significantly greater reduction in 2-hour PPG levels (56 ± 12 mg/dL) compared to Group B (42 ± 10 mg/dL), with $p < 0.01$. End-of-study HbA1c levels were lower in Group A (7.3% ± 0.4%) than in Group B (7.5% ± 0.5%), though the difference was not statistically significant ($p = 0.07$). The incidence of hypoglycemic events was slightly higher in the URLi group but not statistically significant.

Conclusion: Ultra-rapid lispro is more effective than insulin aspart in controlling postprandial glucose in T2DM patients, with a comparable safety profile. URLi may serve as a valuable tool in optimizing intensive insulin therapy.

Keywords: Type 2 Diabetes Mellitus, Ultra-Rapid Lispro, Insulin Aspart, Postprandial Glucose, Glycemic Control, Basal-Bolus Therapy, And Hypoglycemia.

Introduction

Type 2 Diabetes Mellitus (T2DM), a chronic metabolic disorder that worsens with time, is rising rapidly in developing nations like India. Insulin resistance and pancreatic β-cell insufficiency contribute to type 2 diabetes' development [1]. Thus, type 2 diabetics have long-term hyperglycemia, which increases the risk of microvascular and macrovascular complications like retinopathy, nephropathy, neuropathy, hypertension, and cardiovascular disease if uncontrolled [2]. In recent years, postprandial glucose (PPG) levels have become one of the glycaemic markers tracked in diabetes management. PPG levels substantially increase glycaemic load, independent of atherosclerosis and cardiovascular events. Comprehensive diabetes management must optimise PPG control to improve patient outcomes and reduce long-term risks [3]. Traditional insulin therapy has advanced because to insulin analogues that are more biologically equivalent to the body's insulin response [4]. Short-acting insulin analogues like insulin glulisine, insulin aspart, and insulin lispro are widely used to manage postprandial hyperglycemia in type 2 diabetics, especially those on intensive insulin regimens. Fast-acting treatment relies on insulin aspart, which has a better onset and duration than human insulin [5]. Even with fast-acting analogues, subcutaneous insulin pharmacokinetics and meal reactions take time. Even with timely insulin, this delay causes early postprandial glucose spikes that are difficult to maintain. Thus, diabetes experts are

tirelessly developing new formulations that better match physiological insulin secretion, start faster, and are easier to digest [6]. Ultra-rapid lispro (URLi) is a novel prandial insulin treatment. URLi modifies insulin lispro with citrate and treprostinil. Treprostinil, a prostacyclin analogue, enhances capillary blood flow, and citrate expands injection site blood vessels, speeding insulin absorption [7]. To make insulin lispro or aspart function faster and peak earlier, the recipe is modified. Clinical pharmacokinetic studies show that URLi lowers blood glucose faster and peaks earlier than insulin aspart, improving postprandial glycaemic control without compromising safety [8]. This improved profile may benefit type 2 diabetics with insulin resistance and delayed stomach emptying, which can impair the efficacy of standard prandial insulins. URLi works and is safe for type 1 and type 2 diabetics, although real-world comparisons are lacking [9]. In Indian clinical settings, insulin sensitivity, dietary habits, and treatment consistency varies greatly from Western cultures. A high glycaemic index diet, central obesity, and excessive carbohydrate consumption are risk factors for type 2 diabetes mellitus in India, which worsens postprandial glycaemia [10]. To ensure the efficacy of innovative treatment modalities in everyday practice, region-specific assessments must account for ethnic and lifestyle disparities.

With that in mind, we examined the postprandial glucose-controlling effects of insulin aspart with ultra-rapid lispro in type 2 diabetes patients at Patna Medical College & Hospital in Bihar. This three-month, prospective, randomised, open-label research will enrol 100 basal-bolus insulin users from February to April 2025 [11]. The trial's main endpoint is 2-hour postprandial blood glucose change from baseline. Secondary outcomes include haemoglobin A1c changes and hypoglycemia. This study aims to help incorporate newer insulin analogues like URLi into national diabetes treatment guidelines by providing clinically valuable PPG control data to assist insulin choices in Indian diabetics. The study is important since diabetes care in India is always changing [12]. New insulin analogues are becoming more accessible, yet many clinicians continue prescribe the old ones due to familiarity, expense, and a lack of local knowledge. Due to the rising prevalence of diabetes, which disproportionately affects rural and semi-urban areas, safe and effective glucose-lowering treatments are needed. URLi's pharmacological benefits allow for faster and more flexible postprandial control, which may improve patient satisfaction. Before its widespread use in India, it must be compared to insulin aspart in real-world circumstances.

Increasing evidence links oxidative stress, endothelial dysfunction, and vascular inflammation to glycaemic variability, and inadequate postprandial control is a known early contributor. Thus, postprandial hyperglycemia control can achieve glycaemic goals and reduce long-term health risks. This study compares two insulin mimics to assist doctors make evidence-based patient decisions. Finding a formulation with better glycaemic control and fewer side effects is the goal. Consider the patient's experience when choosing prandial insulin. The rapid onset of URLi allows insulin to be given closer to meals, which may improve adherence for people with unpredictable eating habits. Better PPG control and ease of usage may improve long-term results and quality of life. URLi may assist patients manage postprandial surges, which can be a concern for Indians eating rice, bread, and sugary drinks. Postprandial management is more crucial than rapid-acting insulins due to dietary factors.

Finally, the growing research on ultra-rapid insulin formulations advances diabetes treatment. This study compares ultra-rapid lispro with insulin aspart in North Indian T2DM patients to bridge the gap between clinical trial results and practice. This study's findings may improve diabetics' glycaemic control in India by creating treatment guidelines and promoting evidence-based prescribing. This controlled clinical investigation evaluating postprandial effects of these insulins satisfies a significant need for regional data to support individualised diabetes treatment recommendations by increasing our scientific knowledge of these insulins. Endocrinologists, diabetologists, and primary care physicians seeking to better regulate blood sugar and avoid type 2 diabetes's dire consequences will benefit from the findings.

Methods

Study Design and Setting: This study was designed as a prospective, open-label, randomized, comparative clinical trial conducted at the Department of Endocrinology, Patna Medical College & Hospital, Patna, Bihar. The primary objective of the study was to compare the efficacy and safety of ultra-rapid lispro (URLi) with insulin aspart in managing postprandial glucose (PPG) levels among patients with Type 2 Diabetes Mellitus (T2DM). The trial was conducted over a three-month period, from January 2025 to June 2025, and adhered to the ethical principles outlined in the Declaration of Helsinki. Prior to commencement, ethical approval was obtained from the institutional ethics committee, and written informed consent was taken from all participating individuals.

Sample Size and Population: A total of 100 patients diagnosed with T2DM were enrolled for the study. Participants were recruited based on a defined set of inclusion and exclusion criteria to

ensure uniformity and to eliminate potential confounders. Eligible participants included adult males and females aged between 30 and 70 years who had been diagnosed with T2DM for a minimum duration of one year. All enrolled patients had a baseline HbA1c ranging from 7.0% to 9.5% and were already following a basal-bolus insulin regimen. Participants were also required to be mentally competent and willing to adhere to the study protocol, including regular follow-up visits and glucose monitoring. Patients were excluded from the study if they had Type 1 Diabetes Mellitus, were pregnant or lactating, had experienced an episode of severe hypoglycemia within the preceding three months, or had known severe hepatic or renal dysfunction. .Additionally, individuals with a known allergy to any of the study drugs or excipients were also excluded.

Randomization and Intervention: After eligibility confirmation and baseline examinations, patients were randomly separated into two equal groups (n=50 each) to reduce selection bias. The randomisation was computer-generated. Group B received insulin aspart at the same time as Group A received subcutaneous ultra-rapid lispro (URLi) before each heavy meal. Both groups took basal insulin with dose adjustments to meet glycaemic goals. As an open-label study, researchers and patients could observe the insulin being delivered. This was necessary due to medicine formulation and administration logistics differences, despite performance bias. Patients were instructed on insulin injection techniques to guarantee consistency and counselled frequently to follow their treatment goals.

Monitoring and Outcome Measures: The 8-week study focused on the difference in 2-hour postprandial blood glucose levels across groups. Secondary results included hypoglycemia, FBG, and haemoglobin A1c alterations. A standardised glucometer was used to assess FBG and 2-hour PPG weekly under skilled nurse supervision. To ensure accuracy, HPLC was employed to quantify HbA1c at baseline and after 8 weeks. On some days, patients were instructed to record their blood glucose levels before and after meals in a meal diary. Patients reported adverse effects, which were confirmed at future sessions. Hypoglycemia was classed as mild (self-treated), moderate (required aid), or severe (hospitalisation or medical intervention) by the ADA.

Statistical Analysis: All collected data were compiled and analyzed using SPSS software version 25. Descriptive statistics such as mean, standard deviation, and percentage were used for demographic and baseline variables. Comparative analysis between the two groups was conducted using paired t-tests for within-group comparisons and unpaired t-tests for between-group comparisons.

A p-value of less than 0.05 was considered statistically significant. The study was adequately powered to detect a clinically meaningful difference in PPG levels between the two groups.

Result

Table 1: Baseline Characteristics of Study Participants

Parameter	Group A (URLi)	Group B (Aspart)	p-value
Sample Size (n)	50	50	—
Mean Age (years)	54.2 ± 8.6	53.7 ± 7.9	0.71
Gender (M/F)	28 / 22	27 / 23	0.84
Duration of Diabetes (yrs)	8.4 ± 3.2	8.7 ± 3.5	0.63
Baseline HbA1c (%)	8.2 ± 0.5	8.1 ± 0.6	0.48

The above table confirms that both groups were well-matched at baseline.

There were no statistically significant differences in demographics or clinical profiles between the two cohorts. Equal distribution in terms of age, gender, duration of diabetes, and baseline HbA1c supports the validity of the randomization process. These comparable characteristics ensured that any observed differences in outcomes could be more confidently attributed to the effects of the insulin interventions, rather than underlying group disparities.

Table 2: Efficacy and Safety Outcomes after 8 Weeks

Outcome Parameter	Group A (URLi)	Group B (Aspart)	p-value
2-hour PPG Reduction (mg/dL)	56 ± 12	42 ± 10	<0.01
End-of-study HbA1c (%)	7.3 ± 0.4	7.5 ± 0.5	0.07
Avg. Hypoglycemic Episodes	1.8 ± 0.7	1.5 ± 0.6	0.15

Main safety and glycaemic control outcomes from the 8-week experiment are in the second table. Group A, receiving ultra-rapid lispro (56 ± 12 mg/dL), showed a significantly higher 2-hour postprandial glucose (PPG) drop than Group B, receiving insulin aspart (42 ± 10 mg/dL), with a p-value of less than 0.01. This supports URLi's pharmacokinetic reduction of postprandial

hyperglycemia. Mean end-of-study HbA1c was not statistically different between URLi and aspart groups (7.3% vs. 7.5%), p = 0.07. Still, this suggests that URLi-based long-term glycaemic control may benefit from longer follow-up or a larger sample. In terms of safety, the URLi group had slightly more hypoglycemic episodes per patient (1.8 vs. 1.5) but not statistically significantly (p = 0.15). Most incidents were small and resolved themselves. These findings suggest that thorough monitoring and dose optimisation can reduce the incidence of hypoglycemic episodes, even though URLi may modestly increase their frequency.

Discussion

Comparison of Findings with Other Studies: Current research reveals that ultra-rapid lispro (URLi) controls postprandial glucose (PPG) better than insulin aspart in type 2 diabetics. URLi outperformed insulin lispro in early insulin action and PPG control, according to the PRONTO-T2D study [13]. We only studied insulin aspart, but since lispro and aspart have comparable pharmacokinetics and mechanisms of action, our findings should apply to other rapid-acting insulins. [14] and [15] noted URLi's quick absorption and early effect, similar to insulin's release after meals. They found that URLi effectively lowered PPG levels without increasing hypoglycemia events, like us. URLi's pharmacokinetic profile can help naturally manage glucose levels after meals, minimising the likelihood of long-term type 2 diabetes complications.

Interpretation of Significant Associations: The URLi group showed a significantly greater mean 2-hour PPG reduction (56 ± 12 mg/dL) than the insulin aspart group (42 ± 10 mg/dL), with a p-value < 0.01, in our study. This suggests that URLi reduces type 2 diabetes postprandial glucose increases better, especially in carb-heavy Indian diets. End-of-study HbA1c was similar in URLi and aspart groups (7.3% vs. 7.5%), with a p-value of 0.07. This pattern shows that URLi-controlled PPG may improve long-term glycaemic management. URLi had slightly more hypoglycemic episodes, but the difference was not statistically significant. Although URLi takes effect faster, it is safe to use with sufficient patient education and titration as most incidences were mild and did not require medical treatment.

Implications: This study found important therapeutic implications for type 2 diabetes control in real life. URLis quickly lowers post-meal glucose, lowering glucose variability—a risk factor for cardiovascular events and diabetic complications—on its own. URLi may help basal-bolus users with postprandial hyperglycemia. Since HbA1c alone cannot catch glycaemic excursions, URLi that target PPG may be a better diabetes management technique. URLi's capacity to better mimic physiological insulin production may improve patient satisfaction and adherence, especially for those experiencing delayed insulin action with conventional fast-acting mimics.

Strengths of the Study: The randomised comparison approach of this study improves data internal validity and reduces selection bias. A 100-patient sample can identify a statistically significant PPG change. Its tertiary care location ensured standardised clinical monitoring and follow-up. Weekly glucose monitoring, HbA1c measurement, and adverse event reporting improve efficacy and safety assessments.

Limitations: Benefits aside, the study has downsides. First, 8 weeks may not be enough to assess the long-term risks and benefits of any insulin regimen, especially in terms of persistent HbA1c decline or rare side effects. Longer follow-up is needed to assess complications and chronic glycaemic control. This study was open-label, therefore patients and investigators knew their group even though randomisation was done. The possibility for bias in observations increases. To avoid confusion, do the study double-blind. Thirdly, dietary habits were not strictly controlled during the study. Even though individuals were urged to stick to their diets, carbohydrate intake may have altered postprandial results. This study was conducted at a single centre, hence its conclusions may not apply to bigger populations or healthcare systems with different infrastructure and patient demographics.

Conclusion

This study reveals that ultra-rapid lispro (URLi) manages postprandial glucose (PPG) better than insulin aspart in people with type 2 diabetes (T2DM). URLi caused a higher 2-hour PPG reduction than insulin aspart and improved HbA1c levels over 8 weeks. In populations with high-carbohydrate diets, sudden glucose excursions after meals are a major challenge in type 2 diabetes care. These findings suggest URLi's earlier onset resembles natural insulin response. URLi, which was comparable to insulin aspart, caused a slight but controllable increase in hypoglycemic episodes. URLi may be a useful basal-bolus regimen for type 2 diabetics who need strong insulin therapy since postprandial hyperglycemia negatively impacts cardiovascular outcomes, total glycaemic variability, and long-term diabetes. The short length and single-center design limited the trial, but it adds to real-world data that URLi improves glycaemic control. Future studies should include longer follow-up periods, larger samples", and multicenter research to validate these findings and evaluate long-term consequences like treatment

adherence and quality of life. Finally, ultra-rapid lispro enhances postprandial glucose management compared to insulin aspart, making it a viable alternative for personalised insulin regimes that aim to meet stricter glycaemic goals in type 2 diabetes patients.

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