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Research Article

Efficacy and Safety of Insulin Degludec/Aspart (Ryzodeg) In Type 2 Diabetes Mellitus

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ABSTRACT

Background: Type 2 diabetes mellitus (T2DM) is a major global health problem requiring progressive treatment intensification. Insulin degludec/aspart (IDegAsp; Ryzodeg 70/30) is a soluble co-formulation containing 70% ultra-long-acting insulin degludec and 30% rapid-acting insulin aspart, providing basal and prandial glycaemic coverage in a single injection.

Objective: To evaluate the efficacy and safety of insulin degludec/aspart in patients with T2DM.

Methods: This prospective observational study included 170 adults with T2DM who were initiated on or switched to IDegAsp and followed for 24 weeks. Glycaemic parameters, insulin dose, body weight, hypoglycaemia, and adverse events were recorded at baseline, 12 weeks, and 24 weeks. The primary efficacy outcome was change in glycated haemoglobin (HbA1c). Safety outcomes included overall, nocturnal, and severe hypoglycaemia.

Results: The mean age was 54.8 +/- 10.9 years, and 88 patients (51.8%) were male. Mean baseline HbA1c was 9.3 +/- 1.1%, which decreased to 8.1 +/- 0.9% at 12 weeks and 7.5 +/- 0.8% at 24 weeks ($p < 0.001$). Mean fasting plasma glucose decreased from 181.4 +/- 39.6 mg/dL to 124.8 +/- 28.7 mg/dL, while postprandial plasma glucose decreased from 270.6 +/- 54.2 mg/dL to 174.3 +/- 43.5 mg/dL ($p < 0.001$). Overall hypoglycaemia occurred in 31 patients (18.2%), nocturnal hypoglycaemia in 8 patients (4.7%), and severe hypoglycaemia in 1 patient (0.6%).

Conclusion: IDegAsp was associated with significant improvement in HbA1c, fasting glucose, and postprandial glucose over 24 weeks, with a low frequency of severe and nocturnal hypoglycaemia. It appears to be an effective and generally safe insulin intensification option for patients with uncontrolled T2DM.

Keywords: Type 2 Diabetes Mellitus; Insulin Degludec/Aspart; Ryzodeg; Hba1c; Hypoglycaemia; Insulin Therapy.

INTRODUCTION

Type 2 diabetes mellitus is among the most important chronic metabolic disorders worldwide. The International Diabetes Federation estimates that 589 million adults aged 20-79 years are living with diabetes, with the number projected to rise to 853 million by 2050 [1,2]. The rising prevalence of diabetes increases the burden of microvascular and macrovascular complications and creates a continuing need for effective, safe, and practical glycaemic management strategies.

Progressive beta-cell dysfunction is central to the natural history of T2DM. Although lifestyle modification and non-insulin agents remain important, many patients eventually require insulin because of persistent hyperglycaemia despite combination therapy [3,4]. Timely insulin initiation and intensification are recommended when glycaemic targets are not achieved, especially in patients with symptomatic hyperglycaemia, high HbA1c, or evidence of catabolism [3].

Premixed insulin regimens are frequently used in routine practice because they provide both basal and mealtime coverage with fewer injections than basal-bolus regimens. However, conventional premixed insulins may be associated with variability in fasting glucose control, difficulty with meal timing, and hypoglycaemia risk, particularly nocturnal hypoglycaemia [5].

Insulin degludec/aspart (IDegAsp; Ryzodeg 70/30) is the first soluble co-formulation of two insulin analogues. It contains insulin degludec, which provides an ultra-long and stable basal effect, and insulin aspart, which provides rapid prandial coverage [6,7]. Pharmacokinetic and pharmacodynamic studies suggest that the two components maintain their distinct action profiles within the co-formulation [7].

Randomized clinical trials have demonstrated that IDegAsp improves HbA1c and fasting plasma glucose in patients with T2DM and may reduce nocturnal hypoglycaemia compared with some premixed insulin regimens [8-10]. The present study was conducted to evaluate the efficacy and safety of IDegAsp in 170 adults with T2DM in routine clinical practice.

METHODOLOGY

Study design and setting

This prospective observational study was conducted in the outpatient diabetes clinic of a tertiary care hospitals of Abbottabad. A total of 170 patients with T2DM were enrolled and followed for 24 weeks after initiation or switching to insulin degludec/aspart.

Study duration

The study period was six months from November 2025 to May 2026. Study assessments were performed at baseline, 12 weeks, and 24 weeks.

Sample size and sampling technique

A total of 170 patients fulfilling the eligibility criteria were included through non-probability consecutive sampling.

Inclusion criteria

Patients were included if they were aged 30-75 years, had confirmed T2DM for at least one year, had inadequate glycaemic control with oral antidiabetic drugs and/or previous insulin therapy, and were prescribed IDegAsp as part of routine clinical management.

Exclusion criteria

Patients with type 1 diabetes mellitus, pregnancy, diabetic ketoacidosis, severe renal impairment, severe hepatic disease, active malignancy, recurrent severe hypoglycaemia, or incomplete follow-up data were excluded.

Treatment protocol

IDegAsp was prescribed once daily or twice daily with main meals according to baseline glycaemic profile, previous insulin exposure, and clinician judgement. Dose titration was performed using fasting and pre-meal self-monitoring blood glucose values. Oral antidiabetic drugs such as metformin and DPP-4 inhibitors were continued where clinically appropriate. Sulfonylureas were reduced or stopped in patients at higher risk of hypoglycaemia.

Data collection

Demographic data, duration of diabetes, body mass index (BMI), comorbidities, previous antidiabetic treatment, HbA1c, fasting plasma glucose, postprandial plasma glucose, body weight, insulin dose, and adverse events were recorded using a structured proforma.

Outcome measures

The primary efficacy outcome was mean change in HbA1c from baseline to 24 weeks. Secondary efficacy outcomes included changes in fasting plasma glucose, postprandial plasma glucose, body weight, insulin dose, and proportion of patients achieving HbA1c targets. Safety outcomes included overall hypoglycaemia, nocturnal hypoglycaemia, severe hypoglycaemia, injection-site reactions, and treatment discontinuation due to adverse events.

Operational definitions

Overall hypoglycaemia was defined as symptomatic or documented blood glucose <70 mg/dL. Nocturnal hypoglycaemia was defined as hypoglycaemia occurring between midnight and 6:00 AM. Severe hypoglycaemia was defined as any episode requiring assistance from another person.

Statistical analysis

Data were analyzed using SPSS version 26. Continuous variables were expressed as mean +/- standard deviation, while categorical variables were expressed as frequency and percentage. Paired t-test was used to compare baseline and follow-up glycaemic parameters. A p-value <0.05 was considered statistically significant.

RESULTS

A total of 170 patients with T2DM were included in the final analysis. Baseline demographic and clinical characteristics are shown in Table 1. The mean age was 54.8 +/- 10.9 years, and the mean duration of diabetes was 8.6 +/- 4.7 years. Hypertension was present in 96 patients (56.5%), dyslipidaemia in 89 patients (52.4%), and obesity in 68 patients (40.0%).

Table 1. Baseline Characteristics of Study Participants (N = 170)

Variable	Value
Age, years	54.8 +/- 10.9
Male sex	88 (51.8%)
Female sex	82 (48.2%)
Duration of T2DM, years	8.6 +/- 4.7
BMI, kg/m2	28.6 +/- 4.2
Hypertension	96 (56.5%)
Dyslipidaemia	89 (52.4%)
Obesity	68 (40.0%)
Previous oral antidiabetic drugs only	74 (43.5%)
Previous basal insulin	51 (30.0%)
Previous premixed insulin	45 (26.5%)
Baseline HbA1c, %	9.3 +/- 1.1

Data are presented as mean +/- SD or n (%). BMI: body mass index; T2DM: type 2 diabetes mellitus.

HbA1c decreased significantly from 9.3 +/- 1.1% at baseline to 8.1 +/- 0.9% at 12 weeks and 7.5 +/- 0.8% at 24 weeks ($p < 0.001$). Fasting and postprandial plasma glucose levels also decreased significantly during follow-up (Table 2; Figures 1 and 2).

Table 2. Glycaemic and Clinical Outcomes after 24 Weeks of Idegasp Therapy

Parameter	Baseline	12 weeks	24 weeks	p-value
HbA1c (%)	9.3 +/- 1.1	8.1 +/- 0.9	7.5 +/- 0.8	<0.001
Fasting plasma glucose (mg/dL)	181.4 +/- 39.6	143.2 +/- 31.8	124.8 +/- 28.7	<0.001
Postprandial plasma glucose (mg/dL)	270.6 +/- 54.2	209.5 +/- 48.1	174.3 +/- 43.5	<0.001
Body weight (kg)	78.4 +/- 12.6	79.1 +/- 12.4	79.6 +/- 12.3	0.021
Daily insulin dose (units/day)	32.8 +/- 11.4	38.6 +/- 12.7	42.3 +/- 13.5	<0.001

Data are presented as mean +/- SD. IDegAsp: insulin degludec/aspart.

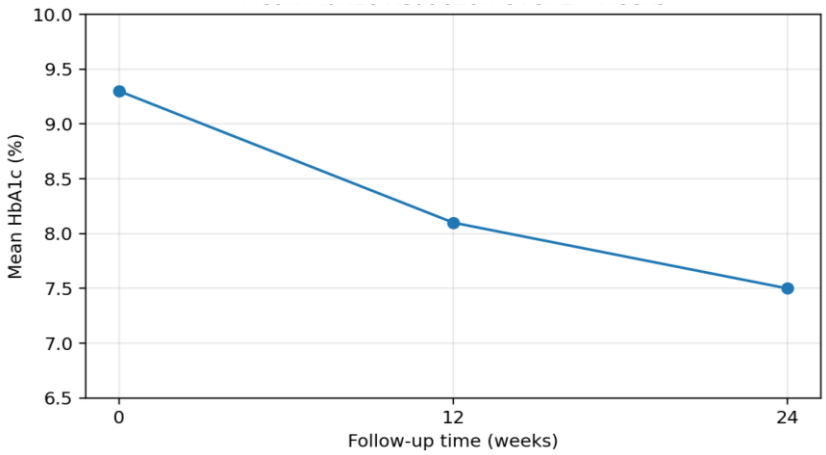

Figure 1. Mean Hba1c Reduction from Baseline to 24 Weeks

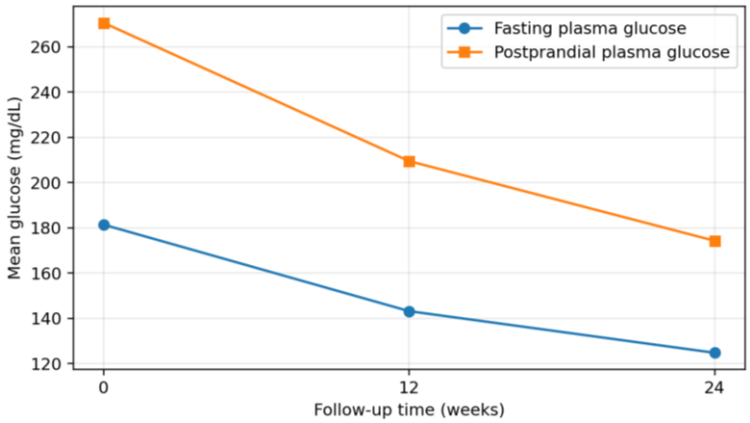

Figure 2. Changes in Fasting and Postprandial Plasma Glucose during Follow-Up

At 24 weeks, HbA1c <7.0% was achieved in 61 patients (35.9%), HbA1c between 7.0% and 7.5% in 62 patients (36.5%), and HbA1c >7.5% persisted in 47 patients (27.6%) (Table 3).

Table 3. Glycaemic Target Achievement at 24 Weeks

HbA1c category	Number of patients	Percentage
HbA1c <7.0%	61	35.9%
HbA1c 7.0-7.5%	62	36.5%
HbA1c >7.5%	47	27.6%

Overall hypoglycaemia occurred in 31 patients (18.2%). Nocturnal hypoglycaemia was reported in 8 patients (4.7%), while severe hypoglycaemia occurred in only 1 patient (0.6%). No diabetic ketoacidosis or treatment-related death was reported (Table 4; Figure 3).

Table 4. Safety Profile of Idegasp during 24 Weeks of Follow-Up

Safety outcome	Number of patients	Percentage
Any hypoglycaemia	31	18.2%
Nocturnal hypoglycaemia	8	4.7%
Severe hypoglycaemia	1	0.6%
Injection-site reaction	6	3.5%
Significant weight gain >3 kg	14	8.2%
Diabetic ketoacidosis	0	0.0%
Treatment discontinuation due to adverse events	3	1.8%

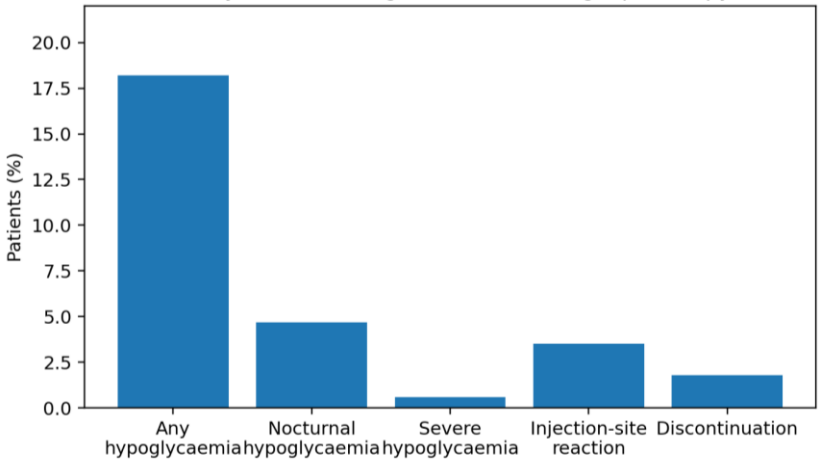

Figure 3. Frequency of Selected Safety Events during 24 Weeks of Idegasp Therapy

DISCUSSION

The present study demonstrated that IDegAsp produced significant improvement in glycaemic control among adults with T2DM over 24 weeks. Mean HbA1c decreased by 1.8%, while fasting and postprandial plasma glucose also improved significantly. These findings are consistent with randomized controlled trials and real-world studies showing that IDegAsp is effective for insulin initiation or intensification in T2DM [11-13].

The dual pharmacological action of IDegAsp is clinically relevant. The degludec component provides stable basal coverage, while the aspart component targets meal-related glycaemic excursions. This allows simultaneous management of fasting and postprandial hyperglycaemia, an important advantage in patients who are not adequately controlled with oral therapy or basal insulin alone [14,15].

In this study, 35.9% of patients achieved HbA1c <7.0% and 72.4% achieved HbA1c <7.5% at 24 weeks. This is meaningful because the baseline HbA1c was high, indicating poor glycaemic control before IDegAsp therapy. Trials comparing IDegAsp with biphasic insulin aspart 30 have reported similar HbA1c reduction, improved fasting glucose, and favourable hypoglycaemia outcomes in different populations [16-18].

The safety profile observed in this study was favourable. Overall hypoglycaemia occurred in 18.2% of patients, nocturnal hypoglycaemia in 4.7%, and severe hypoglycaemia in only 0.6%. Previous analyses have reported that IDegAsp provides effective glycaemic control with low rates of nocturnal or severe hypoglycaemia, especially when doses are titrated carefully and sulfonylureas are reduced in high-risk patients [19-21].

The mild weight gain observed during follow-up was expected with insulin therapy and was not clinically excessive. Weight gain after insulin intensification may reflect reduced glycosuria, improved metabolic control, and anabolic insulin effects. Use of weight-neutral or weight-lowering agents, dietary counselling, and individualized insulin titration can help minimize this limitation [22].

Real-world evidence has become increasingly important because routine clinical populations differ from randomized trial populations. Multicountry real-world studies have reported improved glycaemic control and reduced hypoglycaemia after initiation or switching to IDegAsp [23,24]. Recent Southeast Asian data also support sustained glycaemic improvement and a favourable safety profile during routine IDegAsp use [25].

The present study has several limitations. It was observational, had no active comparator group, and the follow-up duration was limited to 24 weeks. Dietary intake, physical activity, medication adherence, and self-monitoring frequency were not objectively measured. Continuous glucose monitoring was not used, so asymptomatic or unrecognized hypoglycaemia may have been underestimated. Despite these limitations, the study provides useful practical evidence for IDegAsp use in routine diabetes care.

CONCLUSION

Insulin degludec/aspart was effective in improving HbA1c, fasting plasma glucose, and postprandial glucose among patients with T2DM over 24 weeks. It was generally safe, with low rates of nocturnal and severe hypoglycaemia. IDegAsp may be considered a practical insulin intensification option for patients with uncontrolled T2DM, especially when simplified basal and prandial coverage is desired.

Limitations

The main limitations were the observational design, lack of a comparator arm, short follow-up duration, and reliance on reported hypoglycaemic events. Larger randomized or comparative real-world studies with longer follow-up and continuous glucose monitoring are recommended.

Declarations

Ethical approval

The study should be submitted for approval to the relevant institutional review board/ethical review committee before journal submission.

Informed consent

Written informed consent should be obtained from all participants or documented according to institutional policy.

Conflict of interest

The authors declare no conflict of interest.

Funding

No external funding was received.

Data availability

Data may be made available from the corresponding author upon reasonable request, subject to institutional approval.

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