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ABOUT COVER

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AIMS AND SCOPE

The primary aim of *World Journal of Diabetes* (*WJD*, *World J Diabetes*) is to provide scholars and readers from various fields of diabetes with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

WJD mainly publishes articles reporting research results and findings obtained in the field of diabetes and covering a wide range of topics including risk factors for diabetes, diabetes complications, experimental diabetes mellitus, type 1 diabetes mellitus, type 2 diabetes mellitus, gestational diabetes, diabetic angiopathies, diabetic cardiomyopathies, diabetic coma, diabetic ketoacidosis, diabetic nephropathies, diabetic neuropathies, Donohue syndrome, fetal macrosomia, and prediabetic state.

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ORIGINAL ARTICLE

Clinical Trials Study

Efficacy, safety and treatment satisfaction of transition to a regimen of insulin degludec/aspart: A pilot study

Na Yang, Lu Lv, Shu-Meng Han, Li-Yun He, Zi-Yi Li, Yu-Cheng Yang, Fan Ping, Ling-Ling Xu, Wei Li, Hua-Bing Zhang, Yu-Xiu Li

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Abstract

BACKGROUND

There is a lack of clinical evidence on the efficacy and safety of transitioning from a thrice-daily pre-mixed insulin or basal-prandial regimen to insulin degludec/aspart (IDegAsp) therapy, with insufficient data from the Chinese population.

AIM

To demonstrate the efficacy, safety, and treatment satisfaction associated with the transition to IDegAsp in type 2 diabetes mellitus (T2DM).

METHODS

In this 12-week open-label, non-randomized, single-center, pilot study, patients with T2DM receiving thrice-daily insulin or intensive insulin treatment were transitioned to twice-daily injections of insulin IDegAsp. Insulin doses, hemoglobin A1c (HbA1c) levels, fasting blood glucose (FBG), hypoglycemic events, a Diabetes Treatment Satisfaction Questionnaire, and other parameters were assessed at baseline and 12-weeks.

RESULTS
This study included 21 participants. A marked enhancement was observed in the FBG level (P = 0.02), daily total insulin dose (P = 0.03), and overall diabetes treatment satisfaction (P < 0.01) in the participants who switched to IDegAsp. There was a decrease in HbA1c levels (7.6 ± 1.1 *vs* 7.4 ± 0.9, P = 0.31) and the frequency of hypoglycemic events of those who switched to IDegAsp decreased, however, there was no statistically significant difference.

CONCLUSION
The present findings suggest that treatment with IDegAsp enhances clinical outcomes, particularly FBG levels, daily cumulative insulin dose, and overall satisfaction with diabetes treatment.

Key Words: Insulin degludec/aspart; Type 2 diabetes management; Basal-bolus insulin therapy; Pre-mixed insulin; Diabetes treatment satisfaction questionnaire

Core Tip: This study aimed to prospectively assess the efficacy, safety, and treatment satisfaction of switching from thrice-daily pre-mixed insulin or basal-bolus insulin to a twice-daily insulin degludec/aspart (IDegAsp) regimen in Chinese patients with type 2 diabetes mellitus. The results demonstrated significant improvements in fasting blood glucose levels, reduction in total insulin dosage, and enhanced patient satisfaction. These findings suggest that IDegAsp simplifies insulin therapy while maintaining effective glycemic control, thereby offering a promising alternative for optimizing diabetes management in this population.

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INTRODUCTION

Type 2 diabetes mellitus (T2DM) is an intricate and progressive disease that affects > 90% of the population with diabetes mellitus[1]. A substantial number of individuals require insulin therapy to effectively manage glycemic levels[2]. Basal insulin products have a prolonged release profile, and play a role in supplying a steady insulin level throughout the day, contributing to improved fasting blood glucose (FBG)[3]. Rapid-acting insulin formulations (also called bolus insulin) are used to counteract increases in blood glucose levels following meals[4]. The adoption of basal–bolus regimens, involving the separate administration of basal and bolus insulin[5], increases the treatment burden and inconvenience for individuals, potentially reducing medication adherence[6]. To address these challenges, pre-mixed insulin provides an established proportion of slow-release (protamine-bound) and rapid acting (unbound) insulin combined in a single administration[7]. Despite these advantages, pre-mixed insulin formulations have limitations, including the reliance on correct resuspension for accurate dosing[8], elevated glycemic variability[9], and an extended peak effect that may excessively lower glucose levels[10].

In recent years, products have been formulated at a set ratio that combines the two glucose-lowering agents[11]. Although administered as a combined formulation, these products preserve their individual kinetic and dynamic properties related to drug action and metabolism[12,13]. Insulin degludec/aspart (IDegAsp) is a combined formulation consisting of 70%IDeg for long-acting basal regulation and 30% insulin aspart (IAsp) for a quick response[14]. When administered with meals, IDegAsp provides both basal and prandial insulin coverage[15]. Administered through a pre-loaded pen, IDegAsp simplifies usage by eliminating the need for mixing[10]. Compared with pre-mixed insulin regimens, IDegAsp closely mimics physiological insulin secretion patterns, potentially reducing the injection burden for patients compared with basal-bolus insulin regimens[2,5,12,14]. Additionally, a study in Chinese patients with T2DM suggests that, with favorable blood glucose control, basal insulin accounts for 66.7% ± 6.8% of the total daily insulin[16], which is similar to the proportion of IDeg included in IDegAsp. However, there is a lack of clinical evidence on the efficacy and safety of transitioning to IDegAsp therapy from a thrice-daily pre-mixed insulin or basal-prandial regimen, and there is insufficient data in the Chinese population.

In addition to achieving blood glucose control, higher levels of treatment satisfaction are understood to significantly improve adherence[17]. Enhanced adherence can positively affect glycemic control and potentially alleviate diabetes distress[18]. The globally recognized Diabetes Treatment Satisfaction Questionnaire (status version) (DTSQs), an instrument for patient-reported outcomes, evaluates patient satisfaction with diabetes management[19]. This questionnaire has received official approval from the World Health Organization (WHO) and International Diabetes Federation (IDF)[20].

This is the first prospective study, to the best of our knowledge, to demonstrate the efficacy, safety, and treatment satisfaction associated with the transition from three-times-daily pre-mixed insulin or basal–bolus insulin to a twice-daily IDegAsp co-formulation in Chinese patients diagnosed with T2DM.

MATERIALS AND METHODS

Study design

This was a 12-week, open-label, non-randomized, single-center, pilot study in participants with T2DM switching from three-times-daily pre-mixed insulin or basal-bolus insulin therapy to a twice-daily regimen of IDegAsp. The screening process began in September 2020 and concluded with full recruitment by September 2022. Ethical approval for this study was obtained from the relevant Ethics Committee of Peking Union Medical College Hospital (approval number HS-2449). The study adhered to the ethical principles outlined in the Declaration of Helsinki.

Participants

Every participant provided written agreement prior to any research activity, with the study team verifying eligibility at initial screening. The inclusion criteria were as follows: (1) Patients aged ≥ 18 years with T2DM; (2) T2DM diagnosis for > 6 months; (3) Treatment with pre-mixed insulin three times daily or a combination of basal and prandial insulin, with or without oral antidiabetic drugs (OADs), for a minimum of 12 weeks. OADs include metformin, alpha-glucosidase inhibitors, DPP-4 inhibitors, and SGLT2 inhibitors. Basal insulin comprises long-acting insulin analogs, such as glargine, detemir, neutral protamine Hagedorn, and IDeg. Prandial insulin includes rapid-acting or short-acting insulin, such as lispro, IAsp, regular human insulin, and recombinant insulin analogs (IAsp, insulin lispro). Pre-mixed insulin formulations include: 30/50 mixed IAsp and 25/50 mixed injectable suspension of recombinant insulin lispro with protamine and recombinant IAsp with protamine; and (4) Body mass index (BMI) ≤ 35 kg/m^2.

Patients meeting any of the following conditions were excluded from the study: (1) Insulin allergy; (2) Total daily insulin dose > 100 U/day; (3) Prior use of medications that may interfere with glucose metabolism; (4) Pregnancy, lactation, or women planning pregnancy; (5) History of acute or chronic infections, or a history of tumors; (6) History of cardiovascular events within the past 3 months, including stroke, decompensated heart failure (NYHA III or IV), myocardial infarction, coronary artery bypass grafting, or vascular angioplasty; (7) Untreated or uncontrolled severe hypertension, defined as systolic blood pressure ≥ 180 mmHg and/or diastolic blood pressure ≥ 100 mmHg; (8) Severe liver or kidney dysfunction; (9) Recurrent severe hypoglycemic episodes, hypoglycemic coma, or hospitalization owing to diabetic ketoacidosis within the past 3 months; and (10) Presence of mental or psychological disorders, or alcohol dependence, that might interfere with study compliance.

Study procedures

Consented eligible patients participated in the screening phase, where baseline evaluations were conducted: Hemoglobin A1c (HbA1c) assessment *via* high-performance liquid chromatography, demographics (date of birth, sex), medical history, alcohol consumption, smoking, concomitant medications, occurrence of hypoglycemia, and measurements of weight, height, blood pressure, heart rate, waist circumference, hip circumference, and physical examination of insulin injection sites.

Blood samples were assayed, and data including the DTSQs and other relevant information were collected at both baseline and the 12th week after transitioning to the IDegAsp regimen. The insulin dosage was calibrated as follows: The starting quantity of IDegAsp was equivalent to the preceding dose and partitioned into two identical subcutaneous injections. Dosage adjustments were then made in response to pre-prandial self-monitoring blood glucose (SMBG) levels, with the objective of achieving blood sugar levels within the range 4.4–7.2 mmol/L. If necessary, IAsp could be added before lunch. All additional pre-existing medications were maintained at unchanged doses throughout the study period. An episode of hypoglycemia was recorded when SMBG levels were < 3.9 mmol/L or when external aid was necessary.

Endpoints and assessments

The primary endpoint was the change in HbA1c levels at 12 weeks of treatment relative to baseline. Secondary endpoints were the change from baseline in fasting plasma glucose (FPG), insulin dose, and incidence of adverse reactions, notably hypoglycemia. Patient satisfaction with treatment, also a secondary endpoint, was measured using the translated Chinese version of the DTSQs.

The DTSQs consists of eight distinct items[19,20]. An aggregate of six queries evaluates overall treatment satisfaction, including aspects of satisfaction with current treatment, convenience, flexibility, understanding of diabetes, recommendation of treatment to others, and willingness to continue. Rated on a scale of 0 (“very dissatisfied”) to 6 (“very satisfied”), the scores of these questions reflect the degree of patient satisfaction. Cumulative scoring generated a combined index of treatment satisfaction ranging 0–36, where higher scores denote increased satisfaction. The second and third items of the DTSQs specifically gauge the perceived regularity of excessively high and low blood glucose levels, with a scoring bandwidth from 0 (none of the time) to 6 (most of the time).

Statistical analyses

Descriptive statistical techniques included the calculation of percentages and mean values with their corresponding SD, and these were used to provide the basic features of the data, according to the evaluation of distribution for normality. A

paired-sample *t*-test or Wilcoxon signed-rank test was used for normally distributed continuous variables of baseline and follow-up parameters. Statistical significance was set at $P < 0.05$. Data analysis was conducted using the IBM SPSS software (version 26.1, IBMCorp, 2019, Armonk, NY, United States).

RESULTS

Twenty-six participants consented to participate in this initial investigation, and 21 participants completed the study. Five subjects voluntarily withdrew from the study owing to incomplete follow-up. Table 1 presents the baseline demographics and clinical characteristics of participants. The study group included 8 men and 13 women, having a mean age of 59.1 ± 12.6 years. A total of 47.6% of the participants had a T2DM duration of 5–10 years. An insulin therapy duration of < 5 years was noted in 47.6% of the patients. Eight patients exhibited diabetic retinopathy and 11 presented with diabetic nephropathy.

By week 12, there was a decrease in HbA1c levels in those who switched to IDegAsp, however, this was not statistically significant (7.6% ± 1.1% *vs* 7.4% ± 0.9%, $P = 0.31$) (Table 2). There is a significant decrease in FBG (10.4 ± 3.7 *vs* 7.9 ± 2.5 mmol/L, $P = 0.02$), along with a notable reduction in insulin dosage (53.3 ± 25.9 *vs* 43.3 ± 18.1 units, $P = 0.03$) (Table 2). There appeared to be a decreasing trend in the frequency of hypoglycemic events; however, this was not statistically significant ($P = 0.07$) (Table 2). Switching to IDegAsp significantly reduced the number of injections (3.95 ± 0.2 *vs* 2.1 ± 0.3, $P < 0.01$) (Table 2). Prior to the transition, 1 patient received three-times-daily pre-mixed insulin, and 20 patients received basal-bolus insulin (four total injections/day) (Table 1). After 12 weeks, 2 patients received insulin injections three times daily (twice-daily IDegAsp and once-daily as part), and 19 patients received twice-daily IDegAsp.

At week 12, the participants exhibited a statistically significant increase in scores for the following DTSQs items compared with baseline: Satisfaction with current treatment ($P = 0.01$), convenience ($P < 0.01$), willingness to continue ($P < 0.01$), understanding of diabetes ($P = 0.02$), and recommendation of treatment to others ($P = 0.01$) (Table 3). By the 12th week, participants demonstrated a marked and statistically significant elevation in their assessment of overall treatment satisfaction when compared with baseline (23.1 ± 5.4 *vs* 31.0 ± 5.8, $P < 0.01$) (Table 3). A considerable decrease in the reported incidence of unacceptable hyperglycemia was noted ($P = 0.03$) (Table 3), whereas there was no significant change in the perceived frequency of unacceptable hypoglycemia ($P = 0.11$).

No significant differences were detected in relation to alterations in fasting C-peptide, liver function (alanine transaminase and aspartate aminotransferase), renal function (creatinine), or lipid concentrations (total cholesterol, triglycerides, and low-density lipoprotein-cholesterol) between baseline and 12 weeks (Figure 1).

DISCUSSION

This 12-week, open-label, non-randomized, single-center, pilot study revealed significant improvements in FBG, daily total insulin dose, and overall diabetes treatment satisfaction with a switch to the IDegAsp co-formulation from three-times-daily pre-mixed insulin or basal–bolus insulin in patients with T2DM. Additionally, a declining trend was noted in both HbA1c levels and the rate of hypoglycemic events.

This study showed a significant improvement in FBG control upon transitioning to IDegAsp, with a reduction in HbA1c compared to baseline, although the latter did not achieve statistical significance, aligning with findings from previous studies. A meta-analysis encompassing eight studies comparing twice-daily IDegAsp to twice-daily traditional pre-mixed insulin[10,14,21-26] showed a significant reduction in HbA1c levels for both regimens, yet the difference between the groups did not reach statistical significance. Twice-daily IDegAsp exhibited a significant reduction in FBG levels compared to twice-daily traditional pre-mixed insulin treatment. The observed glycemic reduction, as indicated by FBG levels, was primarily owing to the prolonged action of IDeg present in IDegAsp[2]. A recent meta showed that compared with BIAsp30, IDegAsp could significantly reduce FPG levels, insulin dosage, and the risk of nocturnal hypoglycemic events in T2D patients, without increasing the overall risk of adverse events[27]. Earlier studies have highlighted the advantages of twice-daily regimens using long-acting insulin for better glycemic management over other methods[28,29]. For instance, transitioning from a single daily injection to a twice-daily dose of insulin glargine has been shown to enhance blood glucose regulation in patients with inadequate diabetes control[29]. When examining studies comparing basal-bolus insulin therapy with twice-daily IDegAsp injections, some revealed no difference in HbA1c between the two groups[30,31], whereas others demonstrated a significant improvement in HbA1c[5,32]. To our knowledge, this is the first investigation of the transition from three-times-daily pre-mixed insulin or basal–bolus insulin to IDegAsp in a Chinese population, which found an improvement in blood glucose control, fewer daily injections, and no increased susceptibility to hypoglycemia. A previous study showed that the proportional demand for basal insulin in Chinese patients with T2DM also changed. Recent studies suggest that, with favorable blood glucose control, basal insulin accounts for 66.7% ± 6.8% of total daily insulin[16], which is similar to the proportion of IDec included in IDegAsp. Therefore, the use of IDegAsp may reduce the number of injections while providing effective blood glucose control in Chinese patients with T2DM. Although the changes in HbA1c levels were not statistically significant, it is important to note that this study is a preliminary evaluation. However, the emergence of the new drug iGlarLixi appears to provide more options for patients with T2DM. A study showed that in Chinese people with T2D suboptimally controlled with OADs, once-daily iGlarLixi provided better glycaemic control with BW benefit and lower hypoglycemia event rates vs IDegAsp[33]. Larger-scale and longer-term studies are warranted to confirm these findings.

Table 1 Baseline characteristics of the participants, *n* (%)/mean ± SD

Characteristic	Patients (*n* = 21)
Age (year)	59.1 ± 12.6
Male, No. patients	8 (38.1)
BMI (kg/m^2)	24.5 ± 3.5
WC (cm)	90.9 ± 9.6
WHR	0.9 ± 0.1
SBP (mmHg)	126.1 ± 18.7
DBP (mmHg)	74.8 ± 8.0
HR (bpm)	79.9 ± 11.8
Smoking, No. patients	5 (23.8)
Alcohol drinking, No. patients	4 (19.0)
Duration of diabetes (year)	
< 10	3 (14.3)
10-20	10 (47.6)
> 20	8 (38.1)
Baseline insulin regimen, No. patients	
Three times-daily premixed insulin	1 (4.8)
Basal–bolus insulin	20 (95.2)
Duration of insulin therapy (year)	
< 5	9 (42.9)
5-10	6 (28.6)
> 10	6 (28.6)
Oral antidiabetic medicine, No. patients	
Metformin	8 (38.1)
α-Glucosidase inhibitor	8 (38.1)
DPP-4 inhibitor	4 (19.0)
SGLT2 inhibitor	5 (23.8)
Complications, No. patients	
Retinopathy	8 (38.1)
Nephropathy	11 (52.4)
Comorbidity, No. patients	
CVD	4 (19.0)
Stroke	2 (9.5)

WHR: Waist-to-hip ratio; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; HR: Heart rate; CVD: Cardiovascular disease.

Our investigation revealed a decrease in the number of daily injections administered once participants had transitioned to IDegAsp. The implications of reducing the number of insulin injections for clinical practice and patients are noteworthy. This shift may address certain barriers to insulin intensification and reduce clinical inertia. Additionally, the more manageable insulin regimen could boost patient confidence and adherence to treatment. Furthermore, our study revealed a reduction in the total insulin dosage with IDegAsp. Previous studies have consistently demonstrated that the daily insulin dose of once-daily IDegAsp is either lower than[34,35] that of basal insulin or comparable to[36-38] it. Real-world data shows that patients in the IDegAsp group received a significantly lower mean daily dose than patients in the basal-bolus or pre-mixed insulin groups[5,14,31]. These reductions may translate into fewer adverse events.

Our research revealed a decreasing trend in the occurrence of hypoglycemic events by the 12th week from baseline, although the difference was not statistically significant. The occurrence of hypoglycemic episodes poses a significant

Table 2 Comparison of blood glucose control, insulin dosage, and hypoglycemic events, *n* (%)/mean ± SD

Characteristic	Baseline	At 12 weeks	*P* value
HbA1c (%)	7.6 ± 1.1	7.4 ± 0.9	0.31
FBG (mmol/L)	10.4 ± 3.7	7.9 ± 2.5	0.02
Insulin dose, unit	53.3 ± 25.9	43.3 ± 18.1	0.03
Number of injections	3.95 ± 0.2	2.1 ± 0.3	< 0.01
Hypoglycemic events, n times *per* month			0.07
0	6 (28.6)	10 (47.6)	
1-2	9 (42.9)	8 (38.1)	
3-5	2 (9.5)	1 (4.8)	
> 5	4 (19.0)	2 (9.5)	

FBG: Fasting blood glucose; HbA1c: Hemoglobin A1c.

Table 3 Comparison of diabetes treatment satisfaction questionnaire, *n* (%)/mean ± SD[1]

Question	Baseline	At 12 weeks	*P* value
Satisfaction with current treatment	4.0 ± 1.3	5.4 ± 0.9	0.01
The occurrence rate of unacceptable hyperglycemia	2.1 ± 1.7	0.8 ± 1.5	0.03
The occurrence rate of unacceptable hypoglycemia	1.5 ± 1.8	0.7 ± 1.3	0.11
Convenience	3.6 ± 1.5	5.4 ± 0.08	< 0.01
Flexibility	4.6 ± 1.3	5.0 ± 1.1	0.12
Understanding of diabetes	4.3 ± 1.0	5.0 ± 1.1	0.02
Recommend treatment to others	3.1 ± 1.8	5.0 ± 1.8	0.01
Willingness to continue	3.6 ± 1.6	5.3 ± 1.0	< 0.01
Overall treatment satisfaction	23.1 ± 5.4	31.0 ± 5.8	< 0.01

[1]The aggregate score for treatment satisfaction is calculated by totaling the scores for item 1 and items 4 to 8 of the Diabetes Treatment Satisfaction Questionnaire.

challenge to achieving optimal metabolic control, especially in individuals with insulin-treated T2DM. Prior investigations have demonstrated that relative to traditional pre-mixed insulin, twice-daily IDegAsp demonstrates a similar overall hypoglycemic profile, yet with a notably lower incidence of nocturnal hypoglycemia[39]. Prolonged basal insulin release from IDeg contributes to a reduced risk of hypoglycemia, enhancing the safety profile of IDegAsp[28,40-43]. Real-world evidence from Turkey aligns with our findings, illustrating a significant reduction in hypoglycemic events after transitioning from pre-mixed and intensive insulin to the twice-daily IDegAsp co-formulation in patients with T2DM over a 12-week period[14]. Our study also implies, to some extent, that the shift to IDegAsp did not lead to an increase in the occurrence of hypoglycemic events, instead demonstrating a declining trend.

The DTSQs, validated and officially endorsed by the WHO and IDF, has been translated into over 100 Languages and is utilized in many countries[44]. In our study, despite the relatively modest sample size, we observed a high satisfaction score, measuring 31.0 ± 5.8 out of 36. This score represents a significant improvement from the baseline score of 23.1 ± 5.4. Moreover, the participants rated the IDegAsp regimen highly on convenience. Importantly, they were more inclined to recommend this regimen to others and expressed a greater willingness to continue with the treatment.

This study represents the first prospective investigation of the effectiveness and safety of transitioning from three-times-daily pre-mixed or basal–bolus insulin to twice-daily IDegAsp in a Chinese population. However, this study has some limitations. Given the open-label nature of this study, the possibility of observer bias and extraneous variables influencing the data cannot be excluded. Another limitation relates to the small sample size. Considering the abbreviated duration of the intervention, further long-term follow-up is necessary to ascertain enduring efficacy.

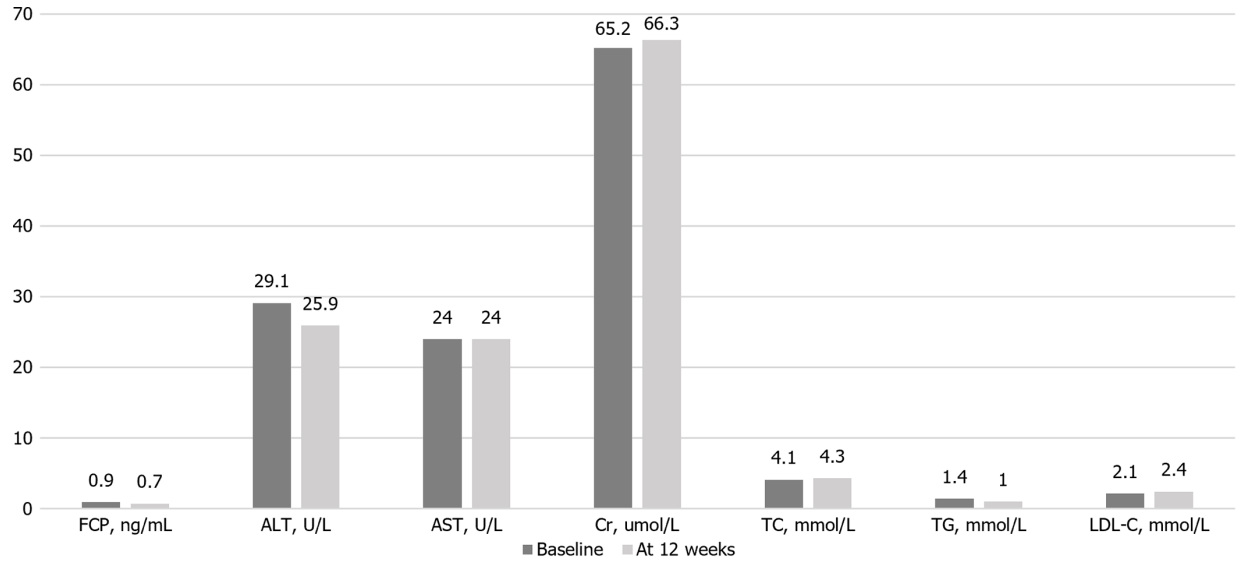

Figure 1 Comparison of biochemical characteristics. FCP: Fasting c-peptide; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; TC: Total cholesterol; TG: Triglycerides; LDL-C: Low-density lipoprotein cholesterol.

CONCLUSION

In conclusion, lower FBG levels, a reduction in overall insulin dosage, and higher diabetes treatment satisfaction were revealed following transition from three-times-daily pre-mixed insulin or basal–bolus insulin to twice-daily IDegAsp. IDegAsp therapy has the potential to aid diverse patient populations, and future research is warranted to explore its full spectrum of benefits.

FOOTNOTES

Author contributions: Zhang HB, Li YX participated in the conceptualization, data curation, investigation, methodology, project administration, resources, and supervision; Yang N was involved in the formal analysis and writing of the original draft; Lv L, Han SM, He LY, Li ZY, Yang YC were involved in the formal analysis; Ping F, Xu LL, Li W were involved in writing-review and editing.

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REFERENCES

1 **Sun H**, Saeedi P, Karuranga S, Pinkepank M, Ogurtsova K, Duncan BB, Stein C, Basit A, Chan JCN, Mbanya JC, Pavkov ME, Ramachandaran A, Wild SH, James S, Herman WH, Zhang P, Bommer C, Kuo S, Boyko EJ, Magliano DJ. IDF Diabetes Atlas: Global, regional and country-level diabetes prevalence estimates for 2021 and projections for 2045. *Diabetes Res Clin Pract* 2022; **183**: 109119 [PMID: 34879977 DOI: 10.1016/j.diabres.2021.109119]

2 **Moon S**, Chung HS, Kim YJ, Yu JM, Jeong WJ, Park J, Oh CM. Efficacy and Safety of Insulin Degludec/Insulin Aspart Compared with a Conventional Premixed Insulin or Basal Insulin: A Meta-Analysis. *Metabolites* 2021; **11** [PMID: 34564455 DOI: 10.3390/metabo11090639]

3 **Sims EK**, Carr ALJ, Oram RA, DiMeglio LA, Evans-Molina C. 100 years of insulin: celebrating the past, present and future of diabetes therapy. *Nat Med* 2021; **27**: 1154-1164 [PMID: 34267380 DOI: 10.1038/s41591-021-01418-2]

4 **Ritzel R**, Ghosh S, Emral R, Malek R, Zeng L, Mabunay MA, Landgraf W, Guyot P, Serafini P, Pushkarna D, Malik RA. Comparative efficacy and safety of Gla-300 versus IDegAsp in insulin-naïve people with type 2 diabetes mellitus uncontrolled on oral anti-diabetics. *Diabetes Obes Metab* 2023; **25**: 2495-2504 [PMID: 37312665 DOI: 10.1111/dom.15121]

5 **Güneş E**, Güneş M. Efficacy of switching from basal-bolus insulin therapy to twice-daily insulin degludec/insulin aspart co-formulation plus insulin aspart in patients with poorly controlled type 2 diabetes. *Eur Rev Med Pharmacol Sci* 2023; **27**: 6691-6699 [PMID: 37522680 DOI: 10.26355/eurrev_202307_33139]

6 **Katabami T**, Eriksen KT, Yamamoto Y, Ishigaki Y. Long-Term Safety and Clinical Outcomes with Insulin Degludec/Insulin Aspart Treatment in Japanese Patients with Diabetes: A Real-World, Prospective, Observational Study. *Adv Ther* 2022; **39**: 544-561 [PMID: 34800283 DOI: 10.1007/s12325-021-01978-2]

7 **Mehta R**, Chen R, Hirose T, John M, Kok A, Lehmann R, Unnikrishnan AG, Yavuz DG, Fulcher G. Practical use of insulin degludec/insulin aspart in a multinational setting: beyond the guidelines. *Diabetes Obes Metab* 2020; **22**: 1961-1975 [PMID: 32618405 DOI: 10.1111/dom.14128]

8 **Rosenstock J**, Emral R, Sauque-Reyna L, Mohan V, Trescolí C, Al Sifri S, Lalic N, Alvarez A, Picard P, Bonnemaire M, Demil N, McCrimmon RJ; SoliMix Trial Investigators. Advancing Therapy in Suboptimally Controlled Basal Insulin-Treated Type 2 Diabetes: Clinical Outcomes With iGlarLixi Versus Premix BIAsp 30 in the SoliMix Randomized Controlled Trial. *Diabetes Care* 2021; **44**: 2361-2370 [PMID: 34183429 DOI: 10.2337/dc21-0393]

9 **Wang H**, Zhou Y, Wang Y, Cai T, Hu Y, Jing T, Ding B, Su X, Li H, Ma J. Basal Insulin Reduces Glucose Variability and Hypoglycaemia Compared to Premixed Insulin in Type 2 Diabetes Patients: A Study Based on Continuous Glucose Monitoring Systems. *Front Endocrinol (Lausanne)* 2022; **13**: 791439 [PMID: 35574003 DOI: 10.3389/fendo.2022.791439]

10 **Yang W**, Ma J, Hong T, Liu M, Miao H, Peng Y, Wang C, Xu X, Yang T, Nielsen AM, Pan L, Liu W, Zhao W. Efficacy and safety of insulin degludec/insulin aspart versus biphasic insulin aspart 30 in Chinese adults with type 2 diabetes: A phase III, open-label, 2:1 randomized, treat-to-target trial. *Diabetes Obes Metab* 2019; **21**: 1652-1660 [PMID: 30869183 DOI: 10.1111/dom.13703]

11 **Demir T**, Turan S, Unluhizarci K, Topaloglu O, Tukek T, Gogas Yavuz D. Use of Insulin Degludec/Insulin Aspart in the Management of Diabetes Mellitus: Expert Panel Recommendations on Appropriate Practice Patterns. *Front Endocrinol (Lausanne)* 2021; **12**: 616514 [PMID: 33776914 DOI: 10.3389/fendo.2021.616514]

12 **Shigiyama F**, Liu L, Nordahl H, Suzuki R, Yamamoto Y, Hirose T. A Real-World, Prospective, Non-interventional Study of Adults with T2D Switching to IDegAsp from Glargine U100 or U300 in Japan. *Diabetes Ther* 2021; **12**: 2405-2421 [PMID: 34304385 DOI: 10.1007/s13300-021-01117-8]

13 **Glastras SJ**, Cohen N, Dover T, Kilov G, MacIsaac RJ, McGill M, Fulcher GR. The Clinical Role of Insulin Degludec/Insulin Aspart in Type 2 Diabetes: An Empirical Perspective from Experience in Australia. *J Clin Med* 2020; **9** [PMID: 32290465 DOI: 10.3390/jcm9041091]

14 **Özçelik S**, Çelik M, Vural A, Aydın B, Özçelik M, Gozu H. Outcomes of transition from premixed and intensive insulin therapies to insulin aspart/degludec co-formulation in type 2 diabetes mellitus: a real-world experience. *Arch Med Sci* 2021; **17**: 1-8 [PMID: 33488849 DOI: 10.5114/aoms.2020.93264]

15 **Kesavadev J**, Saboo B, Kovil R, Joshi S, Shankar A, Ashik A, Ashok AD, Basanth A, Krishnan G. Insulin degludec/insulin aspart safely improves HbA1c: A long-term real-world cohort study (IDEA). *Diabetes Obes Metab* 2023; **25**: 306-309 [PMID: 35986629 DOI: 10.1111/dom.14847]

16 **Gao GQ**, Dong QY, Li SJ, Zhang YY, Li WX, Du WH, Liang CG, Wang YL. Investigation of the insulin dose and characteristics of continuous subcutaneous insulin infusion in Chinese people with type 2 diabetes. *Diabetes Technol Ther* 2011; **13**: 1135-1138 [PMID: 21919776 DOI: 10.1089/dia.2011.0109]

17 **Danne T**, Joish VN, Afonso M, Banks P, Sawhney S, Lapuerta P, Davies MJ, Buse JB, Lin D, Reaney M, Guillonneau S, Snoek FJ, Bailey TS, Polonsky WH. Improvement in Patient-Reported Outcomes in Adults with Type 1 Diabetes Treated with Sotagliflozin plus Insulin Versus Insulin Alone. *Diabetes Technol Ther* 2021; **23**: 70-77 [PMID: 32721228 DOI: 10.1089/dia.2020.0068]

18 **Bajaj HS**, Aberle J, Davies M, Donatsky AM, Frederiksen M, Yavuz DG, Gowda A, Lingvay I, Bode B. Once-Weekly Insulin Icodec With Dosing Guide App Versus Once-Daily Basal Insulin Analogues in Insulin-Naive Type 2 Diabetes (ONWARDS 5) : A Randomized Trial. *Ann Intern Med* 2023; **176**: 1476-1485 [PMID: 37748181 DOI: 10.7326/M23-1288]

19 **Ishii H**, Oura T, Takeuchi M. Treatment Satisfaction and Quality of Life with Tirzepatide Versus Dulaglutide Among Japanese Patients with Type 2 Diabetes: Exploratory Evaluation of the SURPASS J-mono Trial. *Diabetes Ther* 2023; **14**: 2173-2183 [PMID: 37843771 DOI: 10.1007/s13300-023-01485-3]

20 **Naous E**, Boulos M, Sleilaty G, Achkar AA, Gannagé-Yared MH. Quality of life and other patient-reported outcomes in adult Lebanese patients with type 2 diabetes during COVID-19 pandemic. *J Endocrinol Invest* 2022; **45**: 763-772 [PMID: 34780052 DOI: 10.1007/s40618-021-01701-6]

21 **Fujimoto K**, Iwakura T, Aburaya M, Matsuoka N. Twice-daily insulin degludec/insulin aspart effectively improved morning and evening glucose levels and quality of life in patients previously treated with premixed insulin: an observational study. *Diabetol Metab Syndr* 2018; **10**:

64 [PMID: 30127860 DOI: 10.1186/s13098-018-0366-x]

22 **Onishi Y**, Yamada K, Zacho J, Ekelund J, Iwamoto Y. Insulin degludec/insulin aspart vs biphasic insulin aspart 30 twice daily in Japanese patients with type 2 diabetes: A randomized controlled trial. *J Diabetes Investig* 2017; **8**: 210-217 [PMID: 27560769 DOI: 10.1111/jdi.12569]

23 **Kaneko S**, Chow F, Choi DS, Taneda S, Hirao K, Park Y, Andersen TH, Gall MA, Christiansen JS; BOOST: Intensify All Trial Investigators. Insulin degludec/insulin aspart versus biphasic insulin aspart 30 in Asian patients with type 2 diabetes inadequately controlled on basal or pre-/self-mixed insulin: a 26-week, randomised, treat-to-target trial. *Diabetes Res Clin Pract* 2015; **107**: 139-147 [PMID: 25498130 DOI: 10.1016/j.diabres.2014.09.026]

24 **Franek E**, Haluzík M, Canecki Varžić S, Sargin M, Macura S, Zacho J, Christiansen JS. Twice-daily insulin degludec/insulin aspart provides superior fasting plasma glucose control and a reduced rate of hypoglycaemia compared with biphasic insulin aspart 30 in insulin-naïve adults with Type 2 diabetes. *Diabet Med* 2016; **33**: 497-505 [PMID: 26435365 DOI: 10.1111/dme.12982]

25 **Fulcher GR**, Christiansen JS, Bantwal G, Polaszewska-Muszynska M, Mersebach H, Andersen TH, Niskanen LK; BOOST: Intensify Premix I Investigators. Comparison of insulin degludec/insulin aspart and biphasic insulin aspart 30 in uncontrolled, insulin-treated type 2 diabetes: a phase 3a, randomized, treat-to-target trial. *Diabetes Care* 2014; **37**: 2084-2090 [PMID: 24812432 DOI: 10.2337/dc13-2908]

26 **Niskanen L**, Leiter LA, Franek E, Weng J, Damci T, Muñoz-Torres M, Donnet JP, Endahl L, Skjøth TV, Vaag A. Comparison of a soluble co-formulation of insulin degludec/insulin aspart vs biphasic insulin aspart 30 in type 2 diabetes: a randomised trial. *Eur J Endocrinol* 2012; **167**: 287-294 [PMID: 22660026 DOI: 10.1530/EJE-12-0293]

27 **Niu YL**, Zhang Y, Song ZY, Zhao CZ, Luo Y, Wang Y, Yuan J. Efficacy and Safety of Insulin Degludec/Insulin Aspart versus Biphasic Insulin Aspart 30 in Patients with Type 2 Diabetes: A Meta-Analysis of Randomized Controlled Trials. *Iran J Public Health* 2024; **53**: 313-322 [PMID: 38894842 DOI: 10.18502/ijph.v53i2.14916]

28 **Semlitsch T**, Engler J, Siebenhofer A, Jeitler K, Berghold A, Horvath K. (Ultra-)long-acting insulin analogues versus NPH insulin (human isophane insulin) for adults with type 2 diabetes mellitus. *Cochrane Database Syst Rev* 2020; **11**: CD005613 [PMID: 33166419 DOI: 10.1002/14651858.CD005613.pub4]

29 **Eledrisi M**, Suleiman NN, Salameh O, Khair Hamad M, Rabadi O, Mohamed A, Al Adawi R, Salam A. Twice-daily insulin glargine for patients with uncontrolled type 2 diabetes mellitus. *J Clin Transl Endocrinol* 2019; **15**: 35-36 [PMID: 30619716 DOI: 10.1016/j.jcte.2018.12.002]

30 **Home PD**, Meneghini L, Wendisch U, Ratner RE, Johansen T, Christensen TE, Jendle J, Roberts AP, Birkeland KI. Improved health status with insulin degludec compared with insulin glargine in people with type 1 diabetes. *Diabet Med* 2012; **29**: 716-720 [PMID: 22150786 DOI: 10.1111/j.1464-5491.2011.03547.x]

31 **Rodbard HW**, Cariou B, Pieber TR, Endahl LA, Zacho J, Cooper JG. Treatment intensification with an insulin degludec (IDeg)/insulin aspart (IAsp) co-formulation twice daily compared with basal IDeg and prandial IAsp in type 2 diabetes: a randomized, controlled phase III trial. *Diabetes Obes Metab* 2016; **18**: 274-280 [PMID: 26592732 DOI: 10.1111/dom.12609]

32 **Fulcher GR**, Akhtar S, Al-Jaser SJ, Medina J, Mohamed M, Nicodemus NA Jr, Olsen AH, Singh KP, Kok A. Initiating or Switching to Insulin Degludec/Insulin Aspart in Adults with Type 2 Diabetes: A Real-World, Prospective, Non-interventional Study Across Six Countries. *Adv Ther* 2022; **39**: 3735-3748 [PMID: 35752730 DOI: 10.1007/s12325-022-02212-3]

33 **Liu M**, Gu W, Chen L, Li Y, Kuang H, Du J, Alvarez A, Lauand F, Souhami E, Zhang J, Xu W, Du Q, Mu Y; SoliD trial investigators. The efficacy and safety of iGlarLixi versus IDegAsp in Chinese people with type 2 diabetes suboptimally controlled with oral antidiabetic drugs: The Soli-D randomized controlled trial. *Diabetes Obes Metab* 2024; **26**: 3791-3800 [PMID: 38922731 DOI: 10.1111/dom.15724]

34 **Philis-Tsimikas A**, Astamirova K, Gupta Y, Haggag A, Roula D, Bak BA, Fita EG, Nielsen AM, Demir T. Similar glycaemic control with less nocturnal hypoglycaemia in a 38-week trial comparing the IDegAsp co-formulation with insulin glargine U100 and insulin aspart in basal insulin-treated subjects with type 2 diabetes mellitus. *Diabetes Res Clin Pract* 2019; **147**: 157-165 [PMID: 30448451 DOI: 10.1016/j.diabres.2018.10.024]

35 **Heise T**, Tack CJ, Cuddihy R, Davidson J, Gouet D, Liebl A, Romero E, Mersebach H, Dykiel P, Jorde R. A new-generation ultra-long-acting basal insulin with a bolus boost compared with insulin glargine in insulin-naive people with type 2 diabetes: a randomized, controlled trial. *Diabetes Care* 2011; **34**: 669-674 [PMID: 21285389 DOI: 10.2337/dc10-1905]

36 **Shimoda S**, Sakamoto W, Hokamura A, Matsuo Y, Sekigami T, Ichimori S, Iwashita S, Ishii N, Otsu K, Yoshimura R, Nishiyama T, Sakaguchi M, Nishida K, Araki E. Comparison of the efficacy and safety of once-daily insulin degludec/insulin aspart (IDegAsp) and long-acting second-generation basal insulin (insulin degludec and insulin glargine 300 units/mL) in insulin-naïve Japanese adults with type 2 diabetes: a pilot, randomized, controlled study. *Endocr J* 2019; **66**: 745-752 [PMID: 31308304 DOI: 10.1507/endocrj.EJ19-0179]

37 **Cho KY**, Nakamura A, Oba-Yamamoto C, Tsuchida K, Yanagiya S, Manda N, Kurihara Y, Aoki S, Atsumi T, Miyoshi H. Switching to Once-Daily Insulin Degludec/Insulin Aspart from Basal Insulin Improves Postprandial Glycemia in Patients with Type 2 Diabetes Mellitus: Randomized Controlled Trial. *Diabetes Metab J* 2020; **44**: 532-541 [PMID: 31769240 DOI: 10.4093/dmj.2019.0093]

38 **Jang HN**, Yang YS, Lee SO, Oh TJ, Koo BK, Jung HS. Favorable Glycemic Control with Once-Daily Insulin Degludec/Insulin Aspart after Changing from Basal Insulin in Adults with Type 2 Diabetes. *Endocrinol Metab (Seoul)* 2019; **34**: 382-389 [PMID: 31884738 DOI: 10.3803/EnM.2019.34.4.382]

39 **Taneda S**, Hyllested-Winge J, Gall MA, Kaneko S, Hirao K. Insulin degludec/insulin aspart versus biphasic insulin aspart 30 twice daily in insulin-experienced Japanese subjects with uncontrolled type 2 diabetes: Subgroup analysis of a Pan-Asian, treat-to-target Phase 3 Trial. *J Diabetes* 2017; **9**: 243-247 [PMID: 27059529 DOI: 10.1111/1753-0407.12407]

40 **Nasrallah SN**, Reynolds LR. Insulin Degludec, The New Generation Basal Insulin or Just another Basal Insulin? *Clin Med Insights Endocrinol Diabetes* 2012; **5**: 31-37 [PMID: 22879797 DOI: 10.4137/CMED.S9494]

41 **Liu W**, Yang X, Huang J. Efficacy and Safety of Insulin Degludec versus Insulin Glargine: A Systematic Review and Meta-Analysis of Fifteen Clinical Trials. *Int J Endocrinol* 2018; **2018**: 8726046 [PMID: 29721018 DOI: 10.1155/2018/8726046]

42 **ElSayed NA**, Aleppo G, Aroda VR, Bannuru RR, Brown FM, Bruemmer D, Collins BS, Hilliard ME, Isaacs D, Johnson EL, Kahan S, Khunti K, Leon J, Lyons SK, Perry ML, Prahalad P, Pratley RE, Seley JJ, Stanton RC, Gabbay RA; on behalf of the American Diabetes Association. 9. Pharmacologic Approaches to Glycemic Treatment: Standards of Care in Diabetes-2023. *Diabetes Care* 2023; **46**: S140-S157 [PMID: 36507650 DOI: 10.2337/dc23-S009]

43 **Vargas-Uricoechea H**. Efficacy and Safety of Insulin Glargine 300 U/mL versus 100 U/mL in Diabetes Mellitus: A Comprehensive Review of the Literature. *J Diabetes Res* 2018; **2018**: 2052101 [PMID: 29619381 DOI: 10.1155/2018/2052101]

44 **Saisho Y**. Use of Diabetes Treatment Satisfaction Questionnaire in Diabetes Care: Importance of Patient-Reported Outcomes. *Int J Environ Res Public Health* 2018; **15** [PMID: 29747423 DOI: 10.3390/ijerph15050947]

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