VIA MEDICA
RESEARCH PAPER
ISSN 2450–7458
e-ISSN 2450–8187

Duha Ayad Alidrisi[1], Haider Ayad Alidrisi[2], Ali Mohammed Hadi[1]
[1]University of Basrah, College of Pharmacy, Department of Clinical Pharmacy, Basrah, Iraq
[2]University of Basrah, College of Medicine, Faiha Specialized Diabetes, Endocrine, and Metabolism Center, Basrah, Iraq

Effect of Short-Term Basal Insulin Initiation in Newly Diagnosed Type 2 Diabetes on One-Year Glycemic Control: Prospective Cohort, Interventional, Two-Arm Study

ABSTRACT

Objective: To determine the efficacy and safety of early intensive insulin on treatment-naïve, newly diagnosed type 2 diabetes (T2D) patients over one year.

Materials and methods: The study is a prospective cohort, interventional, 2-arm study. It included 243 newly diagnosed, treatment-naïve T2D adult participants who were divided into 2 treatment groups. Both groups (1 and 2) were treated with triple combination glucose-lowering medications for one year. Group 1 participants also were treated with insulin glargine U100 once daily for 2 weeks. The outcomes were glycated hemoglobin (HbA1c), bodyweight changes, and hypoglycemia over one year.

Results: At 3-month evaluation, the achievement of HbA1c < 7% (53 mmol/mol) was 98/119 (82.4%) in group 1 and 61/124 (49.2%) in group 2, (p < 0.0001). At the 12-month evaluation, HbA1c <6.5% (48 mmol/mol) was achieved in 42/109 (38.5%) of group 1 and 27/114 (23.7%) of group 2, (p = 0.01). The 2 groups had significant bodyweight reduction compared to the baseline. The proportion of participants with hypoglycemia was 8.4% in group 1 and 2.4% in group 2.

Conclusions: Two weeks of basal insulin in newly diagnosed T2D with severe hyperglycemia resulted in rapid, more effective, and maintained glycemic control at one-year follow-up. It was safe with less mild hypoglycemia and without weight gain.

ClinicalTrials.gov number: NCT06107153.

Keywords: type 2 diabetes, basal insulin, insulin glargine, metformin, dipeptidyl peptidase inhibitors, pioglitazone

Introduction

Type 2 diabetes (T2D) is characterized by hyperglycemia resulting from insulin resistance and beta-cell dysfunction [1]. There is a gradual and persistent decline in beta-cell function and mass implicating insulin resistance, glucotoxicity, lipotoxicity, and inflammation in T2D patients. Initially, beta cells compensate for insulin resistance by producing more insulin, but this compensatory mechanism eventually fails, leading to glucose intolerance, fasting hyperglycemia, and overt diabetes. By the time T2D is diagnosed, around 40–50%

Address for correspondence:
Haider Ayad Alidrisi MD FIBMS CABM (Med) CABM (Endo) FACE
University of Basrah, College of Medicine, Basrah, 61001 Basrah, Iraq
E-mail: haider.alidrisi@fdemc.iq; haider.alidrisi@uobasrah.edu.iq
Clinical Diabetology
DOI: 10.5603/cd.104242
Received: 27.12.2024 Accepted: 18.01.2025
Early publication date: 17.02.2025

of beta-cell function is already compromised, with an additional annual decline of 4–5% [2].

In Iraq, T2D is diagnosed using a similar diagnostic criterion based on the American Diabetes Association recommendation. The diagnostic criteria of T2D include a fasting plasma glucose level equal to or exceeding 126 mg/dL (6.99 mmol/L), a plasma glucose level of at least 200 mg/dL (11.1 mmol/L) in a patient experiencing symptoms, and a glycosylated hemoglobin (HbA1c) level equal to or more than 6.5% (48 mmol/mol) [3, 4].

A healthy lifestyle is fundamental to diabetes management, but medications may be required besides lifestyle to achieve glycemic control and delay or avoid complications. A comparative efficacy meta-analysis indicates that adding each new class of noninsulin medication to initial treatment typically reduces HbA1c by 0.9–1.1% [3, 5].

The UK Prospective Diabetes Study (UKPDS) and A Diabetes Outcome Progression Trial (ADOPT) indicated that medications aimed at boosting endogenous insulin secretion, such as sulfonylureas, ultimately fail when the stressed beta-cells reach the limit of their ability to respond [6, 7]. Also, these studies endorse the importance of early aggressive glycemic control. Effective lowering of the blood glucose from the start of T2D diagnosis can result in better long-term glycemic control [8].

Insulin is usually advised as a final resort in the progressive treatment protocol for T2D, but it may also be initiated at any time from the onset of T2D, especially in the presence of severe hyperglycemia, weight loss, and during hospitalization [3, 5, 9]. Several studies imply the importance of early initial intensive insulin treatment in newly diagnosed T2D [10]. The rationale for this treatment approach is that insulin has a more potent glucose-lowering potential, protects pancreatic beta-cells, and helps rapid correction of glucotoxicity and lipotoxicity, thereby reducing insulin resistance and improving beta-cell function through the induction of beta-cell rest.

However, there is controversy about the regimen and duration of insulin treatment as an initial treatment for newly diagnosed T2D. Furthermore, patients with T2D frequently refuse to start insulin. In a study from Iraq, most of the patients refused to start insulin when it was indicated, thinking that inulin would affect their social life and other false perceptions of the side effects of insulin [11].

The study aimed to determine the efficacy and safety of early, 2-week basal insulin treatment in combination with multiple glucose-lowering medication on one-year glycemic control

Materials and methods

The study is a prospective cohort, interventional, 2-arm study conducted in Faiha Specialized Diabetes, Endocrine, and Metabolism Center (FDEMC) and Al-Rafidain Endocrine clinic in Basra southern Iraq from June 2023 to October 2024. The study included adult participants (18–65 years old) with newly diagnosed, treatment-naïve T2D. The participants were divided into 2 treatment groups. Group 1 participants were treated with insulin glargine U100 once daily for 2 weeks only plus oral glucose-lowering medications for 12 months. Group 2 participants were treated with glucose-lowering medications, without insulin, for 12 months. ClinicalTrials.gov number, NCT06107153.

Inclusion criteria

- Newly diagnosed T2D, treatment naïve,
- Age between 18 and 65 years,
- HbA1c equals or more than 9% (75 mmol/mol) and random blood glucose (RBG) equal to or more than 300 mg/dl (16.5 mmol/L) and/or fasting blood glucose (FBG) equal to or more than 200 mg/dL (11.1 mmol/L),
- HbA1c more than 10% (86 mmol/mol).

Exclusion criteria

- Patients with type 1 diabetes mellitus,
- Urine ketone dipstick + and above at baseline or at any time throughout the study,
- Pregnancy,
- Current or recent steroid use,
- History of coronary heart disease and heart failure,
- Glomerular filtration rate (GFR) less than 60 mL/min/1.73 m^2.

A total of 243 participants were included in this study; group 1 included 119 participants, and group 2 included 124 participants. In group 1, a total of 119, 119, 113, and 109 participants were actively evaluated at 3, 6, 9, and 12 months, respectively. In group 2, a total of 124, 124, 118, and 114 participants were actively evaluated at 3, 6, 9, and 12 months, respectively.

Clinical data collection

These data include age at diagnosis, gender, history of hypertension, dyslipidemia, cardiovascular disease in the form of ischemic heart disease, heart failure, and stroke. For each participant, office blood pressure was measured using an automatic blood pressure monitor. The participant was considered to have hypertension if he or she was known to have hypertension and was on anti-hypertensive medication or had a blood pressure equal to or more than 140/90 mmHg on

2 occasions [12]. For every participant on each visit, the bodyweight in kilograms (kg) and height in meters (m) were measured with bare feet and light clothes. Body mass index (BMI) was calculated by the formula of bodyweight in kilograms (kg) divided by the square height in meters (m). The participants were considered obese if they had a BMI of 30 (kg/m^2) based on the World Health Organization criteria of obesity classification.

Biochemical data collection

At the inclusion time and from each participant, 10 mL of blood were drawn and put into 2 tubes for laboratory analysis: first, an ethylene diamine tetra acetic acid tube for HbA1c (%) measurement by ion exchange high-performance liquid chromatography using a Bio-Rad® D10, and second, a clot activator tube for the measurement of serum glucose and creatinine using COBAS INTEGRA® 400 PLUS. The GFR was estimated by the equation of the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI). The samples that were taken after 8 hours of fasting were considered as fasting samples. The HbA1c was analyzed in the same method at 3, 6, 9, and 12 months.

Study interventions

Lifestyle measures

Each participant received instructions about lifestyle measures to control the blood glucose and the bodyweight. These instructions were in the form of dietary advice for glycemic control and bodyweight reduction [13].

Oral glucose-lowering medications

The participants in groups 1 and 2 were treated with a combination of 3 oral glucose-lowering medications throughout the 12 months of the study. These medications included metformin extended release (XR) in a dose of 1000 mg once per day and dipeptidyl peptidase 4 inhibitor (DPP4i) (teneligliptin 20 mg or saxagliptin 2.5 mg) once per day. These 2 medications were given in the form of a single-pill combination once daily. The third medication was thiazolidinedione (pioglitazone 30 mg) once per day.

Insulin therapy

The participants in group 1 were treated with basal insulin. The insulin was initiated in a dose of 10 units of glargine U100 at bedtime. The participants were instructed to up-titrate the insulin by adding 2 units every 2 days to reach a FBG between 80 and 130 mg/dL (4.4–7.2 mmol/L) using a home glucometer, and to down-titrate the insulin by subtracting 2 units when the FBG was below 80 mg/dL (4.4 mmol/L). The participants discontinued the basal insulin after 2 weeks or less when FBG was persistently below 100 mg/dL (5.5 mmol/L) on a dose of 10 units of basal insulin.

Efficacy outcomes

The participants in both study groups were evaluated at 3, 6, 9, and 12 months. These evaluations included the measurements of HbA1c (%) and bodyweight (kg). Efficacy measures were as follows:

- The mean HbA1c (%) reductions at 3, 6, 9, and 12 months.
- The percentage of the participants who achieved HbA1c <7% (53 mmol/mol) at 3, 6, 9, and 12 months.
- The percentage of the participants who achieved HbA1c <6.5% (48 mmol/mol) at 3, 6, 9, and 12 months.

Safety outcomes

The participants in both study groups were instructed to have serial monitoring of their blood glucose using a home glucometer at least twice daily or whenever there were symptoms of hypoglycemia. Confirmed hypoglycemia was defined in this study whenever the blood glucose level was below 70 mg/dL (3.8 mmol/L) with or without symptoms. Further evaluation was performed for each participant at each visit in the form of bodyweight measurement.

Statistical analysis

Cochran's formula was used to calculate the sample size for the study. This was done based on a population proportion of T2D of 15%, a confidence interval of 95% (z-score 1.96), and an alpha value of 0.05. A total of 196 participants with T2D needed to be included. The Statistical Package for the Social Sciences version 26.0 (IBM SPSS Statistics, Armonk, NY) was used for data analysis. The qualitative variables were summarized as numbers (N) and percentages (%), and the quantitative variables were summarized as mean ± standard deviations (SDs). To compare the qualitative variables between the groups, we used the chi-square test. The independent Student's t-test was used to compare the quantitative variables between the groups. To analyze the changes in the HbA1c (%) and bodyweight (kg) at each of the study points from baseline and within each group, the paired sample test was used. To compare the changes between the groups at each point, the independent Student's t-test was used. The percentage of the achieved HbA1c < 7 (53 mmol/mol) %, < 6.5 % (48 mol/mol), and the proportions of confirmed hypoglycemia were compared between the groups at

Table 1. General Characteristics of the Study Participants (N = 243)

Variable	N (%) or mean ± SD		P-value**
	Group 1* (N = 119)	Group 2* (N = 124)	
Age [years]	45.4 ± 11.9	48.1 ± 11.9	0.08
Age ≥ 55 years	31 (26.1)	41 (33.1)	0.2
Gender [men]	63 (52.9)	65 (52.4)	0.9
SBP [mmHg]	137.8 ± 17.1	139.3 ± 21.3	0.5
DBP [mmHg]	85.0 ± 11.9	84.4 ± 13.6	0.7
Hypertension	69 (58.0)	76 (61.3)	0.5
BMI [kg/m2]	31.0 ± 6.0	30.2 ± 4.4	0.2
Bodyweight [kg]	85.6 ± 19.7	81.9 ± 15.8	0.1
Obesity (N = 209)	45/95 (47.4)	63/114 (55.3)	0.2
CVD "stroke"	25 (21.0)	31 (25.0)	0.4
FBG [mg/dl], [mmol/L]	271.2 ± 102.4, 15.0 ± 5.6	223.7 ± 92.9, 12.4 ± 5.1	0.1
RBG [mg/dL], [mmol/L]	311.0 ± 69.1, 17,2 ± 3.8	297.8 ± 99.8, 16.5 ± 5.5	0.3
HbA1c [%], [mmol/mol]	11.2 ± 1.6, 99 ± 5.5	11.2 ± 1.5, 99.0 ± 4.5	0.9
Creatinine [mg/dL], [mmol/l]	0.7 ± 0.2, 61.8 ± 17.6	0.7 ± 0.1, 61.8 ± 8.8	0.5

*Group 1: 2-week insulin glargine plus (metformin, dipeptidyl peptidase inhibitor, and pioglitazone). Group 2: metformin, dipeptidyl peptidase inhibitor, and pioglitazone; **N (%) comparison with chi-square test and mean ± SD comparison with independent Student's t test
BMI — body mass index; CVD — cardiovascular disease; DBP — diastolic blood pressure; FBG — fasting blood glucose; HbA1c — glycated hemoglobin; N — number; RBG — random blood glucose; SBP — systolic blood pressure; SD — standard deviation

each of the study points using the chi-square test. For all the above comparisons, a p-value of less than 0.05 was considered statistically significant.

Results

Table 1 summarizes the general characteristics of the study participants. It shows that the 2 study groups were matched, ($p > 0.05$).

Both study groups showed significant reductions in the HbA1c after 3, 6, 9, and 12 months compared to the baseline, ($p < 0.0001$), as shown in Figure 1. At 3-month evaluation, the participants in group 1 had a more significant reduction in HbA1c compared to group 2 [4.9 ± 1.6 % versus 4.1 ± 1.6 % (30 ± 5.5 vs. 21 ± 5.5 mmol/mol), respectively; $p = 0.0001$]. The degree of the HbA1c reductions also appeared higher within group 1 compared to group 2 at 6-month, 9-month, and 12-month evaluations, but it was not statistically significant.

It was found that in this study, group 1 participants were significantly more likely to achieve glycemic control in comparison to group 2 at 3 months, 6 months, and 12 months, as shown in Figure 2. At 3-month evaluation, achievement of HbA1c < 7% (53 mmol/mol) was attained by 98/119 (82.4%) in group 1 and 61/124 (49.2%) in group 2 [OR 4.8 (2.6–8.6), $p < 0.0001$]. Furthermore, the achievement of HbA1c < 6.5% (48 mmol/mol) was 75/119 (63%) in group 1 and 25/124 (20.2%) in group 2, [OR 6.7 (3.7–11.9), $p < 0.0001$].

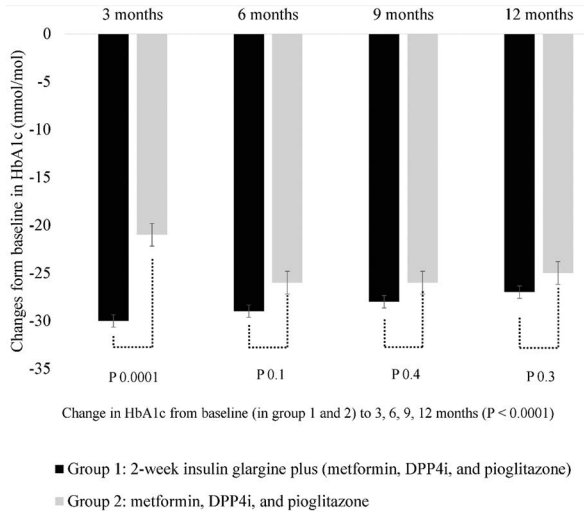

Figure 1. The Changes in the HbA1c from Baseline in the Study Groups Throughout the Study
Baseline to each point comparison was done paired sample t test, for between-group comparison, the independent Student's t test was used
DPP4i — dipeptidyl peptidase 4 inhibitor; HbA1c — glycated hemoglobin

At 6-month evaluation, HbA1c < 7% (53 mmol/mol) was achieved in 97/119 (81.5%) of group 1 and 70/124 (70.2%) of group 2, [OR 1.8 (1.0–3.4), $p = 0.03$]. And HbA1c < 6.5% (48 mmol/mol) was achieved in 60/119 (50.4%) of group 1 and 45/124 (36.3%) of group 2,

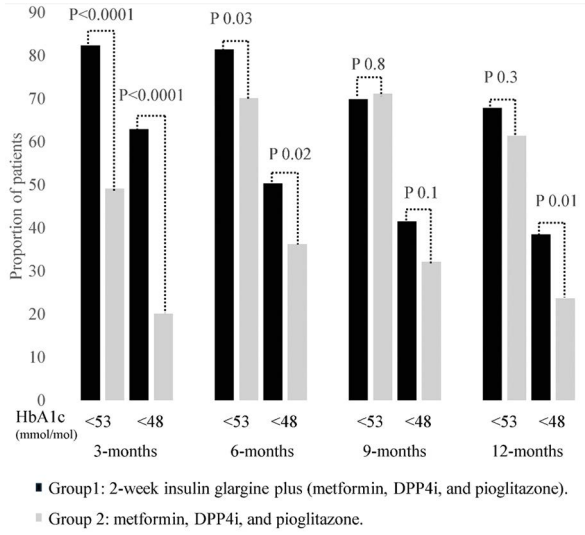

Figure 2. The Targets HbA1c Achievement in the Study Groups Throughout the Study
Comparisons were done using the chi-square test; DPP4i — dipeptidyl peptidase 4 inhibitor; HbA1c — glycated hemoglobin

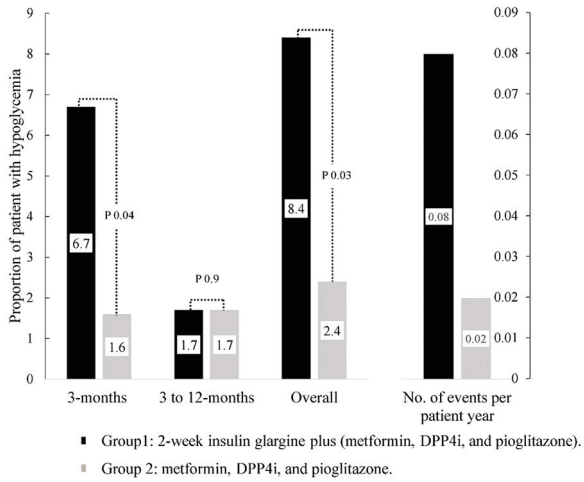

Figure 3. The Development of Confirmed Hypoglycemia in the Study Groups Throughout the Study
Comparison was done with chi-square test; DPP4i — dipeptidyl peptidase 4 inhibitor

[OR 1.7 (1.0–2.9), p = 0.02]. At 12-month evaluation, HbA1c < 6.5% (48 mmol/mol) was achieved in 42/109 [38.5% 0 of group 1 and 27/114 (23.7%)] of group 2, [OR 2.0 (1.1–3.6), p = 0.01]. No significant difference was seen between groups 1 and 2 in the achievement of HbA1c < 7% (53 mmol/mol) at 9 and 12 months, and HbA1c < 6.5% (48 mmol/mol) at 9 months. While the proportion of the participants remaining uncontrolled at 12 months was comparable in both groups, the participants within group 1 had a fast achievement of HbA1c < 7 (53 mmol/mol), [in group 1, 17.6% had HbA1c ≥ 7% (53 mmol/mol) at 3 months, which is nearly comparable to 16.9% with HbA1c ≥ 7% (53 mmol/mol) in group 2 at 9 months]. Throughout the study, more participants remained with HbA1c ≥ 6.5% (48 mmol/mol) in group 2 compared to group 1 (p < 0.0001). At 12 months, 51.7% of the participants in group 2 remained with HbA1c ≥ 6.5% (48 mmol/mol). While at 3 months, only 35.8% of the participants in group 1 remained with HbA1c ≥ 6.5% (48 mmol/mol) (Suppl. Fig. 1).

Both participants in group 2 had significant bodyweight reduction at 3-, 6-, 9-, and 12-month evaluations as compared to the baseline bodyweight, (p < 0.0001) (Suppl. Fig. 2). No significant differences were seen in the bodyweight reductions between the groups through the study (p > 0.05). The average bodyweight loss was 1.7 ± 1.8, 1.7 ± 1.8, 1.6 ± 1.9, and 1.4 ± 2.0 kg at the study points, respectively.

The risk of hypoglycemia was significantly higher in participants of group 1 compared to group 2, as shown in Figure 3. The overall hypoglycemic events were 10/119 (8.4%) in group 1 compared to 3/124 (2.4%) in group 2, [OR 3.7 (0.9–13.7), p = 0.03]. Through the first 3 months, 8/119 (6.7%) had hypoglycemia compared to only 2/124 (1.6%) in group 2, [OR 4.3 (0.9–21.1), p = 0.04]. Only 2 hypoglycemic events occurred between 3 and 12 months, one in each group. These findings resulted in a number of events per patient-year of hypoglycemia of 0.08% in group 1 and 0.02 in group 2.

Discussion

In this study, the combination glucose-lowering medications with or without 2 weeks of basal insulin was associated with significant reductions in HbA1c at the study points. However, in the participants treated with insulin, a higher reduction in HbA1c and a greater proportion of participants achieved HbA1c < 7% (53 mmol/mol) and < 6.5% (48 mmol/mol) at 3 and 6 months and maintained an HbA1c < 6.5% (48 mmol/mol) at 12 months. Many studies have evaluated the benefit of short-term insulin therapy in newly diagnosed T2D by using different types and regimens of insulin and for different durations. Early insulinization was associated with a better outcome in terms of rapidity, degree, and maintenance of glycemic control.

A study that was conducted in India used biphasic insulin for 2 months for newly diagnosed T2D with

HbA1c > 9% (75 mmol/mol). Insulin treatment was associated with rapid glycemic control, maintenance of glycemic control, and improvement in the marker of beta-cell function [14]. Stojanovic et al. [15] studied the effect of one-month insulin (basal or human premixed) on newly diagnosed T2D patients with HbA1c > 9% (75 mmol/mol) as compared to glimepiride. The patients who were treated with an initial insulin had greater improvement in beta-cell function and did better in terms of glycemic and lipid control.

Another study in India recruited 426 treatment-naive T2D patients who received a short course of insulin therapy lasting 4 to 6 weeks in the form of basal once, twice, or premixed twice based on the severity of the baseline hyperglycemia. The study demonstrated a significant improvement in beta-cell function, as indicated by increased serum C-peptide levels, even after 2 years of follow-up [16].

In another study for newly diagnosed T2D and a longer follow-up of 3.5 years, initial intensive insulin plus metformin for 3 months was followed by either a triple glucose-lowering combination (metformin, glibenclamide, and pioglitazone) or insulin plus metformin. No significant difference was found in the glycemic control and preservation of beta-cell function between the groups at 3.5 years. The initial aggressive glucose treatment with insulin for all patients before their assignment to groups may be responsible for the demonstrated comparable achievements. This finding explores the benefit of early aggressive glucose control on long-term glycemic control [17].

In comparison with these studies, the current study used only basal insulin (insulin glargine) for 2 weeks as the maximum duration. The triple (metformin XR, DPP4i, and pioglitazone) glucose-lowering combination was associated with clinically significant reduction of HbA1c in both groups. However, the insulin-treated group showed a higher early reduction in the HbA1c and achievement of HbA1c < 7% (53 mmol/mol) and 6.5% (48 mmol/mol). In our study, we did not measure the markers of beta-cell function. However, more participants from the initial 2-week basal insulin group maintained a more stringent HbA1c of less than 6.5% (48 mmol/mol).

In this study, both participant groups had a significant bodyweight loss. This finding may be explained by the high prevalence of obesity in the studied participants. Consequently, all participants were provided with instructions about a healthy lifestyle including a balanced diet and regular physical activity. This adherence helped in the modest bodyweight loss that was seen even after the short-term insulin therapy. Furthermore, a combination of metformin and DPP4i can be associated with some weight reduction [18]. Interestingly, these bodyweight changes occurred while the participants were treated with pioglitazone. A longer follow-up is needed to ensure the impact of this glucose-lowering combination on bodyweight.

The safety outcome of this short-term basal insulin regimen was documented. The proportion of participants with hypoglycemia who were treated with insulin was 3.5 times higher than the non-insulin group. All the events were mild and self-manageable and were reduced with the follow-up. Hypoglycemia is one of the most feared side effects of early insulin therapy, and it has been observed with mild severity and lower rates in many studies [14, 17, 19]. While similar studies usually used longer, more complex insulin regimens, we tried in this study to use a shorter, less complex regimen that is more convincing to initiate when it is needed.

Conclusions

Two weeks of basal insulin in newly diagnosed T2D with severe hyperglycemia resulted in a rapid and greater reduction in HbA1c at 3 months. More participants achieved glycemic control early and after one year of follow-up. The 2-week basal insulin treatment appeared safe with less mild hypoglycemia and without weight gain.

Article information

Supplementary material

The Supplementary material for this article can be found online at https://journals.viamedica.pl/clinical_diabetology/article/view/104242.

Data availability

The original contributions presented in the study are included in the article and supplementary material and further inquiries can be directed to the corresponding author.

Ethics approval and consent to participate

The study was approved by the Iraqi Ministry of Health and the Institutional Review Board of the Faiha Specialized Diabetes, Endocrine, and Metabolism Center (FDEMC) of the Basrah Directorate of Health (Reference number 56/35/22), and the Scientific and Ethical committee of the University of Basrah, college of medicine (reference number 030408). Intervention and data collection were conducted under the supervision of an endocrinologist. Written informed consent was obtained from each participant.

Author contributions

Haider Ayad Alidrisi: conceptualization, methodology, data curation, formal analysis, investigation, project administration, writing original draft preparation, supervision. Duha Ayad Alidrisi: conceptualization, methodology, data curation, formal analysis, investigation, project administration, writing original draft preparation. Ali Mohammed Hadi: project administration, writing original draft preparation, writing review and editing, supervision.

Funding

No funding.

Acknowledgements

The authors express their sincere gratitude to the medical staff at Faiha Specialized Diabetes, Endocrine, and Metabolism Center and Al-Rafidain Specialized Center.

Conflict of interests

The authors declare no conflict of interest.

REFERENCES

1. Wu Y, Ding Y, Tanaka Y, et al. Risk factors contributing to type 2 diabetes and recent advances in the treatment and prevention. Int J Med Sci. 2014; 11(11): 1185–1200, doi: 10.7150/ijms.10001, indexed in Pubmed: 25249787.
2. Wysham C, Shubrook J. Beta-cell failure in type 2 diabetes: mechanisms, markers, and clinical implications. Postgrad Med. 2020; 132(8): 676–686, doi: 10.1080/00325481.2020.1771047 , indexed in Pubmed: 32543261.
3. Abusaib M, Ahmed M, Nwayyir HA, et al. Iraqi Experts Consensus on the Management of Type 2 Diabetes/Prediabetes in Adults. Clin Med Insights Endocrinol Diabetes. 2020; 13: 1179551420942232, doi: 10.1177/1179551420942232, indexed in Pubmed: 32884389.
4. American Diabetes Association Professional Practice Committee. 2. Diagnosis and Classification of Diabetes:*Standards of Care in Diabetes—2024*. Diabetes Care. 2023; 47(Supplement_1): S20–S42, doi: 10.2337/dc24-s002, indexed in Pubmed: 38078589.
5. American Diabetes Association Professional Practice Committee. 9. Pharmacologic Approaches to Glycemic Treatment: *Standards of Care in Diabetes—2024*. Diabetes Care. 2023; 47(Supplement_1): S158–S178, doi: 10.2337/dc24-s009, indexed in Pubmed: 38078590.
6. King P, Peacock I, Donnelly R. The UK prospective diabetes study (UKPDS): clinical and therapeutic implications for type 2 diabetes. Br J Clin Pharmacol. 1999; 48(5): 643–648, doi: 10.1046/j.1365-2125.1999.00092.x, indexed in Pubmed: 10594464.
7. Viberti G, Kahn SE, Greene DA, et al. A diabetes outcome progression trial (ADOPT): an international multicenter study of the comparative efficacy of rosiglitazone, glyburide, and metformin in recently diagnosed type 2 diabetes. Diabetes Care. 2002; 25(10): 1737–1743, doi: 10.2337/diacare.25.10.1737, indexed in Pubmed: 12351470.
8. Del Prato S, Felton AM, Munro N, et al. Global Partnership for Effective Diabetes Management, Global Partnership for Effective Diabetes Management. Improving glucose management: ten steps to get more patients with type 2 diabetes to glycaemic goal. Int J Clin Pract. 2005; 59(11): 1345–1355, doi: 10.1111/j.1742-1241.2005.00674.x, indexed in Pubmed: 16236091.
9. Korytkowski MT, Muniyappa R, Antinori-Lent K, et al. Management of Hyperglycemia in Hospitalized Adult Patients in Non-Critical Care Settings: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2022; 107(8): 2101–2128, doi: 10.1210/clinem/dgac278, indexed in Pubmed: 35690958.
10. Mohan V, Mukherjee J, Das A, et al. Initiation and intensification of insulin therapy in type 2 diabetes mellitus: Physician barriers and solutions – An Indian perspective. Endocrine and Metabolic Science. 2021; 4: 100103, doi: 10.1016/j.endmts.2021.100103.
11. Alidrisi HA, Bohan A, Mansour AA. Barriers of Doctors and Patients in Starting Insulin for Type 2 Diabetes Mellitus. Cureus. 2021; 13(9): e18263, doi: 10.7759/cureus.18263, indexed in Pubmed: 34712538.
12. McEvoy JW, McCarthy CP, Bruno RM, et al. ESC Scientific Document Group, ESC Scientific Document Group. 2024 ESC Guidelines for the management of elevated blood pressure and hypertension. Eur Heart J. 2024; 45(38): 3912–4018, doi: 10.1093/eurheartj/ehae178, indexed in Pubmed: 39210715.
13. Evert AB, Dennison M, Gardner CD, et al. Nutrition Therapy for Adults With Diabetes or Prediabetes: A Consensus Report. Diabetes Care. 2019; 42(5): 731–754, doi: 10.2337/dci19-0014, indexed in Pubmed: 31000505.
14. Mokta JK, Mohan V, Mokta K, et al. Early Intensified Insulin Therapy in Newly Diagnosed Type 2 Diabetes Leads to Sustained Improvement in Glycemic Control and Improved Beta Cell Function. J Assoc Physicians India. 2018; 66(9): 37–40, indexed in Pubmed: 31321927.
15. Stojanovic J, Andjelic-Jelic M, Vuksanovic M, et al. The effects of early short-term insulin treatment vs. glimepiride on beta cell function in newly diagnosed type 2 diabetes with HbA1c above 9. Turk J Med Sci. 2023; 53(2): 552–562, doi: 10.55730/1300-0144.5616, indexed in Pubmed: 37476884.
16. Madnani S, Anjana RM, Warade SB, et al. Short-term insulin therapy at the time of diagnosis of Type 2 diabetes leads to better glycemic control and improved beta cell function. Journal of Diabetology. 2019; 10(3): 97, doi: 10.4103/jod.jod_39_18.
17. Harrison LB, Adams-Huet B, Raskin P, et al. -cell function preservation after 3.5 years of intensive diabetes therapy. Diabetes Care. 2012; 35(7): 1406–1412, doi: 10.2337/dc11-2170, indexed in Pubmed: 22723578.
18. Göke B, Gallwitz B, Eriksson J, et al. D1680C00001 Investigators. Saxagliptin is non-inferior to glipizide in patients with type 2 diabetes mellitus inadequately controlled on metformin alone: a 52-week randomised controlled trial. Int J Clin Pract. 2010; 64(12): 1619–1631, doi: 10.1111/j.1742-1241.2010.02510.x, indexed in Pubmed: 20846286.
19. Liu L, Liu J, Xu L, et al. Lower mean blood glucose during short-term intensive insulin therapy is associated with long-term glycemic remission in patients with newly diagnosed type 2 diabetes: Evidence-based recommendations for standardization. J Diabetes Investig. 2018; 9(4): 908–916, doi: 10.1111/jdi.12782, indexed in Pubmed: 29193795.