Original Article

Intensive Insulin Titration with Insulin Glargine in Insulin-Naive Type 2 Diabetic Patients in Turkey: LANTIT Study

Türkiye'de İnsülin-Naiv Tip 2 Diyabet Hastalarında İnsülin Glarjin ile İntensif İnsülin Titrasyonu: LANTIT Çalışması

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Abstract

Purpose: This open-label, single-arm, phase 4 study was designed to evaluate the efficacy of intensive insulin glargine titration in type 2 diabetes mellitus (T2DM) patients for 6 months to reach good glycaemic control.

Material and Method: Two hundred-forty one insulin-naive T2DM patients were included. The primary efficacy variable was the glycaemic control (HbA1c level of ≤7%). The secondary variables were a fasting blood glucose (FBG) level of <100 mg/dL, the final dose of basal insulin, number of dose adjustments, time to dose titration in reaching target HbA1c level of ≤7%, weight gain and treatment satisfaction using the Diabetes Treatment Satisfaction Questionnaire (DTSQ). Hypoglycemia, severe hypoglycemia and adverse events were also assessed.

Results: The mean (±SD) HbA1c level of 8.8±0.6% at baseline decreased to 7.4±0.9% on day-90 (p<0.001) and to 7.3±0.9% on day-180 (p<0.001). The percentage of patients with HbA1c≤%7 was 36.9% on day-90 and 40% on day-180. The mean FBG of 186.3±52.5 mg/dL at baseline decreased to 111.5±36.6 mg/dL on day-90 (p<0.001) and to 114.1± 34.8 mg/dL on day-180 (p<0.001). The mean insulin glargine dose on the last day of FBG measurement (day-89) was 32.7±15.5 IU and the mean number of titrations was 12.7±6.6. These values on day-179 were 36.8±19.4 IU and 5.8±5.7, respectively. The total DTSQ score (20.3±7.7) and scores for each item at baseline showed improvement on day-180 (p<0.001). The most frequently reported adverse reactions were hypoglycaemia (49.7%) and weight gain (9.5%). Serious hypoglycaemia cases reported during the first and the second 3-month periods were 11.2% and 13.3%, respectively.

Discussion: In conclusion, the use of insulin glargine with intensive dose titration is effective and safe in T2DM patients. *Turk Jem 2015; 19: 83-88*

Key words: Type 2 diabetes mellitus, basal insulin, insulin glargine, titration

Özet

Amaç: Bu açık-etiketli, tek-kollu faz 4 çalışma, insulin glarjin ile tedavi edilen tip 2 diabetus mellitus (T2DM) hastalarında iyi glisemik kontrol için etkili dozlara ulaşmada yoğunlaştırılmış insülin titrasyonunu değerlendirmek amacıyla tasarlanmıştır.

Gereç ve Yöntem: Önceden insülin kullanmamış 241 T2DM hastası çalışmaya alınmıştır. Birincil değerlendirme kriteri glisemik kontrol (HbA1c seviyesi ≤%7), ikincil kriterler ise açlık kan şekeri (AKŞ) <100 mg/dL, son bazal insülin dozu, doz ayarlama sayısı, hedef HbA1c seviyesine ulaşıldığı an doz titrasyonuna kadar geçen zaman, kilo alımı ve tedavi memnuniyetinin Diyabet Tedavi Memnuniyet Anketi (DTSQ) ile değerlendirilmesi olmuş, ayrıca hipoglisemi, ciddi hipoglisemi ve advers olaylar da değerlendirilmiştir.

Bulgular: Başlangıçtaki ortalama ± SD HbA1c seviyesi %8,8±0,6, 90. günde %7,4±0,9 seviyesine (p<0,001), 180. günde ise %7,3±0,9 seviyesine (p<0,001) düşmüştür. HbA1c seviyesi ≤%7 olan hastaların oranı 90. günde %36,9 iken 180. günde %40 olmuştur. Ortalama AKŞ başlangıçta 186,3±52,5 mg/dL iken 90. günde 111,5±36,6 mg/dL'ye (p<0,001), 180. günde ise 114,1± 34,8 mg/dL'ye düşmüştür (p<0,001). Son AKŞ ölçümü sırasında (89. gün) ortalama insülin glarjin dozu 32,7±15,5 IU ve ortalama titrasyon sayısı ise 12,7±6,6 idi. Bu değerler 169. gün 36,8±19,4 IU ve 5,8±5,7 idi. Total DTSQ skoru (20,3±7,7) ve her bir madde için 180. günde başlangıç vizitine göre bir iyileşme izlendi (p<0,001). En sık bildirilen advers olay hipoglisemi (%49,7) ve kilo alımı (%9,5) idi. İlk ve ikinci 3 aylık dönemlerde bildirilen ciddi hipoglisemi olayları sırasıyla %11,2 ve %13,3 idi.

Tartışma: Sonuç olarak yoğunlaştırılmış doz titrasyonu ile insülin glarjin kullanımı T2DM hastalarında etkili ve güvenli bir tedavi seçeneğidir. *Turk Jem 2015; 19: 83-88*

Anahtar kelimeler: Tip 2 diabetes mellitus, bazal insülin, insülin glarjin, titrasyon

Introduction

Despite long years of research, diabetes mellitus (DM) still remains one of the most significant causes of morbidity and mortality in the world, and its global impact is likely to accelerate over the coming decades. Much of the medical and economic consequences of diabetes are attributable to its associated microvascular and macrovascular complications.

A large percentage of individuals with type 2 DM will eventually require insulin treatment to achieve and maintain glycemic control. This is partly due to the impairment of insulin secretion with progressive decline in beta-cell function, as was observed in the United Kingdom Prospective Diabetes Study (UKPDS) (1). In cases with poor glycemic control by oral treatment in type 2 DM patients, addition of basal insulin treatment is accepted as the most effective treatment approach both by American Diabetes Association/European Association for the Study of Diabetes (ADA/EASD) consensus declaration (2) and Diabetes Mellitus Diagnosis, Treatment and Follow-up Guideline of Turkish Endocrinology and Metabolism Society (3). However, insulin treatment is perceived by many patients as more invasive than diet and/or oral drug-based regimens. Factors contributing to reluctance to insulin treatment from the patient's point of view include anxiety due to giving an injection, preparing the correct dose of insulin, and experiencing hypoglycemia and/or weight gain.

On the other hand, nearly 50% of type 2 DM patients fail to achieve targeted glycemic levels for an effective control of their medical condition as HbA1c levels stay well above 7% (4,5). This inadequacy in reaching treatment targets is mainly due to ineffective insulin dosage titration (6). This low dosage and lack of titration might be caused by the fears of hypoglycemia; thus, effective communication with patients during the initial phases of insulin treatment and titration of daily insulin dosages seem to be useful tools for achieving successful glycemic control in patients.

The current national, open-label, single-arm, phase 4 study was designed to evaluate the efficacy of intensive insulin titration with insulin glargine for the duration of 6 months to reach good glycemic control (A1c ≤7%) in type 2 diabetic patients. The secondary objectives of the study were to determine the dose adjustment and safety profile of insulin glargine during the follow-up.

Materials and Methods

Study Population

Type 2 DM patients, who have not achieved target glycemic levels by means of oral antidiabetic drug (OAD) treatment and who were planned to receive insulin treatment, were invited to participate in this study. The study included 241 patients from 23 centers (university hospitals and training and research hospitals) in Turkey. Male or female insulin-naive patients with type 2 DM, who were aged 18 years or older, under treatment with OADs for more than three months and for whom addition of a basal insulin to the treatment was considered to be appropriate, were included to study. The patients had poor glycemic control (7.5%<HbA1c<10%) and body mass index (BMI) of <40 kg/m^2. Insulin glargine was used as basal insulin. Type 1 DM patients and those with impaired renal function and/or kidney disease and/or metabolic acidosis, and pregnant/breast feeding women were excluded. All patients signed informed consent form before enrollment.

Study Design

This study was designed as an open-label, non-randomized, single-arm, prospective phase 4 study. All subjects fulfilling the eligibility criteria were included in the study and treated with insulin glargine together with a selected OAD. Titration of insulin glargine was done according to the algorithm recommended by the physician until the fasting blood glucose (FBG) level reached <100 mg/dL. When the targeted FBG level was achieved, the patient continued with this same dose until the end of the study. In case of deviation from the targeted glycemic levels, titration procedure was re-started.

Insulin glargine was initiated subcutaneously at a dose of 10 IU once daily. After the initial dosing, patients were asked to monitor their blood glucose levels on a daily basis (every morning) and calculate their mean blood glucose levels every 3 days. Intensive dosage titration was performed by means of regular phone calls. During the calls, the patients' last self-measured FBG levels were recorded and the dose was adjusted in a dose range of 2 to 4 IU once daily for 6 months, if required. The patients were instructed to adjust their insulin dose as follows: if the mean blood glucose level was <100 mg/dL, no dose change was to be done; if it was >100 mg/dL, bed-time dose was to be increased by 2 IU/day; if it was >180 mg/dL, bed-time dose was to be increased by 4 IU/day. At baseline visit (day-0), demographic characteristics, medical and family history, laboratory findings indicative of glycemic control were obtained and the patients' satisfaction level with their diabetes treatment was evaluated using the Diabetes Treatment Satisfaction Questionnaire (DTSQ). At the first follow-up visit (day-90), the patients were evaluated considering glycemic control and safety. At the final visit (day-180), glycemic control and safety parameters were re-assessed along with DTSQ.

Efficacy Parameters

The primary efficacy variable was "achieving glycemic control as defined by a HbA1c level of ≤7%". The secondary variables were reaching FBG level of <100 mg/dl, the final dose of insulin glargine, number of dose adjustments, time to dose titration in reaching target HbA1c level of ≤7%, weight gain and DTSQ scores during the course of study.

Safety Parameters

The presence of hypoglycemia, severe hypoglycemia and adverse events noted by the investigator were assessed. All adverse events were monitored for each patient, from the time informed consent forms were obtained until 30 days after the last dose of insulin glargine.

Statistical Analysis

Assuming that the success rate would be 70% (i.e. 70% of all participants would achieve target HbA1c level), minimum 220 patients were required to be enrolled for the efficacy of treatment to be proven within 10% precision error, alpha=0.05, and power (1-beta) =0.90. Since 10% of patients were expected to be missing in the course of the study, minimum 240 patients were planned

to be enrolled in the study. Efficacy populations of this study were defined as the ITT (intent to treat) and per-protocol populations. Safety population included patients who received at least one dose of insulin glargine.

Comparisons between visits were performed by the Wilcoxon test. Comparisons between the subgroups (e.g. patients who did versus who did not achieve targeted HbA1c levels) were performed by the Mann-Whitney U test. Since there were three visits, type-I error level was adjusted downward to 0.017 (0.05 divided by three pairwise comparisons) for p values corresponding to pairwise visit comparisons. Otherwise, statistical significance was assigned to p values of lower than 0.05.

Hypoglycemia incidence and hypoglycemia attack frequency data were calculated using Open Source Epidemiologic Statistics for Public Health, Version 2.3.1 and IBM SPSS Statistics Release 20.0.0.1 software packages.

Results

Demographic Characteristics

The number of screened patients was 359 and the number of patients, who received at least one dose of study medication, was 241. Among a total of five withdrawn patients, only one was due to an adverse event, the rest four were withdrawn due to investigator decision. Thus, the statistical analysis was conducted on 236 patients.

As demonstrated in Table 1, 53.8% of the study population was female and the mean age was 53.4±9.5 years. The mean body weight was 81.4±13.4 kg, BMI was 29.9±4.4 kg/m^2 and the mean waist circumference was 103.1±12.3 cm. The patients were diabetic for 9.0±5.5 years at baseline (median 7.5 years). The mean FBG level at baseline was 186.3±52.5 mg/dL (median 178.0 mg/dL) and the mean HbA1c was 8.8%±0.6% (median 8.8%).

The most common concomitant diseases were hypertension (61.0%), cardiovascular disease (20.3%) and lipid disorders (65.3%). Retinopathy and neuropathy were present in 26.1% and 23.9% of patients, respectively. The most common OAD which was being used by the study population was sulphonylurea (40.2%) followed by metformin (38.3%). Nearly half of the patients was receiving two OADs (49.6%) and 35% were receiving three OADs at baseline.

Glycemic Control

As shown in Table 2, the mean HbA1c level of 8.8±0.6% at baseline decreased to 7.4±0.9% on day-90 (p<0.001) and to 7.3±0.9% on day-180 (p<0.001). The change in HbA1c levels between two visits was not significant (p=0.172). The percentage of patients who achieved target HbA1c of ≤7 level was 36.9% on day-90 and 40.0% on day-180 by intensive follow-up of blood glucose levels and titration of insulin glargine.

The mean FBG of 186.3±52.5 mg/dL at baseline decreased to 111.5±36.6 mg/dL on day-90 (p<0.001). Although FBG on day-180 (114.1±34.8 mg/dL) was not different from that on day-90, it was significantly lower in comparison to baseline value (p<0.001). The percentage of patients achieved both FBG<100 mg/dL and HbA1c≤7 levels were 25.7% and 23.3% on day-90 and day-180 visits, respectively.

Table 1. Baseline characteristics of the study population	
Characteristics	**% or Mean (±SD)**
Gender (%)	
Male / Female	46.2 / 53.8
Age (years)	53.5 (±9.5)
Body weight (kg)	81.4 (±13.4)
BMI (kg/m^2)	29.9 (±4.4)
Waist circumference (cm)	103.1 (±12.3)
Duration of diabetes (years)	9.0 (±5.5)
Fasting blood glucose (mg/dL)	186.3 (±52.5)
HbA1c (%)	8.8 (±0.6)
Concomitant diseases (%)	
Arterial hypertension	61.0
Cardiovascular disease	20.3
Lipid disorders	65.3
Medications (%)	
Antihypertensive drugs	39.1
Antihyperlipidemic drugs	23.4
Antithrombotic drugs	14.3
OADs (%)	
Sulfonylurea	40.2
Metformin	38.3
Thiazolidinediones	11.4
Acarbose	9.0
DPP4	1.1
Diabetes complications (%)	
Retinopathy	26.1
Neuropathy	23.9
Proteinuria	15.7
Angina	10.4
Myocardial Infarction	10.4
Peripheral vascular disease	7.5
Heart failure	3.7
Foot ulcers	0.7
Amputation	0.7
Stroke	0.7
BMI: Body mass index	

Table 2. Mean (±SD) fasting blood glucose and HbA1c levels of the study population at baseline and study visits			
	Baseline	**Day-90**	**Day-180**
FBG (mg/dL)	186.3 (±52.5)	111.5 (±36.6)*	114.1 (±34.8)*
HbA1c (%)	8.8 (±0.6)	7.4 (±0.9)*	7.3 (±0.9)*
*p<0.001, compared to baseline by Wilcoxon test. FBG: Fasting blood glucose			

Titration of Insulin Glargine

Table 3 shows the dose of insulin glargine and FBG levels in the patients during the course of the study. During the first follow-up period, the mean insulin glargine dose on the last day of home FBG measurement (day-89) was 32.7±15.5 IU (median=30.0 IU) and the mean number of titrations during this period was 12.7±6.6 (median=13.0).

During the second follow-up period, the mean dose of insulin glargine on the last day of FBG measurement (day-179) increased to 36.8±19.4 IU (median=32.0 IU). The mean number of titrations during the second follow-up period was 5.8±5.7 (median=4.0).

Weight Control

As shown in Table 4, waist circumference values in the study population did not show statistically significant alterations throughout the follow-up period (p=0.760), however, a statistically significant increase was observed in the mean body weight (p<0.001) and the BMI values (p<0.001).

Diabetes Treatment Satisfaction

Evaluation of treatment satisfaction assessed in patients by using DTSQ revealed a total score of 20.3±7.7 at baseline. The higher satisfaction scores at baseline were observed for items "recommend to others" (3.6±1.8) and "convenience" (3.6±1.6). The high score for "perceived frequency of hyperglycemia" (4.2±1.4) indicated a low level of satisfaction. As given in Table 5, the change in DTSQ scores obtained on day-180 demonstrated significant improvements in all items compared to baseline, including those of "perceived frequency of hyperglycemia" and "perceived frequency of hypoglycemia".

Comparison of total DTSQ scores between patients who did and did not achieve target HbA1c values on day-180 showed no significant difference (14.0±4.8 and 12.9±5.0; p=0.104, respectively). When these two groups of patients were compared in terms of DTSQ items separately, a significant difference was observed only in the DTSQ scores for "flexibility" being higher in patients who achieved target HbA1c level (p=0.019) (Table 6).

Safety

The patients experienced a total of 147 adverse events during the follow-up period. The most common adverse event was hypoglycemia (49.7%) that followed by weight gain (9.5%) and hypertension (2.7%).

Cases of serious hypoglycaemia (a blood glucose level of ≤ 52 mg/dL) reported during the first and the second 3-month periods were 11.2% and 13.3%, respectively.

During the course of the study, a total of 53 patients (21.9%) experienced hypoglycemia reporting a median of 4.0 (inter-quartile range=7.0) attacks. In a total of 53 patients (21.9%) who experienced hypoglycemia attacks, 12.4% reported 1-5 attacks, 6.6% had 5-15 attacks and 2.9% had >25 attacks.

In this study, a total of 17 cases of serious adverse events were reported in 14 patients. One patient withdrew from the study, however, this patient was diagnosed with small cell lung cancer before initiation of the investigational product and withdrawn. Reported serious adverse events were rated as unrelated with the study medication by the investigators, as all patients presenting serious adverse events had underlying co-morbidities.

Discussion

The findings of the current analysis demonstrated successful glycemic control (as measured by FBG and HbA1c levels) rates along with high safety profile in type 2 DM patients receiving treatment with insulin glargine titrated intensively during 6 months of follow-up. Another important finding of the study was the marked improvement in study patients' treatment satisfaction level as assessed by DTSQ scores.

Patients with type 2 DM are frequently maintained in poor glycemic control for prolonged periods, increasing the risk of serious complications (7). Insulin is the most effective treatment to achieve glycemic goals in these patients (8). Basal insulin analogs have

Table 3. Final insulin glargine dose and the fasting blood glucose levels of study patients on the last day of glucose measurements		
	Day-89	**Day-179**
Final İnsulin Dose (IU/day)		
Mean (±SD)	32.7 (±15.5)	36.8 (±19.4)
Median (min-max)	30.0 (8.0-86.0)	32.0 (8.0-126.0)
FBG (mg/dL)		
Mean (±SD)	98.9 (±21.3)	95.8 (±16.0)
Median (min-max)	95.0 (59.0-194.0)	95.0 (53.0-153.0)
FBG: Fasting blood glucose		

Table 4. Body weight, body mass index and waist circumference of the study population at baseline and study visits				
	Baseline	**Day-90**	**Day-180**	**p**
Weight (kg)				
Mean (±SD)	81.4 (±13.4)	82.2 (±12.7)	82.9 (±13.3)	<0.001 *
Median (min-max)	80.0 (51.0-80.0)	81.2 (55.0-118.0)	82.0 (55.0-122.0)	
BMI (kg/m^2)				
Mean (±SD)	29.9 (±4.3)	30.7 (±4.3)	30.9 (±4.4)	<0.001 *
Median (min-max)	30.0 (17.0-39.0)	30.2 (17.8-42.0)	30.4 (19.4-122.0)	
Waist Circumference (cm)				
Mean (±SD)	103.1 (±12.3)	103.0 (±12.0)	102.9 (±12.2)	0.760 **
Median (min-max)	103.0 (65.0-145.0)	103.0 (64.0-134.0)	102.0 (65.0-148.0)	
*Day-180 compared to baseline by Wilcoxon test. **Day-180 compared to baseline by paired sample test. BMI: Body mass index				

been designed to provide consistent, relatively flat, and protracted insulin levels. Horvath et al. (9) have recently published their meta-analysis assessing the effects of long-term treatment with long-acting insulin analogs compared to NPH insulin in patients with type 2 DM and found significantly lower rates of symptomatic, overall and nocturnal hypoglycemia with the use of basal insulin. Twenty-four-hour continuous activity profile of insulin glargine without peaks has been shown to be beneficial in the early periods of type 2 diabetes (10,11). In our study, initial insulinization with insulin glargine at bedtime and continuous monitoring with intensive titration resulted in a reasonable decrease in both HbA1c and FBG levels in nearly half of the patients. About 36% of all patients achieved target HbA1c levels on day-90, and this was increased to 40% after 180 days of follow-up. The mean value of HbA1c decreased from 8.8% to 7.4% in 3 months and to 7.3% in 6 months. The data of The Canadian Implementing New Strategies with Insulin Glargine for Hypoglycemia Treatment (INSIGHT) study demonstrated that adding a daily injection of insulin glargine and titrating the dose by 1 IU/day was 1.7 times more likely to achieve two consecutive HbA1c levels ≤6.5% than conventional treatment with oral glucose-lowering agents (12). In the LANMET study, the patients' HbA1c level averaged 6.96 and 6.97% in the insulin glargine and NPH groups, respectively (6). In the LANMET study, the patients were using only metformin whereas in our

study, sulphonylurea and metformin were the most frequently used OADs. On the other hand, in the treat-to-target study, 60% of the patients using insulin glargine along with sulphonylurea and metformin attained HbA1c of ≤7% (5).

This study provided important data on intensive insulinization by means of continuous titration with insulin glargine for 6 months. The titration data indicated a rather rapid increase in dosage of the drug, from the initial 10 IU/day to 25 IU/day in 25 days. Then, it was 30 IU/day in 60 days when the mean FBG level in the patients was 100 mg/dL. Finally, it maintained a plateau level of about 35 IU/day in the remaining days of the follow-up. The mean number of titrations, which was 12 during the first 90 days of the follow-up period, decreased to 6 during the second period.

As the data demonstrated, insulin glargine was well-tolerated by the study population. Cases of serious hypoglycaemia reported during the first and the second 3-month periods were 11.2% and 13.3%, respectively. Although the mean waist circumference showed slight decrease throughout the follow-up period, these changes did not reach a statistically significant level (p=0.760). On the other hand, with a statistically significant increase, the mean body weight in the population increased 1.5 kg and reached to 82.9 kg at the end of the observation period (p<0.001). Similarly, the mean BMI in the population increased 1 kg/m^2 at day-180 when compared to baseline (p<0.001). Besides, none of the 17

Table 5. DTSQ scores of the study population at baseline and change in scores on Day-180. The data are given as mean (±SD)			
Item	Baseline	Change on Day-180	p*
Total Score	20.3 (±7.7)	13.2 (±5.1)	<0.001
Items			
Satisfaction with current treatment	3.4 (±1.7)	2.4 (±0.9)	<0.001
Convenience of present treatment	3.6 (±1.6)	2.2 (±1.2)	<0.001
Flexibility of present treatment	3.2 (±1.4)	1.8 (±1.4)	<0.001
Satisfaction with own understanding of their diabetes	3.3 (±1.8)	2.0 (±1.4)	<0.001
How likely to recommend present treatment	3.6 (±1.8)	2.5 (±0.9)	<0.001
How satisfied to continue with their present treatment	3.5 (±1.8)	2.3 (±1.1)	<0.001
Perceived frequency of hyperglycemia	4.2 (±1.4)	-0.9 (±2.1)	<0.001
Perceived frequency of hypoglycemia	1.6 (±1.6)	-0.3 (±1.9)	0.028
*by Wilcoxon test. DTSQ: Diabetes Treatment Satisfaction Questionnaire			

Table 6. DTSQ scores in patients who did/did not achieve targeted HbA1c levels (HbA1c< 7%). The data are given as mean (±SD)			
Items	Target HbA1c (+)	Target HbA1c (-)	p*
Satisfaction with current treatment	2.5 (±0.8)	2.4 (±0.9)	0.454
Convenience of present treatment	2.4 (±0.9)	2.1 (±1.3)	0.070
Flexibility of present treatment	2.1 (±1.2)	1.6 (±1.5)	0.019
Satisfaction with own understanding of their diabetes	2.2 (±1.2)	1.9 (±1.5)	0.109
How likely to recommend present treatment	2.5 (±0.9)	2.5 (±0.9)	0.817
How satisfied to continue with their present treatment	2.3 (±1.2)	2.3 (±1.0)	0.849
Perceived frequency of hyperglycemia	-1.0 (±2.1)	-0.8 (±2.1)	0.566
Perceived frequency of hypoglycemia	-0.5 (±2.0)	-0.1 (±1.8)	0.074
Total Score	14.0 (4.8)	12.9 (5.0)	0.104
*by Mann-Whitney U test. DTSQ: Diabetes Treatment Satisfaction Questionnaire			

cases of serious adverse events reported in 14 patients were related to insulin glargine.

Evaluation of DTSQ scores in our study provided valuable data on the level of treatment satisfaction in the study population. The questionnaire which patients were asked to complete at pre-treatment (baseline) showed that patients were not actually satisfied with their current anti-diabetic treatment. On the other hand, DTSQ score change data on day-180 demonstrated higher rates of patient satisfaction with insulin glargine, in accordance with the previous observations. When DTSQ scores for each item on day-180 were re-evaluated in patients who did and did not achieve the treatment goal for HbA1c separately, it was observed that the scores for all items were similar in the two groups of patients except for the "treatment flexibility" item score which was significantly higher in those who reached target HbA1c level. The two groups did not differ also in terms of their scores for "perceived frequency of hyperglycemia" and "perceived frequency of hypoglycemia" as both were very low in two groups.

The limitation of this study was lying in its single arm design. However, as this study intended to evaluate the efficacy and safety of intensive insulinization with a strict follow-up, a comparative approach was not selected for not complicating the outcomes of intensification of treatment.

In conclusion, the findings of the present study demonstrated that the use of insulin glargine in type 2 diabetic patients is effective and safe and that intensive dose titration is an important means to increase the efficacy of treatment, thus, achieving good glycemic control.

Ethics Committee Approval: Approved by the Uludağ University Medical School Ethics Committee, **Informed Consent:** Written informed consent was obtained from each subject following a detailed explanation of the objectives and protocol of the study, which was conducted in accordance with the ethical principles stated in the Declaration of Helsinki, **Concept:** Ercan Tuncel, **Design:** Ercan Tuncel, Mustafa Kanat, Ekrem Algun, Rıfat Emral, **Data Collection or Processing:** Mustafa Kanat, Ekrem Algun, Özen Öz Gül, Rıfat Emral, **Analysis or Interpretation:** Ercan Tuncel, Özen Öz Gül, **Literature Search:** Ercan Tuncel, Özen Öz Gül, **Writing:** Ercan Tuncel **Peer-review:** Externally peer-reviewed, **Conflict of Interest:** No conflict of interest was declared by the authors,

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