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Comparison of Thrice-daily Novomix Insulin Versus Insulin Glargine Once-Daily Combined with Thrice-Daily Insulin Aspart on Glycemic Control in Patients with Type 2 Diabetes Mellitus: A Cross-Sectional Study

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Abstract

Objective: The objective of the present analysis was to compare the effect of these two treatment regimens (Novomix insulin twice or thrice-daily versus once-daily insulin glargine plus twice or thrice-daily insulin aspart) on glycemic control in Iranian patients with T2DM.

Materials and Methods: This cross-sectional study was conducted for one year on people with type 2 diabetes referred to Yazd Medical Research Center. Glycemic control (HbA1C, FBG, and 2hPP) from baseline (week 0) to 24 -48 weeks were recorded in the electronic file of patients receiving Novomix insulin twice or thrice daily. These profiles were compared to those of patients receiving once-daily insulin glargine plus twice or thrice-daily insulin aspart (according to each meal). $P< 0.05$ was considered as a significant level.

Results: Based on the finding, both treatment groups demonstrated significant reductions in FBG, 2hPP, and HbA1c from baseline to the study endpoint (weeks 24 and 48) ($P< 0.05$ for all comparisons). However, the changes in HbA1c, FBG, and 2hPP levels compared to the baseline level during the study were not significant between the two groups.

Conclusion: The insulin glargine regime is effective in reducing HbA1C-FBS-2HPP compared to aspart and Novomix, but no significant difference was seen between the two mentioned regimes. It is recommended to observe more effectiveness and achieve more efficient and reliable results of the studies.

Keywords: Insulin aspart, Insulin Glargine, Glycemic control, Diabetes mellitus, type 2.

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Introduction

An overall prevalence rate for diabetes in Iran is estimated between 1.3% and 14.5% (1). Type 2 diabetes mellitus (T2DM) and its complications, as one of the most common chronic conditions and an important public health concern, imposes a significant burden on the health care system throughout the world (2-5).

Management of patients with T2DM is challenging and complicate; At first, by modifying the lifestyle (careful monitoring of diet and exercise), it is possible to partially control the blood glucose level in type 2 diabetes (6); However, These patients will require oral anti hyperglycemic medications and, eventually,exogenous insulin replacement therapy, due to pancreatic β-cell dysfunction and the progressive nature of the disease, in order to better glycemic control and delay the onset of many vascular and neurological diabetes complications (7-10).

Short-acting regimen (aspart, 2-4 hours effect,2-3injections/day), long-acting regimen (glargine, 18-24 hours effect, single dose), and mixed regimen (premix, 8-12 hours effect, 2-3 injection/day) injectable regimens are insulin (11). Nowadays, regarding insulin therapy, due to discomfort and fear of repeated injections, combination of rapid-acting insulin analogues, such as insulin aspart and Novomix and long-acting insulin analogues such as insulin glargine have been included in treatment regimens (12,13); which, due to a pattern similar to endogenous insulin secretion, facilitates the achievement of appropriate levels of glycemic profiles in patients with type 2 diabetes (14). However, the most appropriate insulin algorithms for T2DM patients are not well defined.

Hence, to bridge the gap between treatment guidelines and the clinical evidence based on the difference in clinical performance of Novomix insulin with insulin glargine plus insulin aspart, current study was designed to confirm the hypothesis that these two insulin regimens had comparable efficacy and safety in improving glycemic control in Iranian patients with T2DM. Hence, the objective of the present analysis was to compare the effect of these two treatment regimens (Novomix insulin twice to thrice-daily versus once-daily insulin glargine plus twice to thrice-daily insulin aspart) on glycemic control in Iranian patients with T2DM.

Material and methods

Study design and participants

This cross-sectional study was conducted for one year on people with T2DM referred to Yazd Medical Research Center (Yazd, Iran).

Eligible patients were men and women, aged 30 years or older, with T2DM, who had been diagnosed with diabetes for at least one year. They were taking Novomix insulin two to three times a day, compared to once-daily insulin glargine plus two to three times a day insulin aspart, for at least one year. Patients with a GFR<30 Child=3 were included, as long as they did not change their insulin diet during the treatment period. Additionally, they needed to have at least three tests of HbA1c, fasting blood glucose (FBG), and two-hour blood glucose (2hPP). The key exclusion criteria were gestational diabetes mellitus and severe kidney and liver failure.

Data collection

Information was obtained from the electronic registration system. Glycemic profiles (HbA1c, FBG, and 2hPP) from baseline (week 0) to weeks 24 and 48 were recorded in the electronic file of patients receiving Novomix insulin twice to thrice daily. These profiles were compared to those who received once-daily insulin glargine plus twice to thrice-daily insulin aspart (according to each meal).

Statistical analysis

SPSS 18 software package was used for statistical analysis (IBM SPSS Inc., Chicago, IL). Data were presented as mean ± standard deviation (SD) or number (percentage). Statistical comparisons were performed using T-test and Chi-square tests. *P*< 0.05 was considered as a significant level.

Ethical considerations

This study has been formally approved by Shahid Sadougi University of Medical Sciences ethical committee (IR.SSU. MEDICINE.REC.1399.198). Due to the retrospective nature of the study, the requirement for written informed consent was waived.

Result

A total of 243 patients were assigned to either the glargine+ aspart diet (n= 130) or the Novomix diet (n= 113). Baseline HbA1c, FBS, and 2hPP, as well as demographic data, were similar between treatment groups (Table 1).

As shown in Tables 2 and 3, both treatment groups demonstrated significant reductions in FBG, 2hPP, and HbA1c from baseline to the study endpoint (weeks 24 and 48) (*P*< 0.05 for all comparisons). However, the changes in HbA1c, FBG, and 2hPP levels compared to the baseline level during the study were not significant between two groups.

Discussion

According to the study data, at the beginning of the study in both groups, HbA1c-FBS-2HPP was significantly higher than the normal level, and after the study, a significant

Table 1. Demographics and baseline characteristics of patients

Variables		Insulin glargine + Insulin Aspart (n= 130)	Novomix insulin (n= 113)	*P*-value
Demographic characteristics				
Age (years)		56.96 (± 9.96)	58.81 (± 10.54)	*P*= 0.16
sex	**Men**	65 (48.5)	60 (4906)	*P*= 0.48
	Women	69 (51.5)	61 (50.4)	
Clinical characteristics				
HbA1c		8.81 (± 1.80)	8.69 (± 1.48)	*P*< 0.61
FBG (mmol/L)		164.25 (± 63.19)	161.63 (± 56.91)	*P*< 0.74
2hPP (mmol/L)		237.60 (± 90.96)	242.41 (± 96.53)	*P*= 0.71

Values are reported as n (%) or mean± SD. *P*-value obtained from chi- square or student T-test.
Abbreviations: HbA1c: Hemoglobin A1C; FBG: Fasting blood glucose; 2hPP: 2-Hour Postprandial Blood Glucose.

Table 1. Changes in variables from baseline to week 24

Variables		Baseline	24 weeks	*P*-value	Change	*P*-value
FBG	Insulin glargine + Insulin aspart group	164.25 (± 63.19)	140.67 (± 44.18)	0.001	22.4 (±5.78)	0.081
	Novomix insulin group	161.63 (± 56.91)	144 (± 42.14)	0.0001	17.63 (±4.92)	
2hPP	Insulin glargine + Insulin aspart group	237.60 (± 90.96)	205.72 (± 64.07)	0.002	32.0 (±10.21)	0.063
	Novomix insulin group	242.41 (± 96.53)	216.10 (± 70.57)	0.015	24.53 (±9.83)	
HbA1c (%)	Insulin glargine + Insulin aspart group	8.81 (± 1.80)	8.01 (± 1.29)	0.0001	0.74 (±0.12)	0.698
	Novomix insulin group	8.69 (± 1.48)	7.83 (± 1.12)	0.0001	0.87 (±0.16)	

- Values are reported as mean± SD. P-value obtained from student T-test.
- Abbreviations: HbA1c: Hemoglobin A1c; FBG: Fasting blood glucose; 2hPP: 2-Hour Post Prandial Blood Glucose.

Table 2. Changes in variables from baseline to week 48

Variables		Baseline	48 weeks	*P*-value	Change	*P*-value
FBG	Insulin glargine + Insulin aspart group	164.25 (± 63.19)	129.58 (± 42.66)	0.004	36.08 (±12.06)	0.495
	Novomix insulin group	161.63 (± 56.91)	132.69 (± 52.15)	0.001	37.46 (±10.28)	
2hPP	Insulin glargine + Insulin aspart group	237.60 (± 90.96)	199.07 (± 69.21)	0.018	26.42 (±7.1)	0.685
	Novomix insulin group	242.41 (± 96.53)	190.96 (± 66.35)	0.002	25.28 (±7.2)	
HbA1c (%)	Insulin glargine + Insulin aspart group	8.81 (± 1.80)	7.70 (± 1.06)	0.001	0.77 (±0.16)	0.135
	Novomix insulin group	8.69 (± 1.48)	7.54 (± 1.00)	0.003	0.83 (±0.17)	

- Values are reported as mean± SD. *P*-value obtained from student T-test.
- Abbreviations: HbA1c: Hemoglobin A1C; FBG: Fasting blood glucose; 2hPP: 2-Hour Post Prandial Blood Glucose.

difference was seen in both groups before and after the study, but it should be noted that HbA1c-FBS-2HPP is in the uncontrolled range, although it decreased during the study and was also significant. Comparison of the data between the studied groups showed that the changes were not significant, so we can conclude that the drug regimen used (insulin glargine and aspart - Novomix) can be effective in reducing blood sugar, but it is sufficient to control the patient's blood sugar naturally during 24 and 48 weeks and it is not clinically significant. It is suggested to use other medications at the same time, and another argument is that there was no difference between the two treatment regimens, so we recommend that based on more accessible and achievable regimen, this medicinal regimen can be used.

The results obtained from the present study are consistent with several studies. In line with the research findings of Weiping et al in 2015, comparing insulin glargine and lispro, they concluded that after 12-24 weeks of intervention, no significant difference was observed in the patients' HbA1c levels (2); Also, in their 2014 study by Yixuan et al., there was no significant difference in the amount of FBS, 2HPP before and after 32 weeks of intervention on elderly people with diabetes, although there was a significant decrease in the amount of FBS, 2HPP within the group during the study (3). Also, in other similar studies that have been conducted with other insulins, no significant difference in HbA1c-FBS-2HPP factors was observed between the two groups after control (6,15,16).

The present study has several limitations: First, due to the retrospective nature of the study, it was not possible to fully control confounding factors. Second, the participants' medication adherence was not measured. Third, the therapeutic dose of insulins was not the same, which can affect the results of the study.

Conclusion

In the end, it can be said that insulin glargine drug regime is effective in reducing HbA1c-FBS-2HPP compared to aspart and Novomix, but no significant difference was seen between the two mentioned regimes and it was recommended to observe more effectiveness and achieve more efficient and reliable results of the studies. A prospective clinical trial with a larger sample size should be designed and carried out in a longer period of time.

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Conflict of Interest

None.

Authors' contributions

SH.M, R.R, R.M, N.N, M.M and R.A. equally contributed to the conception and design of the research. SH.M, N.N and R.A. collected and analyzed the data. M.M contributed to the interpretation of the data. R.R, R.M, N.N and R.A. drafted the manuscript. All the authors critically revised the manuscript, agree to be fully accountable for the integrity and accuracy of the study, and read and approved the final manuscript.

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