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Original Article

Efficacy of Glargine Insulin Compared with Neutral Protamine Hagedorn Insulin in Patients with Type 2 Diabetes not Controlled with Oral Hypoglycemics: A Cohort Study

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ABSTRACT

Objective: To compare the efficacy of Glargine Insulin with Neutral Protamine Hagedorn (NPH) Insulin in patients with uncontrolled type 2 diabetes with oral hypoglycemic.

Study Design: Prospective cohort study.

***Place and Duration of the Study*:** Railway Hospital, Rawalpindi Pakistan, from Nov 2020 to Jul 2021.

Methodology: All patients aged 30-70 years of either gender, presented with uncontrolled diabetes mellitus on oral hypoglycemic for ≥1 year were enrolled. Patients were divided into Insulin Glargine and injection NPH subcutaneously by lottery method. In both groups, patients were compared for a reduction in HbA1c level after three months of treatment with Insulin. The efficacy was achieved after three months based on a>1% HbA1c level reduction compared to baseline HbA1c.

Results: The efficacy of Glargine Insulin was found to be significantly higher, 66(66%), as compared to NPH Insulin, 43(43%) (*p*-value = 0.002). After adjusting for all other covariates, the efficacy of Glargine Insulin was 3.81 times higher as compared to NPH Insulin (aOR 3.81, 95% CI 1.93-7052). Furthermore, efficacy was 6.95 times higher in patients with ≤25 kg/m2 BMI (aOR 6.95, 95% CI 3.16-15.30), 2.52 times higher in patients with ≤16 years of type 2 diabetes (aOR 2.52, 95% CI 1.30-4.87), 2.77 times higher in patients living in urban areas (aOR 2.77, 95% CI 1.43-5.36).

Conclusion: The efficacy of Glargine Insulin was found to be considerably higher than NPH Insulin in patients with type 2 diabetes not controlled with oral hypoglycemia.

Keywords: Efficacy, Glargine insulin, NPH insulin, Type 2 diabetes.

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INTRODUCTION

Diabetes mellitus is one of the most significant public health non-communicable diseases in South-East Asia, including Pakistan.[1] The reported burden of type 2 diabetes mellitus (T2DM) ranged from 7.7 to 13.7% in Asia, with mortality reported to be more than 1 million.[2]

The management of diabetes involves several multi-therapeutic approaches, such as an active physical lifestyle, dietary control, stress, and anxiety reduction, along with pharmacological interventions. Despite the availability of several antihyperglycemic drugs, many people with type 2 diabetes require Insulin.[3] It is recommended to use basal Insulin when initiating Insulin in a previously Insulin naïve patient. Basal Insulin, including basal Insulin analogues, should mimic natural basal Insulin secretion to restore glycemic control while avoiding low blood sugar level.[4]

Currently, basal Insulin options include the neutral protamine Hagedorn (NPH), which has an intermediate action, and Insulin Glargine, which has a prolonged action. Unlike endogenous basal Insulin, Insulin Glargine has a smooth 24-hour time-action profile with no pronounced peak.[5] Insulin Glargine had superior or equivalent glucose-lowering efficacy in clinical studies but was associated with fewer daytime or nocturnal hypoglycemic events when compared to NPH.[6,7]

International guidelines recommend initiation of basal Insulin if the glycaemic target cannot be attained on non-Insulin anti-diabetic drugs.[8,9] The rationale of the study was that the burden of T2DM and its related complications is on the rise in Pakistan. There is a dire need for an effective therapeutic approach, particularly among patients with uncontrolled diabetes. This study was planned to assess the efficacy of Glargine Insulin compared with NPH Insulin in patients with type 2 diabetes not controlled with oral hypoglycemia in our population.

METHODOLOGY

The prospective cohort study was conducted at the General Medicine Department, Railway Hospital of Rawalpindi, from November 2020 to July 2021. Ethical approval was obtained from the Institutional Review

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Committee of the Railway Hospital of Rawalpindi, Pakistan (IRB #: Riphah/IRC/20/226).The sample size calculation was done by using the WHO calculator taking Absolute HbA1c reductions of 0.96% and 0.84% with the respective use of Glargine U100 and NPH6.[9]

Inclusion Criteria: All patients aged 30-70 years of either gender having type 2 diabetes mellitus for more than equal to 1 year, HbA1c >9%, and reporting diabetes mellitus not controlled with oral hypoglycemic were included.

Exclusion Criteria: Patients with a history of Insulin and steroid use were excluded.

All patients were enrolled via a non-probability consecutive sampling technique. Type-2 diabetes mellitus was defined as fasting blood sugar of >126mg/dl, random blood sugar of >180mg/dl, and HbA1c of >6.5%.[10] A brief history of demographic variables, place of residence, and disease duration was taken, followed by a clinical examination. Patients were divided into groups of 100 cases each, allocated randomly by lottery method. Group-A patients were given Insulin Glargine U100 daily, while Group-B patients received injection NPH subcutaneously. In both groups, patients were compared for a reduction in HbA1c level after three months of treatment with Insulin. Efficacy of Insulin was assessed after three months with a reduction in HbA1c level of >1% in comparison to the baseline HbA1c level.

Statistical Package for Social Sciences (SPSS) version 24 was used for statistical analysis. Mean and standard deviation was computed for quantitative variables like age, duration of type 2 diabetes and HbA1c level. Frequency and percentages were calculated for quantitative variables like gender, residence, and efficacy. Cross-tabulation was performed to compare efficacy for the Groups and baseline characteristics. Furthermore, binary logistic regression analysis was also applied. All those variables significantly associated with cross-tabulation were used in binary logistic regression.

RESULTS

Of 200 participants, the mean age was 58.86 ±6.95 years. There were 112(56%) males and 88(44%) females. The mean height, weight, and BMI of the patients were 1.71±0.11m, 78.89±9.27kg, and 27.02±3.98 kg/m2, respectively. Urban residence was observed in 116(58%) patients, while rural in 84(42%). The mean duration of type-2 diabetes mellitus was 15.65±4.66 years (Table-I).

Table-I: Baseline characteristics of the patients in both Groups (n=200)

	Group-A	Group-B	*p*-value
Age, years	59.77±4.75	57.95±8.53	0.064
≤60	56(50.5)	55(49.5)	0.887†
>60	44(49.4)	45(50.6)	
Gender			
Male	59(52.7)	53(47.3)	0.393†
Female	41(46.6)	47(53.4)	
Height, m	1.72±0.11	1.71±0.11	0.775
Weight, kg	78.41±9.91	79.38±8.61	0.461
Body Mass Index, kg/m2	26.62±3.15	27.43±4.64	0.150
≤25	32(49.2)	33(50.8)	0.880†
>25	68(50.4)	67(49.6)	
Duration of type Diabetes Mellitus, years	16.27±3.85	15.03±5.29	0.060
≤16	45(47.4)	50(52.6)	0.479†
>16	55(52.4)	50(47.6)	
Residence			
Urban	57(49.1)	59(50.9)	0.774†
Rural	43(51.2)	41(48.8)	

‡Independent t-test applied, †Chi-square test applied

The mean HbA1c level significantly drops at three months compared to the baseline HbA1c level (*p*-value <0.001) (Table-II).

Table-II: Mean difference of HbA1c between the Groups (n=200)

HbA1c	Group-A	Group-B	*p*-value
At Baseline	10.18 ±0.71	10.30 ±0.52	0.203
At 3 months	8.48 ±0.62	8.71 ±0.44	0.005

Independent t-test applied

The efficacy of Glargine Insulin was found to be significantly higher 66 (66%) as compared to NPH Insulin 43 (43%) (*p*-value 0.002) (Table-III).

Table-III: Comparison of Efficacy in the Study Parcticipants (n=200)

	Efficacy		
	Yes	No	*p*-value
Groups			
Group-A	66(66.0)	34(34.0)	0.002
Group-B	43(43.0)	57(57.0)	
Age, (years)			
≤60	63(56.8)	48(43.2)	0.474†
>60	46(51.7)	43(48.3)	
Gender			
Male	60(53.6)	52(46.4)	0.766†
Female	49(55.7)	39(44.3)	
Body Mass Index, kg/m2			
≤25	52(80.0)	13(20.0)	<0.001
>25	57(42.2)	78(57.8)	
Duration of type 2 Diabetes Mellitus, years			
≤16	60(63.2)	35(36.8)	0.019†
>16	49(46.7)	56(53.3)	
Residence			
Urban	73(62.9)	43(37.1)	0.005†
Rural	36(42.9)	48(57.1)	

‡Independent t-test applied, †Chi-square test applied

The findings of the univariate analysis showed that the efficacy of Glargine Insulin was 2.57 times significantly higher as compared to NPH Insulin (OR 2.57, 95% CI 1.45-4.56). Similarly, significantly higher association was observed in the multivariate analysis as well. The findings of the multivariate analysis revealed that after adjusting for all other covariates, the efficacy of Glargine Insulin was 3.81 times significantly higher compared to NPH Insulin (aOR 3.81, 95% CI 1.93-70.52). Furthermore, the efficacy was 6.95 times significantly higher in patients with ≤25 kg/m2 BMI than those with >25kg/m2 BMI (aOR 6.95, 95% CI 3.16-15.30). The efficacy was 2.52 times significantly higher in patients with ≤16 years of type 2 diabetes as compared to the patients with >16 years of type 2 diabetes (aOR 2.52, 95% CI 1.30-4.87). The efficacy was 2.77 times significantly higher in patients living in urban areas compared to those living in rural areas (aOR 2.77, 95% CI 1.43-5.36) (Table-IV).

DISCUSSION

In the current study, the efficacy of Glargine Insulin was almost four times significantly higher than NPH Insulin. In particular, the mean HbA1c level significantly drops at three months compared to the baseline HbA1c level. Regarding group-wise stratification, an insignificant mean HbA1c level difference was observed at baseline between Glargine and NPH Insulin. However, at baseline, the HbA1c level was significantly lower in Glargine Insulin than that of NPH Insulin. Various studies have reported the efficacy of Insulin Glargine in patients with uncontrolled diabetes mellitus.[11,12] Since its introduction on the market in 2000, Insulin Glargine has become a breakthrough in Insulin therapy.[13] The drug Insulin Glargine has become one of the most thoroughly investigated and prescribed diabetes medications worldwide and has been used for decades.[14,15] Another study reported the use of Insulin Glargine in addition to oral antidiabetic therapy in older individuals with uncontrolled diabetes as an effective strategy compared to NPH Insulin.[16]

As per current study findings, the efficacy was almost seven times significantly higher in patients with ≤25 kg/m2 BMI than those with >25kg/m2 BMI. The efficacy was two times significantly higher in patients with ≤16 years of type 2 diabetes than those with >16 years of type 2 diabetes. The efficacy was almost three times significantly higher in patients living in urban areas compared to those living in rural areas. A large number of the population in Pakistan belongs to rural areas and poor socioeconomic status, therefore. Most patients reported very late due to a lack of medical facilities and financial constraints compared to other developed countries.[17,18] Therefore, it is important to investigate the recent status of it in our country so that treatment of patients with not controlled oral hypoglycemics should be anticipated in the appropriate clinical line, which will help prevent complications of type 2 diabetes mellitus.[19]

LIMITATIONS OF STUDY

The findings of this study could be highlighted in the light of certain limitations. Firstly, several important confounding variables were not observed: physical activity, binge eating, stress, socioeconomic status, and employment status. Secondly, the comorbid history of the patients and laboratory characteristics were also not studied. Further large-scale multicenter studies are recommended with the inclusion of essential variables to preclude the findings of this study.

CONCLUSION

The efficacy of Glargine Insulin was found to be considerably higher than NPH Insulin in type 2 patients with diabetes not controlled with oral hypoglycemia. Furthermore, factors such as normal BMI, less duration of type 2 diabetes mellitus, and urban residence were observed as important predictor variables for the use and efficacy of Insulin Glargine.

Conflict of Interest: None.

Authors Contribution

Following authors have made substantial contributions to the manuscript as under:

EB: & SB: Data acquisition, concept, approval of the final version to be published.

MUS: & NS: Data acquisition, data analysis, data interpretation, critical review, approval of the final version to be published.

MF: Critical review, study design, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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