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Original Article

Comparison of Pre-Mixed Human Insulin with Insulin Analog in Diabetic Control at Tertiary Care Hospital

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ABSTRACT

Objective: To compare the effect of pre-mixed human insulin with insulin analogue in diabetic control among type-2 Diabetes mellitus patients at tertiary care hospital.

Study Design: Comparative cross-sectional study.

Place and Duration of Study: Department of Medicine, Pak Emirates Military Hospital, Rawalpindi, Pakistan, from Jun 2021 to Apr 2022.

Methodology: Eleven hundred and fifty-six patients with poorly controlled type-2 diabetes on oral hypoglycemic agents requiring insulin were recruited for the study. Patients were divided into two groups via a lottery method. Group-A received the pre-mixed human insulin, while Group-B received the Insulin analogue advised by the consultant endocrinologist or medical specialist according to the requirements based on recent investigations. Diabetes control was compared in both groups at the end of twelve weeks of treatment.

Results: Out of 1156 patients with type-2 diabetes mellitus included in the study, 810(70.1%) were male, while 346(29.9%) were female. The mean duration of DM in the study participants was 3.42±4.44 years. At the end of three months, 978(84.6%) patients had good glycemic control, while 178(15.4%) patients had poor glycemic control. Statistical analysis revealed that the type of insulin used to manage these patients had no significant relationship with glycemic control in our study participants (*p*-value>0.05).

Conclusion: No statistically significant difference was observed in the number of patients achieving adequate glycemic control between those using pre-mixed human insulin and those using insulin analogue in our study.

Keywords: Blood glucose; Insulin analog; Mixed human insulin, Type-2 DM, Glycemic control, Glycated hemoglobin.

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INTRODUCTION

Type-2 diabetes mellitus is one of the most prevalent metabolic conditions which affect the lives of millions of individuals across the globe.[1] If diabetes remains poorly controlled, it may prone the patients towards several potentially life-threatening complications and end organ damage of various vital organs of the human body.[2] Clinicians and researchers have been working hard to find the best method for managing diabetes mellitus, and oral hypoglycemic agents and insulin are the most commonly used treatment options.[3,4] Insulin has been classified into various types depending upon origin or pharmacokinetic effects. Each type differs in terms of onset and duration of action, and the dose is tailored according to the needs of the patient.[5]

Comparisons have been published recently regarding the impact of various types of insulin on the control of diabetes mellitus.[6-9]

Pakistan bears a huge burden of non-communicable diseases, including diabetes mellitus. A huge number of patients live in rural areas where administration of insulin is a challenge in addition to other challenges like regular follow-up and blood sugar monitoring. These factors play a huge role in increasing the number of patients with complications of this disease. A local study concluded that a switch from biphasic human insulin 30 to Biphasic Insulin Aspart 30 was beneficial for our population's glycemic control.[10] Limited local data has been available regarding the comparison of pre-mixed human insulin and insulin analogue in our part of the world. The rationale of this study was to generate our data in this regard and provide a basis for local guidelines.

METHODOLOGY

The comparative cross-sectional study was conducted at the Department of Medicine, Pak

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Emirates Military Hospital, Rawalpindi Pakistan, from June 2021 and April 2022, after Ethical Approval (A/28/EC/394/2022). The non-probability consecutive sampling technique was used to gather the sample for the study. The sample size was calculated by using the WHO sample size calculator by taking efficacy of insulin analogue in type-2 diabetes patients as 87%.[11]

Inclusion Criteria: Patients with type-2 diabetes mellitus, aged 25-60 of either gender, with HBA1c levels greater than 6.5 were included.

Exclusion Criteria: Patients who had a history of diabetic coma in recent months or those with a clear diagnosis of type-1 diabetes mellitus, those with any neoplastic conditions of the origin or any uncontrolled metabolic, endocrine or autoimmune conditions, end-organ damage, and Type-2 DM, those taking steroids (oral or parenteral) or any other medications interfering with glycemic control were not included. Patients were also excluded based on not giving informed consent for this study or using insulin to manage their diabetes.

Patients meeting the criteria were recruited and divided into two groups. The research team divided patients via the lottery method, which ensured randomisation Figure).

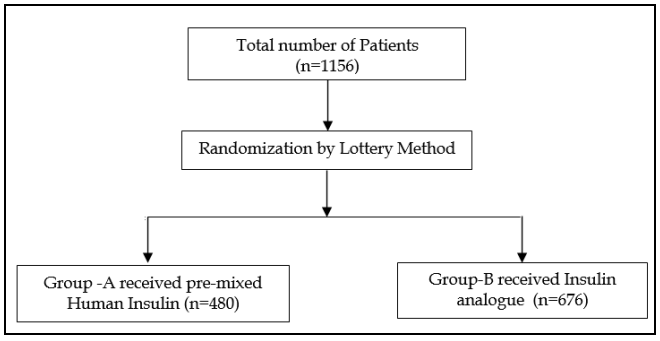

Figure: Patient Flow Diagram (n=1156)

Group-A had the patients who received pre-mixed human insulin, and Group-B had the patients who received insulin analogue. Details of patients and all the readings were recorded in exclusive proforma for each patient.

Glycemic control was checked in all the patients at the end of three months via HBA1c. Training staff performed venipuncture, and the sample was sent to the hospital's laboratory via the set protocol. High-performance liquid chromatography was used to measure the glycosylated haemoglobin levels for all the study participants.[12] Both forms of insulin were given in standard doses set by the treating physician as per requirement based on clinical and laboratory parameters.[13] Body mass index was classed as normal, overweight or obese as per the standard defined by the World Health Organization.[14]

Statistical Package for Social Sciences (SPSS) version 25.0 was used for the data analysis. Quantitative variables were expressed as Mean±SD and qualitative variables were expressed as frequency and percentages. Chi-square test was applied to explore the inferential statistics. The *p*-value of ≤0.05 was set as the cut-off value for significance.

RESULTS

Eleven hundred and fifty-six patients were recruited in the final analysis. Of 1156 patients, 810(70.1%) were male, while 346(29.9%) were female. The mean age of the patients was 44.59±6.175 years. The mean duration of type-2 diabetes mellitus in the study participants was 3.42±4.44 years. Table-I summarises the social and demographic parameters of patients recruited in the analysis. 480(41.5%) patients were managed with pre-mixed human insulin, while 676(58.5%) were managed via insulin analogue. Of the patients, 808(69.8%) had normal body mass index, while 348(30.2%) were overweight or obese. At the end of three months, 978(84.6%) patients had good glycemic control, while 178(15.4%) patients had poor glycemic control. Table-II shows the results of the statistical analysis. The type of insulin used to manage these patients had no significant relationship with glycemic control in our study participants (*p*-value>0.05).

Table-I: Characteristics of study participants (n=1156)

Study parameters	n(%)
Gender	
Male	810(70.1%)
Female	346(29.9%)
Body Mass Index	
Normal	808(69.8%)
Obese and over weight	348(30.2%)
Type of Insulin	
Pre mixed human insulin	480(41.5%)
Insulin analogue	676(58.5%)
Glycemic Control at the end of 6 Months	
Good	978(84.6%)
Poor	178(15.4%)

Table-II: Association of Various Factors Including type of Insulin with Glycemic Control at the end of Three Months (n=1156)

Factors	Good	Poor	*p*-value

	control	control	
Age			
<55 years	719(73.5%)	140(78.6%)	0.143
>55 years	259(26.5%)	38(21.4%)	
Gender			
Male	686(70.1%)	24(69.6%)	0.898
Female	292(29.9%)	54(30.4%)	
Type of Insulin			
Pre mixed human	406(41.5%)	74(41.5%)	0.988
Insulin analogue	572(58.5%)	10(58.5%)	
Body Mass Index			
Normal	672(68.7%)	13(76.4%)	0.036
Overweight orobese	306(31.3%)	42(23.6%)	

DISCUSSION

Diabetes mellitus is known as the mother of many illnesses. If uncontrolled, it may lead to multisystem abnormalities, causing devastating impacts on the overall health of an individual. Recent years have been important regarding various management strategies for this chronic illness. Lifestyle changes, oral medications and insulin types have constantly evolved in the last two decades. Insulin remains the gold standard treatment for these patients. Various types of insulin based on mode or onset of action, route and other parameters have been in clinical practice with distinct merits and demerits. We designed this study to compare the effect of pre-mixed human insulin with insulin analogue in diabetic control at tertiary care hospitals.

Nicolucci *et al*. conducted a meta-analysis regarding the effects of Rapid-Acting Insulin Analogues versus Regular Human Insulin on glycemic control in patients suffering from type-2 Diabetes mellitus.[15] They concluded that rapid-acting insulin analogues were better than regular human insulin in terms of glycemic control and preventing long-term compilations related to diabetes mellitus. Our study was slightly different in methodology and results. We compared pre-mixed human insulin with insulin analogue and found no difference in glycemic control. Melo *et al*. conducted similar systematic review and meta-analysis comparing short-acting insulin analogues versus regular human insulin in patients with Type-1 diabetes mellitus.[16] They concluded that short-acting insulin analogues were superior to regular human insulin in patients managed for Type-1 diabetes mellitus. We made a similar comparison and found no statistically significant difference in many patients achieving adequate glycemic control between those using pre-mixed human insulin and those using insulin analogue.

In 2018, short-acting and regular human insulin analogues were compared for adult, non-pregnant persons with type-2 diabetes mellitus. It was found that both forms of insulin were equally effective in achieving glycemic control in their study participants. The results of our study supported those of Fullerton *et al*.[17] as we also could not establish any difference in the efficacy of the two types used to manage type-2 diabetes mellitus.

A study conducted in Tokyo analysed the change in glycemic control after switching the patients from pre-mixed human insulin to insulin analogue.[18] It concluded that insulin analogue was better for maintaining glycemic control than pre-mixed human insulin. We did not switch the patients from one form to another but made two groups and found no difference in our patients' glycemic control in both groups.

LIMITATION OF STUDY

Glycemic control was observed over a relatively shorter period. Long-term follow-up, with records of adverse effects like hypoglycemic episodes, would have generated a better idea of the effectiveness and safety of both insulin forms compared to our study.

CONCLUSION

Our results showed no statistically significant difference in the number of patients achieving adequate glycemic control between those using pre-mixed human insulin and those using insulin analogue.

Conflict of Interest: None.

Authors' Contribution

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

SFUH & MZH: Data acquisition, critical review, approval of the final version to be published.

IMJ & HS: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

SJ & MTY: Conception, data acquisition, 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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