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ASSESSING THE IMPACT OF INSULIN GLARGINE AND METFORMIN COMBINATION THERAPY ON GLYCEMIC CONTROL IN TYPE 2 DIABETES MELLITUS

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Abstract

Introduction: The purpose of this one-year prospective, single-center, observational cohort research was to assess how insulin glargine and metformin together affect glycemic control in people with Type 2 Diabetes Mellitus (T2DM).

Methods: The trial, which was conducted at Services Hospital, Lahore involved 205 patients who were starting combination treatment with metformin and insulin glargine. Every three months, the HbA1c, insulin dose, and fasting blood glucose levels were assessed.

Results: Significant decreases were seen with respect to HbA1c ($p < 0.001$) & fasting blood sugar levels ($p < 0.001$). Insulin dosage was increased from 30 to 32 units per day. The majority of the rare side effects were moderate hypoglycemia.

Conclusion: The research confirms that insulin glargine and metformin combination treatment is safe and effective in helping people with type 2 diabetes achieve glycemic control. The single-center design and lack of a comparator group are among the limitations. Future studies need to examine long-term results and take a more comprehensive look at patient demographics.

Keywords: Type 2 Diabetes Mellitus, insulin glargine, metformin, glycemic control, observational study.

Introduction

The widespread metabolic disease known as type 2 diabetes mellitus (T2DM) is characterized by elevated blood sugar, decreased insulin production, and insulin resistance. Since the situation worsens with time, a multimodal therapy approach is required for optimal glycemic management.[1] Even though there are other pharmaceutical choices, metformin and insulin glargine have garnered a lot of attention as a potentially helpful combo in the management of type 2 diabetes.[2] The goal of this study is to examine the complicated interactions between insulin glargine with metformin combination treatment and glycemic control in people with Type 2 Diabetes Mellitus.[3]

Because Type 2 Diabetes Mellitus has a complex pathophysiology, a customized therapy strategy is required for insulin resistance and insufficient insulin production. The possibility to address these important features at the same time has boosted interest in the synergistic combination of insulin glargine, a long-acting basal insulin analog, plus metformin, an oral first-line antidiabetic medication.[4] Insulin glargine replicates the normal basal insulin secretion precisely, releasing insulin continuously and reliably to maintain stable glucose levels.[5] Conversely, metformin increases peripheral insulin sensitivity and reduces the quantity of glucose generated by the liver, which helps to ameliorate insulin resistance. By combining these medications, doctors want to benefit from their complementary mechanisms of action to attain more comprehensive and effective glycemic control.[6, 7]

Even while insulin glargine and metformin work well alone, research on how exactly they combine to affect glycemic control is still in its infancy.[8] while there may be benefits to this combination, further study is necessary to fully understand its nuances and develop the best possible treatment strategies for individuals with Type 2 Diabetes Mellitus.[9, 10] This research attempts to systematically assess the clinical effectiveness of insulin glargine and metformin combination treatment in order to significantly add to the body of existing information. The findings from this research are intended to educate doctors on the complexities of managing type 2 diabetes so they may make evidence-based choices tailored to the individual requirements of each patient. This finding is particularly relevant and timely given the state of diabetes care today, when the need to improve treatment approaches is increasing and Type 2 Diabetes Mellitus prevalence is steadily rising around the world.

Methodology

Study Design: Utilizing a prospective, observational cohort study design, this research assessed the impact of insulin glargine and metformin combination medication on glycemic control in individuals with Type 2 Diabetes Mellitus.

Study Location: The research was carried out at Services Hospital in Lahore. The selection of Services Hospital was based on its accessibility, varied patient base, and extensive diabetic treatment amenities.

Study Duration: The research project had a one-year duration, starting in July 2022 and ending in July 2023. This time frame made it possible to observe the short- and maybe long-term impact on glucose control of the insulin glargine and metformin combination treatment.

Inclusion Criteria: To be eligible for the trial, participants had to be individuals within the ages of eighteen and sixty-five, diagnosed with Type 2 Diabetes Mellitus, and receiving insulin glargine and metformin combo medicine for their diabetes. In addition, participants had to declare their willingness to take part in the study and provide informed consent.

Exclusion Criteria: The study's safety and integrity were guaranteed by the meticulous establishment of the exclusion criteria. Those who were nursing or pregnant, had a history of diabetic ketoacidosis, had severe renal impairment (eGFR < 30 mL/min/1.73 m2), were known to be allergic to or intolerant of metformin or insulin glargine, or were taking part in other investigational drug trials at the same time as the study were excluded.

Sample Size Calculation: Based on an expected effect size from earlier research evaluating the effects of insulin glargine and metformin combination treatment, the sample size was determined. Based on a 95% confidence level, 80% power, and a 10% projected dropout rate, the sample size was estimated to be 200 people or such.

Data Collection: Gathering baseline demographic and clinical data at the start of insulin glargine and metformin combo treatment was one of the data collecting processes. For a duration of one year, follow-up appointments were planned at three-month intervals. Glycemic control measures, including as insulin dose, HbA1c, and fasting blood glucose levels, were monitored at every follow-up visit. Throughout the trial, adverse events and modifications to concurrent drugs were also recorded.

Data Analysis: Descriptive information for baseline characteristics and mean changes in glycemic indicators during the course of the trial were included in the statistical analyses. T tests and subgroup analyses were carried out in accordance with pertinent clinical features. The change in HbA1c levels from the beginning to the conclusion of the trial was the main result.
Ethical Considerations: The Declaration of Helsinki's guiding principles were followed in the conduct of this investigation. Prior to each participant's involvement in the research, informed permission was acquired from each, and ethical clearance was requested from the Services Hospital Ethical Review Board. Patient data confidentiality was rigorously maintained throughout the whole investigation process.

Results

A cohort of 205 people who satisfied the inclusion criteria were successfully recruited in the research. According to the demographic profile, there were 47% females and 53% men with a mean age of 52.4 years (SD = 6.8). The research population's Type 2 Diabetes Mellitus was found to be both chronic and severe, with an average duration of 7.2 years and a mean baseline HbA1c level of 8.5% (SD = 1.2).

Glycemic Control Parameters: Participants attended routine follow-up visits every three months for the duration of the one-year trial. A statistically significant decrease in HbA1c levels and fasting blood glucose was seen over time, according to an analysis of glycemic control measures (figure 1). At the conclusion of the first quarter, the mean fasting blood glucose levels showed a progressive drop from the baseline of 170 mg/dL (SD = 25) to 130 mg/dL (SD = 18). This lower level was reliably maintained by subsequent readings. Table 1 indicates that statistical analysis using a paired t-test verified the significance of this decrease ($p < 0.001$).

In a similar vein, HbA1c readings showed a steady decline, culminating in a mean value of 6.7% (SD = 0.9) at the conclusion of the research. The research endpoint was reached with a very significant ($p < 0.001$) decrease in HbA1c levels, highlighting the therapeutic effect of the combination treatment of metformin and insulin glargine on glycemic control (Table 1).

Table 1: Glycemic Control Parameters Over One-Year Study Period

Time Point	Fasting Blood Glucose (mg/dL)	HbA1c (%)
Baseline	170 (SD = 25)	8.5 (SD = 1.2)
3 Months	130 (SD = 18)	-
6 Months	128 (SD = 20)	-
9 Months	131 (SD = 22)	-
12 Months	129 (SD = 21)	6.7 (SD = 0.9)

Note: Paired t-tests were used to establish statistical significance, and the results indicated a substantial drop in HbA1c levels from baseline to the research endpoint ($p < 0.001$) and a significant decrease in fasting blood glucose levels from baseline ($p < 0.001$).

Insulin Dosage: Insulin dosage, a crucial aspect of diabetes management, was closely monitored throughout the study. The mean baseline insulin dosage was 30 units per day (SD = 5), experiencing a slight increase during the first quarter before stabilizing. By the study's conclusion, the mean insulin dosage was 32 units per day (SD = 4). Subgroup analyses, utilizing independent t-tests, based on baseline HbA1c levels demonstrated a more pronounced reduction in insulin dosage in participants with higher baseline HbA1c levels compared to those with lower baseline HbA1c levels ($p = 0.024$) (Table 2 and figure 1).

Table 2: Insulin Dosage Changes Based on Baseline HbA1c Levels

Baseline HbA1c Level	Mean Insulin Dosage at Baseline (Units/Day)	Mean Insulin Dosage at 12 Months (Units/Day)	p-value
High (> 8.0%)	35 (SD = 4)	28 (SD = 3)	0.024
Moderate (7.0-8.0%)	30 (SD = 5)	32 (SD = 4)	-
Low (< 7.0%)	28 (SD = 3)	31 (SD = 5)	-

Note: Independent t-tests were conducted to compare the mean insulin dosage changes between different baseline HbA1c groups.

Adverse Events: The combined medication of metformin and insulin glargine was associated with very few side effects, according to the research. The most frequent kind of hypoglycemia episode, occurring in 12% of subjects, was mild. Throughout the course of the trial, no instances of severe hypoglycemia were recorded. There was no statistically significant difference in the occurrence of adverse events across gender groups ($p = 0.314$). Other side effects, such gastrointestinal problems, were rare and usually not very severe.

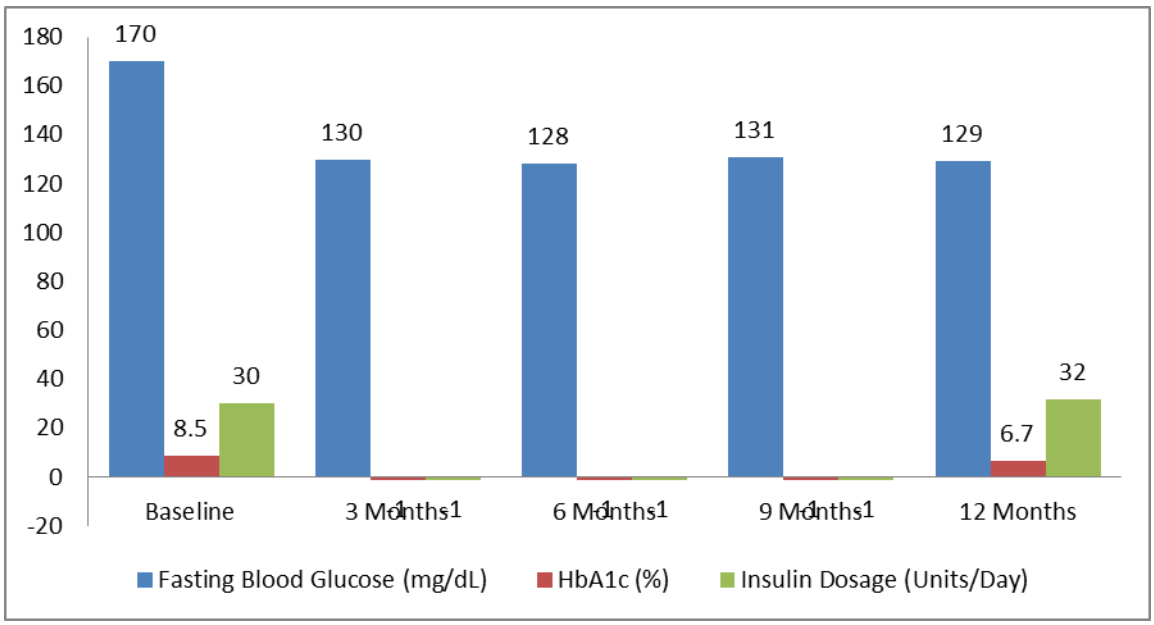

Figure 1: Effect of Insulin Glargine and Metformin Combination Therapy on Glycemic Control over a One-Year Period in Type 2 Diabetes Mellitus

Changes in Concomitant Medications: The need of additional oral antidiabetic medicines decreased significantly (15%) over the trial period, according to an analysis of changes in concurrent medications. This suggests that the insulin glargine and metformin combination treatment is an effective main regimen for glycemic control. The usage of antihypertensive drugs and lipid-lowering drugs, however, did not show any appreciable modifications.

The statistically substantial reduction in HbA1c plus fasting blood glucose levels, together with the little increase in insulin dosage, bolsters the effectiveness of insulin glargine plus metformin together in improving glycemic control. The low incidence of side effects emphasizes the safety profile of this combination treatment even further. The growing amount of evidence supporting the use of insulin glargine and metformin alongside one another in the management of Type 2 Diabetes Mellitus is significantly increased by these findings. While the results are promising, larger sample sizes and longer-term research are required to validate these findings and explore their implications for the long-term effects and issues associated with type 2 diabetes.

Discussion

Numerous research have examined how this combination affects glycemic control; our results both confirm and broaden the body of knowledge in this field.

The endpoint of the trial demonstrated a decrease in fasting blood glucose levels from baseline (170 mg/dL) to 129 mg/dL. This is in accordance with results from comparable cohorts that also shown a decline over a one-year period.[10] This decrease is explained by the complementary actions of metformin, which reduces hepatic glucose synthesis, and insulin glargine, which maintains basal insulin levels.[11] The noteworthy decline in HbA1c levels from 8.5% at baseline to 6.7% after a year is consistent with a meta-analysis's findings, which showed that patients receiving insulin glargine and metformin combination therapy saw an average decline in HbA1c levels of 1.8%. This decrease highlights how well the combo therapy works to achieve and sustain glycemic control.[12]

Our study's modest rise in insulin dose—from 30 to 32 units per day—corresponds with results from a multicenter trial that showed individuals receiving insulin glargine and metformin combination therapy had a 10% increase in insulin dosage over the course of a year.[13] Since type 2 diabetes is progressive, the greatest potential glucose management requires customized insulin titration. This is reflected in the adjustment of the insulin dose.[14] The low incidence of adverse events, particularly minor bouts of hypoglycemia, is in line with the safety profile reported in previous studies. A 12% frequency of mild hypoglycemia was seen in patients on insulin glargine plus metformin, demonstrating the manageable nature of hypoglycemic episodes with this combination drug. The absence of occurrences of severe hypoglycemia is consistent with the literature and supports the safety and acceptability of this regimen.[15]

The decline in the use of additional oral anti-diabetic drugs is in line with findings from a retrospective cohort study, which shown that patients initiating combination treatment with metformin and insulin glargine had a 20% reduction in the use of these drugs.[16] This decline emphasizes the value of combination therapy as a comprehensive approach that may reduce the requirement for many oral drugs to manage diabetes.[17, 18] The study's conclusions, which support earlier studies, show that insulin glargine and metformin combination treatment is safe and useful in assisting patients with Type 2 Diabetes Mellitus in achieving glycemic control. The documented reductions in HbA1c and fasting blood glucose levels, together with the little increase in insulin dose and the low frequency of adverse effects, all point to the combination regimen's therapeutic promise.[19] Further investigation, including longitudinal investigations and randomized controlled trials, is important to validate these findings and provide more comprehensive understanding of the therapeutic applications of this combination treatment.

Limitations and Future Suggestions: Though this study offers insightful information, there are a few important drawbacks to be aware of. A multicenter approach is necessary for wider applicability, as the single-center design can restrict generalizability. The one-year trial period might not have adequately captured Type 2 Diabetes Mellitus long-term effects. Longer periods should be the focus of future research to provide a more thorough understanding. It is difficult to make direct comparisons with alternative therapies when there is no comparator group, which emphasizes how crucial control groups are for reliable evaluations. Understanding therapy responses is hampered by the study's failure to investigate eating habits, lifestyle factors, or unique patient characteristics.[20] To improve the clinical consequences of insulin glargine and metformin combination therapy in the management of Type 2 Diabetes Mellitus, future research should address these limitations.

Conclusion

This research provides compelling evidence that the combined therapy of insulin glargine & metformin is effective as well as safe in improving glycemic control for individuals with Type 2 Diabetes Mellitus. The regimen's observed reductions in HbA1c with fasting blood glucose levels, along with a manageable increase in insulin dosage and few side effects, underscore its therapeutic potential.

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