REDVET - Revista electrónica de Veterinaria - ISSN 1695-7504
Vol 25, No. 1 (2024)
http://www.veterinaria.org
Article Received: 21/02/2024 Revised: 04/03/2024 Accepted: 15/03/2024

Comparative Study Of Insulin Regimens In Hospitalized Patients

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ABSTRACT
Introduction: Diabetes mellitus is a complicated, long-term illness that is impacted by a number of environmental and genetic variables. Type 2 diabetes is associated with insulin resistance that eventually leads to gradual increase in the requirement of insulin either endogenous or exogenous. Diminished β-cell function is an important part of the disease progression in Type 2 diabetes. In the past few years, new research has provided fresh insights into the pathogenesis of this disease, the importance of Glucagon has gained new perspective in type 2 Diabetes.
The hormone insulin, which is produced by the Beta cells of pancreas, is essential for regulating blood sugar levels. Different insulin doses for basal and meals are used in basal-bolus, providing flexibility. Fixed-ratio insulin for meals and basal needs are combined in premix. Basal + OAD combines oral medicine with basal insulin. The efficiency and safety of several insulin regimens for the management of type 2 diabetes are examined and compared in this study.
Objective: A comparative study of insulin regimens in hospitalized patients
Methodology: This study was carefully structured as a prospective and longitudinal investigation, entailing the enrolment of 168 subjects chosen based on specific inclusion and exclusion criteria from the admitted in Sagar Hospitals. The assessment and evaluation of the study were carried out employing suitable statistical methods to ensure robust and accurate analyses.
Results: Out of three regimens included, the study confirms that basal + bolus regimen has better safety and effectiveness. From this study it suggests that basal + bolus regimen is more efficient and safer treatment option, followed by a basal + OAD regimen, based on the study's findings.
Conclusion: Examining insulin therapy in hospitalized type 2 diabetes patients highlights its proper use. The basal-bolus regimen demonstrates superior safety and efficacy compared to other approaches, notably reducing hypoglycemic events. These results underscore its importance as a preferred treatment, enhancing insulin protocols and promoting better patient outcomes.

Keywords: Diabetes, FBS, GRBS, PPBS, Insulin

INTRODUCTION

Insulin, an important anabolic hormone which is used for storing dietary carbon sources, undergoes careful regulation. It is synthesized in pancreatic β-cells, followed by partial liver clearance. It then acts on the vascular endothelium and critical sites like the brain, muscles, and adipocytes, ensuring accurate control over its production, quality, and delivery.

Insulin is transported from pancreatic β-cells to the liver through the portal circulation. There, more than half is removed, then the remaining reaches the systemic circulation through the hepatic vein. After that, it dilates blood vessels and affects liver metabolism in preparation for a second elimination. It enters the muscle and fat cells through smaller capillaries, facilitating the intake of glucose. At last the kidney breaks down the remaining insulin.

Insulin synthesis, processing, and packaging in pancreatic β-cells are directed by genetic instructions. Humans possess a single insulin gene, **INS**, located on chromosome 11, while rodents have two, **ins1** and **ins2**. The human **INS** gene is regulated by upstream enhancer elements that bind key transcription factors like IDX1 (PDX1), MafA, and NeuroD1, alongside various coregulators. These factors are crucial for insulin gene expression, responding to glucose levels and autocrine insulin signaling. Additionally, they influence β-cell components, such as glucose transporter 2 (GLUT2) and insulin-processing enzyme PC1/3, thereby preserving β-cell identity and supporting their secretory function.

The important role of the insulin is to maintain the glucose metabolism, mainly in muscle and adipose tissues. Its main function in these tissues is to increase the uptake of carbohydrates in form of glucose and store them for the energy of the tissue. As the entry of glucose into these cells is a limitation for its storage as glycogen in muscles and triglycerides in fat cells, it is expected that insulin plays a role in controlling this process. This regulation includes different series of signals

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that work together to bring glucose transporters, particularly the GLUT4 isoform, to the cell surface. This process, known as GLUT4 translocation, has been completely studied for three decades, disclosing complicate regulation at various stages within the cell. The movement of GLUT4 transporters to the cell surface in response to insulin binding occurs within a minutes in muscle and fat cells. Mainly, this process happens without the internalization of the hormone.[3]

For the past 15 years, treating hyperglycemia in hospitals has been mainly depend on insulin therapy. In cases of hyperglycemic condition and serious condition, the most recommended treatment is continuous insulin infusion. For the non-critical patients, insulin is the most preferred treatment for the patients experiencing severe hyperglycemia, those who requires high doses of insulin at home, patients with type 1 diabetes, or those with hyperglycemia increased by steroids.[4] Managing blood sugar levels during hospitalization is a main part of patient care. Current guidelines suggests that insulin therapy need to be started when hyperglycemia continues or it exceeds a range of 180 mg/dl. Soon after a patient is admitted to the hospital, blood glucose levels is not controlled due to factors such as acute illness, irregular nutrition intake, and medical interventions like the administration of glucocorticoids. The guidelines published by the Endocrine Society suggest that insulin therapy should be started within a range of 0.2 to 0.5 units per kilogram of body weight as the total daily dose. But in practice this weight-based insulin dosing approach is not followed. This is mainly because of the availability of wide range of insulin doses and the considerable blood glucose level fluctuations immediately after hospital admission. In addition there is a risk of hypoglycemia that may increase when using a regimen that involves basal, nutritional, and correction insulin, as compared to correction insulin alone. As a result, by the prediction of hypoglycemia, many physicians make a choice to use sliding scale correction insulin as the main treatment strategy for hospitalized patients diagnosed with Type 2 diabetes mellitus.[5] However the sliding scale regimen has maximum fallacies.
Three types of insulins have been included in our study, they are BASAL + BOLUS, PREMIX and BASAL + OAD.

Basal + Bolus Insulin:
The basal-bolus insulin regimen works on the principle of precision and adaptation. It has two different types of insulin, each with its unique mechanisms and uses. The basal insulin, is a long-acting or intermediate-acting insulin, it provides a continuous supply of insulin throughout the day. This basal insulin maintains the blood glucose levels which is effective at both fasting and between meals. On the other hand, the bolus insulin, is a fast-acting insulin.it act as a dynamic responder. It is administered before the meals, that increases the insulin secretion that naturally occurs after consumption of food. By administering bolus insulin before a meal, the patients with diabetes can control the blood glucose levels, and can prevent hyperglycemia. The basal insulin steadily controls the glucose level, whereas bolus insulin takes the lead.[6]

Premix insulin:
The biphasic insulin regimen, also known as premix insulin, contains two different insulin analogs in a single formulation. This combination has a fast-acting or short-acting insulin along with an intermediate-acting insulin analog. The main reason of this combination is to imitate the natural pattern of insulin secretion, which gives both mealtime and basal insulin coverage with just one injection. Premix insulins contains different ratios of short-acting to intermediate-acting insulin. The short-acting works by controlling the post-meal glucose level, which reduces blood sugar levels after the consumption of food. The intermediate-acting insulin provides a prolonged insulin action throughout the day, thereby imitating increased insulin production in the human body. The double-action mechanism of premix insulin works by maintaining blood glucose levels in a stable state, preventing both hyperglycemic and hypoglycemic incidents. This mechanism of action reflects the natural pattern of insulin secretion, making premix insulin better for diabetes management.

BASAL INSULIN WITH OAD:
The combination of basal insulin and Oral Antidiabetic Drugs (OAD) is a carefully designed regimen that focus in improving glycemic control for patients with diabetes. The basal insulin acts consistently and OADs are administered to improve the overall efficacy of the treatment. The combination in this regimen is particularly more helpful for the patients with type 2 diabetes. The basal insulin, is a long-acting insulin, which provides a constant level of insulin throughout the day. This insulin reflects the natural secretion of insulin by a healthy pancreas, by always maintaining a minimum level of insulin to satisfy the basic metabolic needs. This Basal insulin also prevents hyperglycemia during both fasting and in between meals. In addition to basal insulin, OADs are also administered to prevent the variations in blood glucose levels. These OADs will differ widely with their mechanisms of action. Some OADs works by reducing insulin resistance, while the others increase insulin secretion, and some will have effect on carbohydrate absorption and an another will push out extra glucose from the kidneys. The selection of appropriate OADs is based on the specific needs and characteristics of the patient.

RESULTS:
TABLE NO.1 COMPARISON OF INSULIN REGIMENS FOR FBS USING STUDENT t TEST

POST-Hoc test for FBS		
GROUPS	T TEST	SIGNIFICANT?

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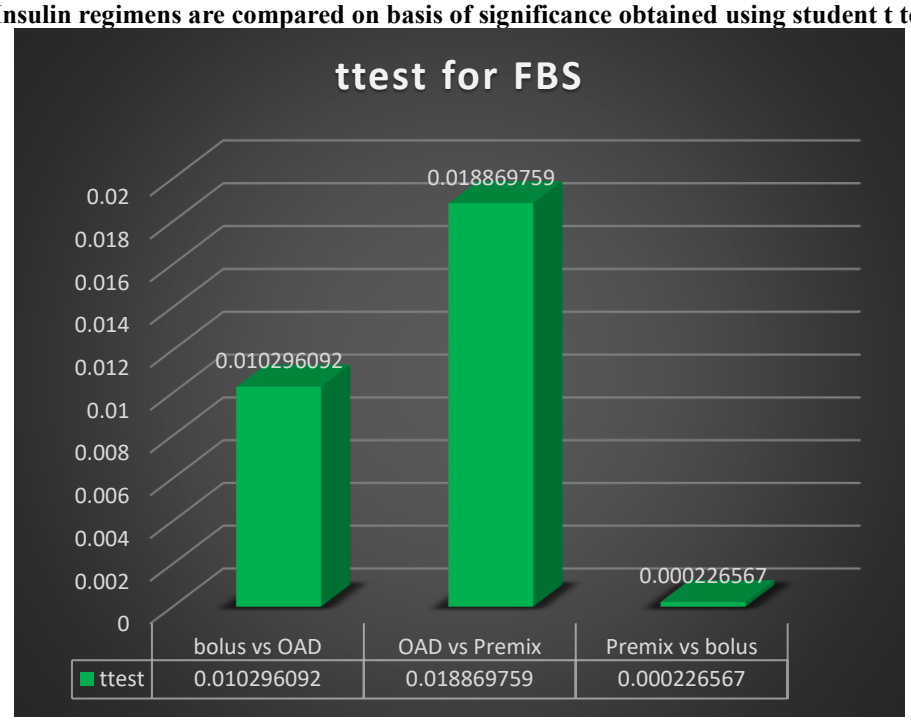
Basal+ bolus vs Basal +OAD	0.010296092	Yes
Basal +OAD vs Premix	0.018869759	No
Premix vs Basal+ bolus	0.000226567	Yes

Figure 1. Insulin regimens are compared on basis of significance obtained using student t test for FBS



From the significance comparison table using t test for the FBS values, premix vs basal+ bolus comparison group showed a greater significance of 0.000226567, significance seen in basal + bolus vs basal + OAD group was 0.010296092 and least significant group was basal+ OAD vs premix of 0.018869759

TABLE NO.2 COMPARISON OF INSULIN REGIMENS FOR GRBS USING STUDENT t TEST

Post -hoc test for GRBS		
GROUPS	T TEST	SIGNIFICANT?
bolus vs OAD	0.002847326	Yes
OAD vs Premix	0.505016588	No
Premix vs bolus	0.007785724	Yes

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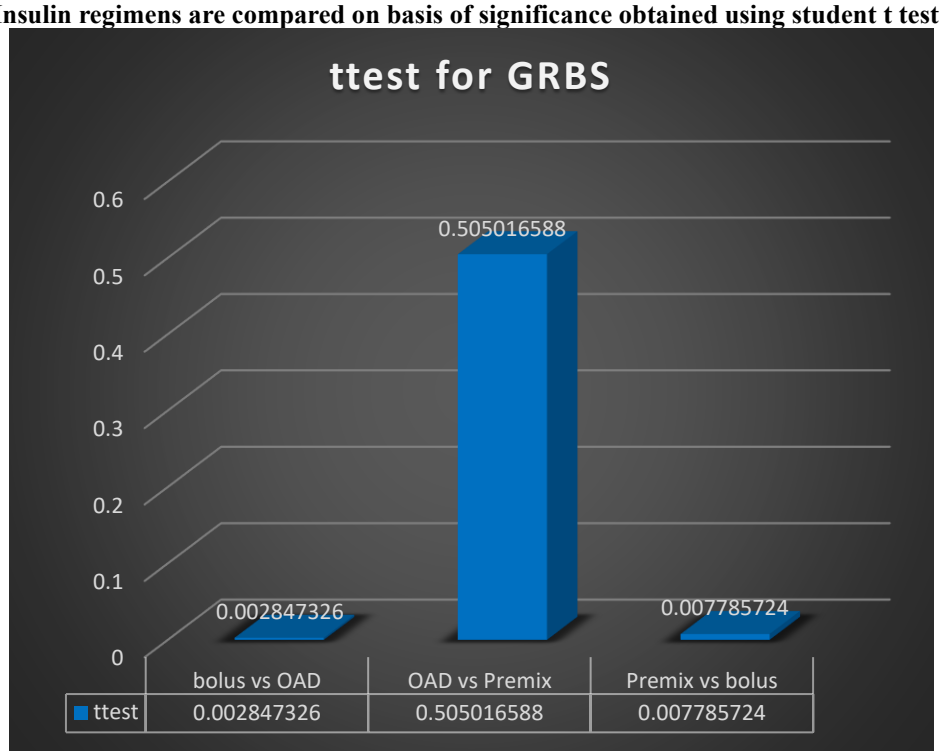
Figure 2. Insulin regimens are compared on basis of significance obtained using student t test for GRBS

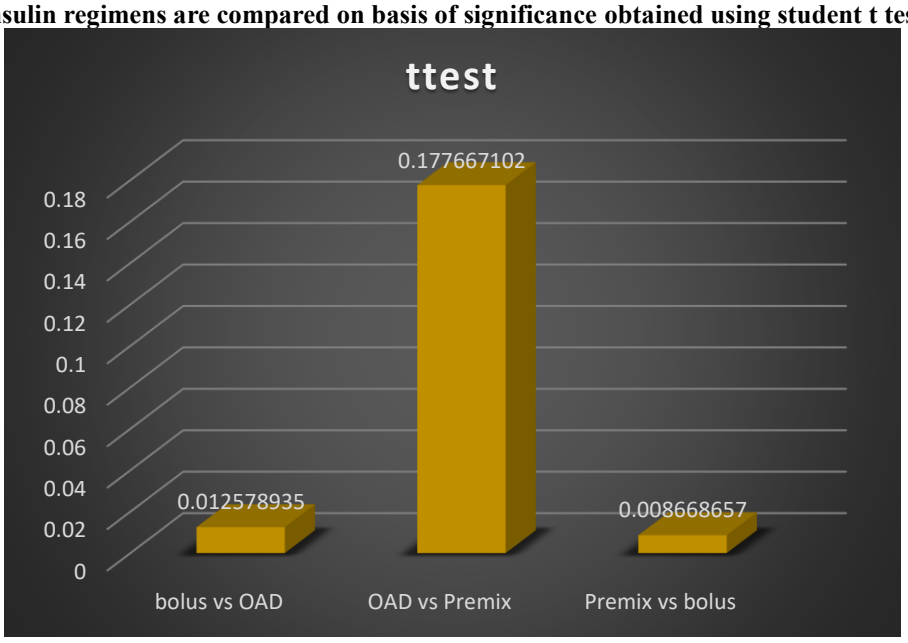


From the significance comparison table using t test for the GRBS values, Basal + bolus vs Basal + OAD comparison group showed a greater significance of 0.0002847326, significance seen in premix vs basal + bolus group was 0.007785724 and least significant group was basal+ OAD vs premix of 0.505016588

TABLE NO.3 COMPARISON OF INSULIN REGIMENS FOR PPBS USING STUDENT t TEST

post -hoc test for PPBS		
GROUPS	T TEST	SIGNIFICANT?
bolus vs OAD	0.012578935	Yes
OAD vs Premix	0.177667102	No
Premix vs bolus	0.008668657	Yes

Figure 3. Insulin regimens are compared on basis of significance obtained using student t test for PPBS



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From the significance comparison table using t test for the PPBS values , premix vs basal+ bolus comparison group showed a greater significance of 0.008668657 , significance seen in basal + bolus vs basal + OAD group was 0.012578935 and least significant group was basal+ OAD vs premix of 0.177667102.

DISCUSSION:
A prospective longitudinal study was conducted on individuals diagnosed with type 2 diabetes mellitus at the diabetes department of Sagar Hospitals in Bengaluru. The study, spanning six months, involved the selection of participants based on defined inclusion and exclusion criteria. Its primary objective was to analyse different insulin regimens, evaluate their effectiveness, and assess their impact on hypoglycemia in patients.

AGE:
In this investigation, participants were grouped into age categories of 30–50, 51–70, 71–90, and 91–110 . The primary findings revealed that individuals aged 51–70 had the highest occurence of type 2 diabetes mellitus, followed by those in the 71–90 ,30–50. The minimum number of cases were seen in the 91–110 age people.

GENDER:
The study incorporated 176 participants, with 98 being males and 78 females. Males constituted 55.68% of the total study population, while females comprised approximately 44.31%. Examination of the study population revealed a higher number of patients having type 2 diabetes mellitus in males as opposed to females. Concluding that the prevalence of type 2 diabetes mellitus was observed to be more prominent among male participants within the examined cohort.

COMORBIDITIES:
Among the study participants, frequently observed comorbidities included hypertension, chronic kidney disease, and cardiovascular disease. Even though several additional comorbid conditions were present, the above mentioned comorbidities were exhibited particularly in higher prevalence rates. The majority of patients experienced the presence of multiple comorbidities simultaneously.

HbA1c:
HbA1c, a vital parameter in diabetes management, which measures the average blood glucose levels over the preceding two to three months. In our investigation, HbA1c levels were classified into four ranges: 6–8, 8.1–10, 10.1–12, and 12.1–14. The majority of patients exhibited HbA1c levels within the 6–8 range indicating a moderate level of glycemic control, followed by 8.1-10 . Conversely, only a limited number of patients demonstrated higher HbA1c levels falling between 10.1 and 14, suggesting a need for closer monitoring and potentially intensified diabetes management strategies.

HYPOGLYCEMIA:
Hypoglycemia is a medical condition marked by an unusually low blood glucose level, commonly linked to diabetes treatment, especially when individuals with diabetes use excessive insulin or other glucose-lowering medications or they miss their diet or vomit after having food. According to ADA hypoglycaemia is considered when the blood glucose reduces below 70 mg/dl. Moderate hypoglycaemia when grbs is less than 60 mg/dl. It serves as a safety parameter and primary objective in our study. The examination of an event of hypoglycemia allows us to identify the safety and efficacy of various insulin regimens in the management of type 2 diabetes mellitus, aiding in the determination of optimal treatment approaches. In our study, we found that the basal + bolus regimen has better safety parameters when compared to other insulin regimens.

EFFECTIVENESS OF INSULIN REGIMENS:
Following a comprehensive statistical analysis of each insulin regimen to gauge effectiveness, the results revealed that although basal and OAD showcased positive safety parameters, their efficacy was relatively inferior to the basal+bolus regimen. Notably, premix insulin exhibited a higher occurrence of hypoglycemia and diminished efficacy, positioning it as the least advantageous among the regimens assessed. The study concludes that the basal+bolus regimen stands out as the most suitable insulin prescription, followed by basal+OAD, while premix insulin ranks as the least favourable option.

ACKNOWLEDGEMENT
We sincerely thank **Dr. Md. Naseeruddin Inamdar, Principal of East West College of Pharmacy**, for his invaluable support and guidance.
Our heartfelt gratitude goes **to Dr. Swathi Ramesh, Pharm.D., Assistant Professor**, for her expert advice and motivation, which were crucial to this dissertation's success.
We also extend our thanks to **Dr. Pratyush Miglani, MBBS, MD, Consultant at Sagar Hospitals, Bengaluru,** for his expertise, time, and guidance in shaping this study's outcomes.

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Conflict of Interest: Each author declares that he or she has no commercial associations that might pose a conflict of interest in connection with the submitted article.

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