Research Article

INTERNATIONAL RESEARCH JOURNAL OF PHARMACY

www.irjponline.com

ISSN 2230-8407 [LINKING]

GLYCEMIC CONTROL IN SUBJECTS WITH TYPE 2 DIABETES MELLITUS ON PREMIXED INSULIN REGIMEN TO BASAL-BOLUS INSULIN

Dr. Subir Kumar Saha,[1] Dr. Priya Yadav[2*]

[1]Associate Professor, Department of General Medicine, Jagannath Gupta Institute of Medical Sciences and Hospital (JIMSH), Kolkata, West Bengal

[2*]MBBS, Resident, Sir Ganga Ram Hospital, Delhi

Corresponding author

dr.y.priya3107@gmail.com

How to cite: Saha SK, Yadav P. Glycemic control in subjects with type 2 diabetes mellitus on premixed insulin regimen to basal-bolus insulin. International Research Journal of Pharmacy, 2022, 13:2:56-60.

DOI:10.7897/2230-8407.1312190

==========

ABSTRACT

Background: Insulin therapy forms the golden management strategy in subjects with diabetes mellitus in most of the subjects with T2D (type 2 diabetes mellitus) owing to it having a progressive and chronic nature.

Aim: In an Indian setting, the current study sought to evaluate the side effects and glycemic control of individuals with type 2 diabetes mellitus on a premixed insulin regimen against basal-bolus insulin.

Methods: 120 participants with Type 2 diabetes mellitus who had had the disease for more than seven years were evaluated for this study. They were split into two groups of 60 at random, with Group I receiving BB management and Group II receiving an OM insulin regimen. At 4 and 12 weeks, changes in glycemic parameters as well as instances of hypoglycemia were evaluated.

Results: FPG (fasting plasma glucose) decreased significantly with PM insulin from baseline at 4 weeks ($p=0.01$), but only at 12 weeks ($p<0.001$) did BB insulin show a meaningful drop. At 4 and 12 weeks, the PM groups showed a greater decrease in FPG than the BB group ($p=0.03$ and 0.02 respectively). There was a substantial decrease in post-prandial plasma glucose from baseline to 4 weeks ($p=0.03$) and at 8 weeks ($p<0.0001$) for both. At 4 weeks, there was no intergroup difference ($p=0.14$). At 12 weeks, nevertheless, it was significant for the PM group ($p=0.008$).

Conclusion, both the BB and PM insulin regimens significantly enhance glycemic control without putting their users at risk for severe hypoglycemia episodes. Therefore, patient-related factors like adherence and eating patterns, as well as insulin-related factors like complexity and posology, should influence the choice of insulin.

Keywords: basal-bolus insulin, Insulin naïve, glycated hemoglobin, hypoglycemia, premixed insulin

INTRODUCTION

The patient's eating habits, insulin therapy compliance, and expected adherence all play a significant role in the insulin selection process for diabetics. Additionally, it is controlled by a number of pre-existing OHAs (oral hypoglycemic agents), medication interactions, and the intricacy of the regimen, all of which have a significant impact on the individuals' adherence to the insulin therapy.[1]

While the Indian National Consensus Group (2013) suggests starting insulin therapy with premix insulin alone, the American Association of Clinical Endocrinologists' 2022 guidelines, the Research Society for the Study of Diabetes in India's 2019 guidelines, and the International Diabetes Federation's 2017 guidelines all recommend starting insulin therapy with either premix insulin or basal insulin.[2]

Based on clinical literature data, Asian individuals with type 2 diabetes mellitus who have a HbA1c (glycated hemoglobin) level greater than 8.5% and for whom basal insulin may not be enough to achieve glycemic control and who are insulin-naïve need aggressive dual pharmacotherapy with prandial and basal insulin to control both post-prandial and fasting glucose levels.[3]

For patients who cannot count carbs or who have consistent eating and lifestyle patterns, premixed insulin treatment, which consists of 70% intermediate-acting and 3% regular insulin, is sufficient. The pancreatic physiological secretion of insulin is replicated by the BB (basal-bolus) regimen. But it requires regular and proactive self-monitoring. Because basal bolus requires more frequent doses than Premix, patient adherence may suffer.[4]

The effectiveness of Pm and BB insulin regimens has been examined in the literature, with mixed findings. While some studies demonstrate that both regimens are equally effective in decreasing HbA1c and controlling blood sugar, others suggest that one of the regimens is more effective. The incidence of hypoglycemia varies between PM and BB regimens, according to literature statistics. However, there is a dearth of information in the literature currently available on the Indian setting.[5]

Therefore, the current study sought to compare the negative effects and glycemic control of premixed insulin regimen to basal-bolus insulin in the Indian context in participants who were insulin-naïve and had type 2 diabetes mellitus.

MATERIALS AND METHODS

Comparative evaluation of the negative effects and glycemic control in individuals with type 2 diabetes mellitus was the goal of the current prospective clinical observational investigation on premixed insulin regimen to basal-bolus insulin in Indian scenario in insulin-naïve subjects. The research participants came from the Institute's Department of Medicine. Prior to their involvement in the study, all individuals gave their written and verbal informed consent.

Participants with type 2 diabetes mellitus who were insulin-naïve and between the ages of 18 and 65 were included in the research. Subjects who were 18 years of age or older, with HbA1c levels greater than 8%, uncontrolled diabetes, uncontrolled lifestyle change, three oral hypoglycemic drugs (by the treating clinician's view), and were willing to participate in the trial were all considered for inclusion. Participants having a history of alcohol misuse, acute sickness, severe concurrent conditions, comorbid chronic kidney or liver disorders, breastfeeding or pregnant women, and those taking beta-blockers or other drugs that interfere with blood sugar levels were excluded from the research, who did not give consent for study participation.

Following the research participants' final inclusion, the following information was collected: age, gender, weight, height, hip circumference, and blood pressure. BMI (body mass index) and the waist-hip ratio were also computed using this. The effectiveness of each regimen was evaluated by measuring changes in HbA1c%, PPG (prandial plasma glucose), and FPG (fasting plasma glucose) at 4 and 12 weeks. The American Diabetes Association and the European Association for the Study of Diabetes categorization systems were used to diagnose hypoglycemia. 6, 7 (ii) Clinically significant hypoglycemia (level 2) <54 mg/dL (3.0 mmol/L), low enough to indicate severe, clinically significant hypoglycemia; (iii) Hypoglycemia alert value (level 1) ≤70 mg/dL (3.9 mmol/L), low enough for fast-acting carbohydrate treatment and dose modification of glucose-lowering therapy; (iii) Severe hypoglycemia (level 3), lack of a defined glucose threshold, hypoglycemia linked to significant cognitive impairment, and the need for outside help to recover.

Both groups received conventional medical attention and care. At the physicians' decision, the majority of participants were on a combination of glimepiride, metformin, and vildagliptin, which was maintained unaltered throughout the research. As directed by the attending doctors, treatment for pre-existing comorbidities, including ischemic heart disease, hypothyroidism, bronchial asthma, chronic obstructive pulmonary disease, dyslipidemia, hypertension, and other conditions, was continued. Two injections of PM insulin were administered daily as part of the PM protocol. The BB regimen includes four daily injections of a single dosage of peakless insulin in addition to three doses of conventional insulin.

The data gathered were statistically analyzed using SPSS (Statistical Package for the Social Sciences) software version 24.0 (IBM Corp., Armonk. NY, USA) for assessment of descriptive measures, one-way ANOVA (analysis of variance), Pearson correlation, Kruskal-Wallis test, and chi-square test. The findings were presented as frequency, percentages, mean, and standard deviation. Statistical significance was defined as a p-value of less than 0.05.

RESULTS

The goal of the current prospective clinical observational study was to compare the negative effects and glycemic control of premixed insulin regimen to basal-bolus insulin in the context of type 2 diabetes mellitus in participants who were insulin-naïve in India. 120 participants with Type 2 diabetes mellitus who had had the disease for more than seven years were evaluated for this study. They were split into two groups of 60 at random, with Group I receiving BB management and Group II receiving an OM insulin regimen. The research participants in the BB and MP groups had mean ages of 54.41±10.13 and 52.41±8.58 years, respectively. This difference was not statistically significant (p=0.43).

There was no statistically significant difference between the two groups in terms of gender, type 2 diabetes mellitus, BMI, weight, dyslipidemia, hypertension, family history, and HbA1c (p=0.32, 0.35, 0.37, 0.25, 0.75, 0.77, 0.97, 0.44, and 0.13, respectively). With a p-value of 0.02, the PM regimen significantly reduced post-prandial glucose more than the BB regimen (Table 1).

In both BB and PM insulin regimens, PPG and FPGs demonstrated a substantial decrease from baseline to 12 weeks. At 4 weeks from baseline, premix insulin levels significantly decreased from 182.04±49.28 to 146.6±30.75 with p=0.01 and from 182.04±49.28 to 131.4±19.39 mg/dl with p<0.0001. FPG decreased from 191.41±44.44 mg/dl at baseline to 141.24±15.15 mg/dl after 12 weeks with a p-value of less than 0.0001 while following the BB regimen.

Moreover, FPG in the PM and BB groups decreased significantly after 4 weeks (146.78±30.75 mg/dl and 167.78±33.12 mg/dl, respectively, with p=0.03) and at 12 weeks (131.58±19.39 mg/dl and 141.28±15.59 mg/dl, respectively, with p=0.02). Between baseline and 4 weeks, PPG significantly decreased in the PM group from 253.44±54.28 mg/dl to 190.1±32.45 mg/dl (p=0.03) and in the BB group from 234.1±66.18 mg/dl to 190.1±22.45 mg/dl (p=0.03). The PM group saw a decline from 253.44±54.28 mg/dl to 171.3±16.60 mg/dl with p<0.0001 after 12 weeks, whereas the BB group experienced a decrease from 234.1±66.18 mg/dl to 158.5±20.19 mg/dl with p<0.0001. At 4 weeks, the PM group had 177.68±24.22 mg/dl compared to 190.28±32.45 mg/dl (p=0.14), and at 12 weeks, they had 158.68±20.19 mg/dl and 171.48±16.60 mg/dl (p=0.08), but there was no intergroup difference.

The percentage change in HbA1c readings was 9.16%, and the drop from 8.36±1.06% at baseline to 7.59±0.59% after 12 weeks was statistically significant (p=0.0002). The mean HbA1c value in patients following the BB regimen changed from 7.88±0.76% to 7.32±0.61% between baseline and 12 weeks (p=0.0007), with a change of 7.06% as a percentage. In comparison to the BB regimen, this demonstrated a superior and larger percentage reduction in HbA1c in the PM group. With p=0.37, the observed intergroup difference was statistically non-significant.

DISCUSSION

120 participants with Type 2 diabetes mellitus who had had the disease for more than seven years were enrolled in the current study. They were split into two groups of 60 at random, with Group I receiving BB management and Group II receiving an OM insulin regimen.

The research participants in the BB and MP groups had mean ages of 54.41±10.13 and 52.41±8.58 years, respectively. This difference was not statistically significant (p=0.43). Type 2 diabetes mellitus, gender, weight, BMI, dyslipidemia, hypertension, family history, and HbA1c were all statistically not significantly different between the two groups (p=0.32, 0.35, 0.37, 0.25, 0.75, 0.77, 0.97, 0.44, and 0.13, respectively). With p=0.02, the PM regimen's reduction in post-prandial glucose was substantially greater than the BB regimen's. These demographics were similar to those of the earlier research conducted by Yavuz DG et al. (2015) and Anyanwagu U et al. (2017), in which the authors evaluated participants with diabetes mellitus and similar demographics to the current study.

In both BB and PM insulin regimens, it was seen that both PPG and FPGs significantly decreased from baseline to 12 weeks. At 4 weeks from baseline, however, there was a substantial decrease in premix insulin levels from 182.04±49.28 to 146.6±30.75 with p=0.01 and from 182.04±49.28 to 131.4±19.39 mg/dl with p<0.0001. FPG decreased from 191.41±44.44 mg/dl at baseline to 141.24±15.15 mg/dl at 12 weeks with a p<0.0001 reduction while following a BB regimen. Moreover, FPG in the PM and BB groups decreased significantly after 4 weeks (146.78±30.75 mg/dl and 167.78±33.12 mg/dl, respectively, with p=0.03) and at 12 weeks (131.58±19.39 mg/dl and 141.28±15.59 mg/dl, respectively, with p=0.02). These findings aligned with those of Bai R et al. (2011) and Testa MA et al. (2010) where Additionally, the authors saw a noteworthy decrease in both BB and PM insulin regimens from baseline to 12 weeks in their individual investigations. From baseline to 4 weeks, PPG (post-prandial glucose) decreased significantly in the PM group from 253.44±54.28 mg/dl to 190.1±32.45 mg/dl with p=0.03, and in the BB group from 234.1±66.18 mg/dl to 190.1±22.45 mg/dl with p=0.03, according

to the study data. By the end of 12 weeks, the PM group had decreased from 253.44±54.28 mg/dl to 171.3±16.60 mg/dl with p<0.0001, while the BB group had decreased from 234.1±66.18 mg/dl to 158.5±20.19 mg/dl with p<0.0001. The PM group, however, did not vary across groups at 4 weeks (177.68±24.22 mg/dl vs. 190.28±32.45 mg/dl, p=0.14) or 12 weeks (158.68±20.19 mg/dl and 171.48±16.60 mg/dl, p=0.08).

These results were consistent with the findings of the current study and the findings of Miser WF et al. (2010) and Miyoshi H et al. (2013), who showed a substantial decrease in PPG with both PM and BB after three months. The HbA1c results showed a statistically significant drop from 8.36±1.06% at baseline to 7.59±0.59% at 12 weeks, with a percentage change of 9.16%. This change was statistically significant with p=0.0002. The mean HbA1c value in patients following the BB regimen changed from 7.88±0.76% to 7.32±0.61% between baseline and 12 weeks (p=0.0007), with a change of 7.06% as a percentage. In comparison to the BB regimen, this demonstrated a superior and larger percentage reduction in HbA1c in the PM group. With p=0.37, the observed intergroup difference was statistically non-significant.

These results were consistent with those of Bellido V et al. (2014) and Ilag LL et al. (2007), whose authors similarly observed significantly lower HbA1c levels with both BB and PM groups, comparable to the current research.

CONCLUSION,

Notwithstanding its limitations, the current study comes to the conclusion that both BB and PM insulin regimens significantly enhance glycemic control without putting their users at risk for severe hypoglycemia episodes. Therefore, the patient's adherence levels and eating habits, as well as the insulin's complexity and posology, should influence the insulin selection.

REFERENCES

1. World Health Organization fact sheet diabetes. https://www.who.int/news-room/fact-sheets/detail/diabetes
2. Pradeepa R, Mohan V. Epidemiology of Type 2 diabetes in India. *Indian J Ophthalmol*. 2021;69:2932-8.
3. Ali MM, Aung KT, Young M, Eligar VS, Davies JS. Different insulin initiation regimens in patients with Type 2 diabetes-a review article. *Int J Diabetes Clin Res*. 2018;5:83.
4. Stratton IM, Adler AI, Neil HA, Matthews DR, Manley SE, Cull CA, et al. Association of glycemia with macrovascular and microvascular complications of Type 2 diabetes (UKPDS 35): Prospective observational study. *BMJ*. 2000;321:405-12.
5. International Diabetes Federation. 2021. [https://diabetesatlas.org/idfawp/resource-files/2021/11/IDFDA10-global-fact-sheet.pdf]
6. American Diabetes Association. 6. Glycemic targets: Standards of medical care in diabetes-2018. *Diabetes Care*. 2018;41:S55-64.
7. International Hypoglycaemia Study Group. Glucose concentrations of less than 3.0 mmol/l (54 mg/dl) should be reported in clinical trials: A joint position statement of the American Diabetes Association and the European Association for the Study of Diabetes. *Diabetologia*. 2017;60:3-6.
8. Yavuz DG, Ozcan S, Deyneli O. Adherence to insulin treatment in insulin-naïve Type 2 diabetic patients initiated on different insulin regimens. *Patient Prefer Adherence*. 2015;9:1225-31.
9. Anyanwagu U, Mamza J, Gordon J, Donnelly R, Idris I. Premixed vs basal-bolus insulin regimen in Type 2 diabetes: Comparison of clinical outcomes from randomized controlled trials and real-world data. *Diabet Med*. 2017;34:1728-36.
10. Testa MA, Gill J, Su M, Turner RR, Blonde L, Simonson DC. Comparative effectiveness of basal-bolus versus premix analog insulin on glycemic variability and patient-centered outcomes during insulin intensification in Type 1 and Type 2 diabetes: A randomized, controlled, crossover trial. *J Clin Endocrinol Metab*. 2012;97:3504-14.
11. Bai R, Batra K, Yap C, Izuora K. Diabetes-related outcomes with basal-bolus vs. premixed insulin among veterans with Type 2 diabetes: A single institutional retrospective study. *Am J Med Sci*. 2021;366:38-43.
12. Miser WF, Arakaki R, Jiang H, Scism-Bacon J, Anderson PW, Fahrbach JL. Randomized, open-label, parallel-group evaluations of basal-bolus therapy versus insulin lispro premixed therapy in patients with Type 2 diabetes mellitus failing to achieve control with starter insulin treatment and continuing oral antihyperglycemic drugs: A noninferiority intensification substudy of the DURABLE trial. *Clin Ther*. 2010;32:896-908

13. Miyoshi H, Baxter M, Kimura T, Hattori M, Morimoto Y, Marinkovich D, et al. A real-world, observational study of the initiation, use, and effectiveness of basal-bolus or premixed insulin in Japanese people with Type 2 diabetes. *Diabetes Ther*. 2021;12:1341-57.
14. Bellido V, Suarez L, Rodriguez MG, Sanchez C, Dieguez M, Riestra M, et al. Comparison of basal-bolus and premixed insulin regimens in hospitalized patients with Type 2 diabetes. *Diabetes Care*. 2015;38:2211-6.
15. Ilag LL, Kerr L, Malone JK, Tan MH. Prandial premixed insulin analog regimens versus basal insulin analog regimens in the management of Type 2 diabetes: An evidence-based comparison. *Clin Ther*. 2007;29:1254-70.

Parameters	BB insulin (n=60)	PM regimen (n=60)	p-value
Mean age (years)	54.41±10.13	52.41±8.58	0.43
Gender			
Males	36 (60)	26 (43.3)	0.32
Females	24 (40)	34 (56.6)	
Type 2 Diabetes duration	7.44±4.13	7.98±3.04	0.35
BMI (kg/m2)	24.61±4.46	25.60±4.42	0.37
Weight (kg)	67.65±9.08	64.45±12.96	0.25
Dyslipidemia	20 (33.3)	16 (26.6)	0.75
Hypertension	30 (50)	26 (43.3)	0.77
Family history	48 (80)	44 (73)	0.97
FPG (mg/dl)	191.38±44.38	182.04±49.28	0.44
Post-prandial glucose (mg/dl)	253.44±54.28	234.08±66.18	0.02
HbA1c%	7.88±0.76	8.36±1.03	0.13

Table 1: Biochemical, clinical, and demographic data in study subjects