ORIGINAL ARTICLE

THE EFFECTIVENESS OF DIFFERENT INSULIN REGIMENS IN DIABETIC PREGNANT PATIENTS- A RANDOMIZED CONTROLLED TRIAL

Samina Aliya Sabir[1], Qudsia Qazi[1], Ghulam Abbas[2], Laila Zeb[3], Sumaira Yasmin[1]

[1]Department of Obstetrics & Gynaecology, MTI, Lady Reading Hospital Peshawar - Pakistan

[2]Department of Medicine, MTI, Khyber Teaching Hospital Peshawar - Pakistan

[3]Department of Medicine, MTI, Lady Reading Hospital Peshawar - Pakistan

ABSTRACT

Objective: To compare the effectiveness of Basal bolus and Premixed Insulin regimen in gestational and type 2 diabetic pregnant patients.

Material and methods: This randomized controlled trial was conducted in Obstetrics and Gynecology department, Lady Reading Hospital (LRH) Peshawar over a period of one year from January to December 2020. A total of 100 patients with Type 2 Diabetes and Gestational Diabetes were included in the study. These 100 patients were divided into two groups. Group 1 was allocated to patients given Basal Bolus Regimen and Group 2 was allocated to patients given Pre-mixed twice daily Insulin. Patients were allocated to each group randomly by lottery method. The patients were put on insulin according to body weight after the first 24-hour blood sugar profile.

Results: The two groups were comparable for maternal age (34.6±4.68, 34.6±5.11, p-value = 0 .775), gestational age (34.2±1.65, 34.0±1.34, and p value = .552), gravidity (7.08±1.65, 6.68±1.5, p-value of 0.434). HBA1C in the two groups were similar (7.40±.742 and 7.39±.751 with a p-value of 0.947), with mean blood glucose (calculated by average of 2 readings of postprandial levels) in the two groups in first 24 hours were comparable (MBG 24Hrs Group 1= 341.54±46, Group 2 =344.08±47 p-value = 0.784). There was a rapid control of blood sugar, on day 7 with Basal Bolus regimen with Mean Blood Glucose (MBG) 152±9.798mg/dL as compared to Premixed split regimen which was 192.4±14.99 mg/dL

Conclusion: The Basal bolus regimen is more effective than the premixed insulin regimen in controlling blood sugar in pregnant patients with diabetes.

Key words: Multiple dose Insulin (MDI), Mean blood glucose (MBG), Gestational Diabetes Mellitus (GDM)

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INTRODUCTION

Diabetes is the most common disorder affecting about 7% of pregnancies where 87.5% of these females have gestational diabetes, 7.5% have type 1 diabetes while 5% have type 2 diabetes.[1,2] Gestational diabetes mellitus is defined as a fasting blood sugar(FBS) of 100 mg/dl or more and 2 hours' random blood sugar (RBS), postprandial of 140 or more on 75 gm OGTT after 24 weeks of gestation. Type II Diabetes is characterized by FBS more than 126mg/dl before 24 weeks of gestation of pregnancy[2].

Correspondence
Dr Sumaira Yasmin
Assistant Professor
Department of Gynae C Lady reading Hospital Peshawar - Pakistan
Email drsumairayasmeen@gmail.com
Cell: +92-345-9136989
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The poor metabolic control in diabetic patients leads to unfavorable fetal outcome. The choice of treatment in pregnancy is insulin. Two types of conventional insulin regimens i.e. the Premixed regimen and the basal bolus regimen are used which mimic endogenous insulin response. Premixed or split regimen is defined as premixed 70/30 formulation having 30% Regular insulin and 70% NPH given BD before meals with 2/3rd of total calculated dose given in the morning and 1/3rd of the dose given in evening. The advent of Insulin analogues with improved pharmacokinetics has resulted in pregnancies with good maternal and fetal outcomes[2,3]. Trials have also shown safety of oral hypoglycemic especially metformin and glyburide to warrant use in pregnancy[4]. Whatsoever be the type or regimen of insulin used the main aim is to achieve a good glycemic control so as to reduce maternal and fetal complications. The best insulin regimen would be the one which controls the mean blood glucose (MBG).

The aim of our study was to compare the conventional regimens so as to device a protocol of which one

is better in pregnancy for use in our patient as both the regimens are in affordable ranges as compared to Insulin analogues.

MATERIAL AND METHODS

This study was done in Obstetrics and Gynecology department of Lady Reading Hospital from January 2020 to December 2020. It was a Randomized controlled open labeled study. The sample size was 100 calculated with WHO formula taking the prevalence of diabetes in pregnancy as 7%, confidence interval 95% and margin of error 5%. The patients were distributed in the two groups randomly by lottery methods. The inclusion criteria were pregnant patients with GDM and type II diabetes, booked in first, second and third trimester before 32 weeks of gestation. The exclusion criteria were patients booked in late 3rd trimester after 32 weeks, Type 1 diabetics, patients already controlled on oral hypoglycemic agents. Data was entered to SPSS 24, mean ±SD was calculated for continuous variable like age, period of gestation, parity and mean blood glucose. Post stratification analysis was done using independent "t" test to calculate p value ≤ 0.05. In this study 50 patients were put on basal bolus regimen in Group 1 and another fifty patients were given premixed regimen in Group 2, after consent from each patient. Patients were booked through antenatal clinic, admitted for work up which included 6 points blood sugar profile and HBA1C. After 24 hours' blood sugar levels patients were put on one of the regimens according to body weight in kilograms with this formula.

Body weight in Kg x 0.6 in first trimester = Total units of insulin to be started for the patient. Body weight in Kg x 0.7 in second trimester = Total units of insulin to be started for the patient.

Body weight in Kg x 0.8 in second trimester = Total units of insulin to be started for the patient. Total units of insulin in premixed regimen were given twice a day in the formulation of 70/30 (two third of NPH in this formulation and with one third of Regular insulin).

Total units of insulin in Basal Bolus Regimen were given according to the following formula with one fourth of NPH given at night at 10 pm and rest of Insulin was given as Regular Insulin and this Regular Insulin was divided into equal dosages as thrice a day (6 hours' interval) and half an hour before meals.

The efficacy parameters were time and doses needed to control the blood sugar. Patients were given dietary counseling sessions with easy pictorial diet charts and were advised to walk for 30 minutes every day. All this information was filled on a proforma, the patients were followed up in the OPD after every 2 weeks with their blood sugar records and fetal surveillance. If the blood sugars were abnormal then the patients were readmitted.

RESULTS

The two groups were similar for maternal age, gestational age, gravidity, mean blood glucose in first 24 hours as shown in Table 1.The first 24 hour MBG was 341.54±46mg/dL and 344.08±47 mg/dL in basal bolus and premixed regimen group respectively with a p-value of 0.784 as given in Table 1. MBG was calculated by average of 2 readings of postprandial levels. The MBG on day 3 being 160.20±8.569 mg/dL in basal bolus group and 222.22±17.57 mg/dL in premixed insulin. There was a rapid control of blood sugar, on day 7 in basal bolus group with 152±9.897 mg/ml as compared to premixed regimen which was 192.42±14.99 mg/dL with a p-value of 0.000 as shown in Table 2.

DISCUSSION

The ultimate goal of using different insulin regimens in pregnant diabetic patients is to attain a near normal glycemic control to avoid fetal complications like fetal congenital anomalies, polyhydramnios, fetal macrosomia which in turn leads to intrapartum and post-partum complications.

Table 1: Demographic data of Pregnant Diabetic patients

Variables	Basal bolus regimen	Premixed Regimen	P value
Maternal age	34.6±4.68	34.6±5.11	.775
Gestational age	34.2±1.65	34.0±1.34	.552
Gravidity	7.08±1.65	6.68±1.56	.434
Hba1c	7.40±.742	7.39±.751	.947

Table 2: Control of mean blood glucose by Basal bolus and premixed regimens

	Group 1 Basal Bolus Regimen	Group 2 Premixed Insulin 70/30
No of patients in each group	50	50
Type 2 Diabetics	38	39
Gestational Diabetics	12	11

Table 3: Time required controlling the blood sugar with basal bolus regimen versus premixed regimen

Variable	Basal bolus regimen	Premixed regimen	P value
MBG 24Hrs	341.54±46	344.08±47	.784
MBG 72Hrs	160.20±8.569	220.22±17.57	.000
MBG 7days	152.00±9.897	192.42 ±14.99	.000

Table 4: Side effects associated with Insulin Regimen

Variable	Basal Bolus Regimen	Premixed regimen	P value
Hypoglycemia	0	5	NC

Current study shows that study basal bolus regimen is more effective in controlling blood sugar levels in gestational as well as type 2 diabetic pregnant patients as compared to pre-mixed regimen in lowering mean blood glucose levels more efficiently. Similar observation was noted in studies done by Nachum S Z and Kernaghan D[5,6]. A basal-bolus routine involves taking a longer acting form of insulin to keep blood glucose levels stable through periods of fasting and separate injections of shorter acting insulin to prevent rises in blood glucose levels resulting from meals. One of the main advantages of a basal-bolus regimen is that it allows to closely match how body releases insulin in a natural way if it was able to do so.

Patients in both the groups upon admission had uncontrolled diabetes as can be seen from their mean 24-hour admission blood glucose levels and HbA1C (as shown in Table. 1), but then had a sustained control of blood sugars in the following weeks of pregnancy with basal bolus regimen.

Although lowering of blood glucose was noticed in the premixed insulin regimen also, but a more rapid control was achieved with basal bolus as compared with premixed insulin (mean blood glucose MBG of 152±9.897 mg/dL vs. 192.42±14.99mg/dL) respectively as shown in Table 2.

This study was performed in low economic resource setting with non-availability of medicines. In our study both types of insulins were less expensive, with the basal bolus regimen giving a good control of blood sugars same as with ultra-short acting insulin[7].

Another study done by Jovanovic supported the use of Basal bolus regimen with good fasting and HBA1c control[8]. Although the four-dose daily regimen involves more injections a day than a twice daily regimen, the twice daily regimen entails frequent changes in the dose adjustment. Additionally, patients with basal bolus regimen may have meals at more flexible intervals as they can adjust the dose of insulin to variables such as exercise and appetite[9,10].

A study done by Ranasingh PD et al. recommends the use of Insulin according to individual cases with the use of multiple dose regimen being the most common[11]. A review of 5 randomized controlled trials revealed no firm conclusions that which Insulin type is better[12]. A review of recent advances and current trends by Nawaz et al showed that multiple insulin injections were one of the best treatments to control diabetes[13]. In our study patients were admitted twice or thrice for control of blood sugars during the antenatal period because of their noncompliance and inability to check blood sugar on glucometer or laboratory. Multiple admissions to hospital lead to better blood sugar control[14]. In our study as shown in Table 4 the incidences of hypoglycemia were low in both groups.[15] With the evidence from our study and comparisons with the other studies we can clearly see that the basal bolus regimen is effective, as compared with premixed regimen. We have not compared other types of Insulin in pregnant diabetic patients. Further large-scale studies are required to compare different Insulin regimen in pregnant diabetic patients. Different types of Insulin are to be compared for a better control of blood glucose levels in our pregnant population.

CONCLUSION

The results of our study revealed that Basal bolus regimen is more effective than the premixed insulin regimen in controlling blood sugar in pregnant patients with diabetes.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under

Sabir SA: Concept/ Idea, Literature, review, Drafting & Final Review

Qazi Q: Manuscript Writing, Literature review, Analysis & Interpretation of Data

Abbas G: Concept/idea, Data Collection

Zeb L: Concept/idea, Literature review, Drafting & Final Review

Yasmin S: Concept/idea, Literature review

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.