Original Article

Metformin vs Insulin in the Management of Gestational Diabetes; A Randomized Controlled Trial

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Abstract

Objectives: To compare the efficacy in terms of glycemic control of insulin versus metformin in gestational diabetes mellitus.
Methodology: This Randomized Controlled trial conducted in Department of Obstetrics & Gynecology at Pakistan institute of medical sciences, Islamabad from January 2022 to July 2022. A total of 100 pregnant women with gestational diabetes mellitus and gestational age of >20 weeks of age 18-40 years were selected. Patients in the group A were given injection regular insulin by subcutaneous route and group B was given tablet metformin 500mg by oral route. Patients were admitted for 1 week in 2nd and 3rd trimester for glycemic control. All the patients were put on 6 hourly sugar profile at which efficacy was noted.
Results: The mean age of women in group A was 27.86 ± 4.17 years, and in group B was 28.22 ± 3.97 years. Majority of the patients 64 (64.0%) were between 18 to 30 years of age. The mean gestational age of women in group A was 25.04 ± 3.26 weeks and in group B was 24.60 ± 3.30 weeks. In this study, the efficacy of metformin versus insulin in terms of glycemic control was 74.0% versus 32.0% respectively, p = 0.0001.
Conclusion: This study concluded that there is better glycemic control with metformin compared to regular insulin in managing gestational diabetes mellitus.
Keywords: Gestational diabetes, metformin, insulin.

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Introduction

Gestational diabetes mellitus (GDM) is commonly associated with pregnancy therefore it is defined as any level of glucose intolerance during the pregnancy.[1] It exposes a greater risk and poses threat to both mother and fetus. And complications that follows both mother and fetus throughout the life. Maternal complications include pre-eclampsia, hyperglycemic crisis, urinary tract infections, cardiovascular complications later in life, including hyperlipidemia and hypertension.[2] Early detection and treatment of gestational diabetes mellitus is of utmost importance not only to mother but fetus in order to prevent lifelong complications.[3]

Therefore, importance of pre-conceptional evaluation and counselling of women with pregestational diabetes mellitus cannot be overstated. In the later stages in pregnancy it increases the risk of macrosomia two to four times.[4] In a comparative study the found out that perinatal mortality rates in diabetic mothers were significantly higher than those with good glycemic control and perinatal morbidity including neonatal hypoglycemia, macrosomia, LGA, birth asphyxia.[5]

The main purpose of treatment is to achieve optimal glycemic control and to prevent its complications.[6] This can be achieved by dietary and lifestyle modifications and in uncontrolled cases, Insulin is drug of choice. Women who begin insulin therapy require education on how to self-administer insulin as prolonged use can cause hypoglycemia and weight gain. And in most of the cases they develop resistance. Therefore, the use of oral

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anti-diabetic drug is advocated with tolerance, better efficacy and enhanced glycemic control. About 20-60% of the patients with GDM need pharmacological treatment .[7]

Metformin is an alternative to insulin in patients with pregnancy induced hyperglycemia or with any familial history. It decreases hepatic gluconeogenesis and improves peripheral glucose uptake.[8] it minimizes the side effects caused by insulin as it does not induce hypoglycemia and it is not associated with appreciable weight gain. Although it crosses the placenta, there is no evidence of adverse fetal effects [9] or increased risk of major malformations when metformin is used in pregnant women.[10] In a study, the efficacy of metformin versus insulin in terms of glycemic control and patient acceptability was 76.6% versus 27.2% respectively. [11]

As metformin and insulin are the two widely used drugs for gestational diabetes mellitus in our country and the better among them with better glycemic control and more patient acceptable is still debatable. This study was planned to compare the glycemic control of insulin versus metformin in gestational diabetes mellitus. So, it will help to decide a drug with better glycemic control and more patient acceptability with reduction in morbidity of both mother and fetus in our population.

Methodology

In this randomized control trial study, all the patients were enrolled after taking permission from the ethical review committee of the hospital. All pregnant patients who were presented to the Department of Obstetrics & Gynecology of Pakistan Institute of Medical Sciences, Islamabad were enrolled for the study. The study was conducted in a period of six months from January 2022 to July 2022. The sample size was calculated by WHO sample size calculator and it turned out to be 100 i.e. 50 in each group with 5% margin of error, 80% power of study, taking efficacy of metformin as 76.6% and that of insulin as 27.2%.[11]

All pregnant women with diagnosed gestational diabetes mellitus and gestational age of >20 weeks (assessed on LMP), having age between 18-40 years and a parity of 1-4 were selected for the study. Women presented with multiple pregnancies (assessed on USG), already taking treatment for gestational diabetes mellitus, known patients of diabetes mellitus (assessed on history) were excluded from the study.

After taking informed written consent and relevant history, patients were divided into two groups i.e. A & B by random number tables. Patients in the group A were given injection regular insulin by subcutaneous route and group B was given tablet metformin 500mg by oral route. Patients were admitted for 1 week in 2nd and 3rd trimester for glycemic control. All the patients were put on 6 hourly sugar profile at which efficacy was noted in both groups. Efficacy was assessed in terms of quantitative variable by measuring one hour posy-prandial fasting plasma glucose levels <92 mg/dl. All the data was recorded on a specially designed proforma for analysis.

Statistical analysis was performed using SPSS version 20.0. Mean and standard deviation were calculated for age, gestational age, parity and body mass index (BMI). Frequency and percentage were calculated for efficacy (yes/no). The efficacy of the two study groups was compared using Chi-Square test between both groups. P-value ≤0.05 was considered as significant.

Effect modifiers like age, gestational age, parity and body mass index were controlled through stratification and post-stratification chi square was applied to see their effect on efficacy. P-value ≤ 0.05 was considered as significant.

Results

The overall mean age of the study sample was 28.04 ± 4.06 years, ranging from 18 to 40 years. The mean age of women in group A was 27.86 ± 4.17 years and in group B was 28.22 ± 3.97 years. There was no statistically significant (p-value > 0.05) difference in the mean age of both groups.

The mean gestational age of women in group A was 25.04 ± 3.26 weeks was similar to the group B 24.60 ± 3.30 weeks without any significant (p-value > 0.05) difference. There was no significant (p-value > 0.05) difference in both groups with respect to mean parity (2.66 ± 0.87 vs 2.76 ± 0.85) and mean BMI (30.60 ± 2.79 vs. 30.72 ± 2.60) kg/m2 between insulin and metformin groups as shown in table I.

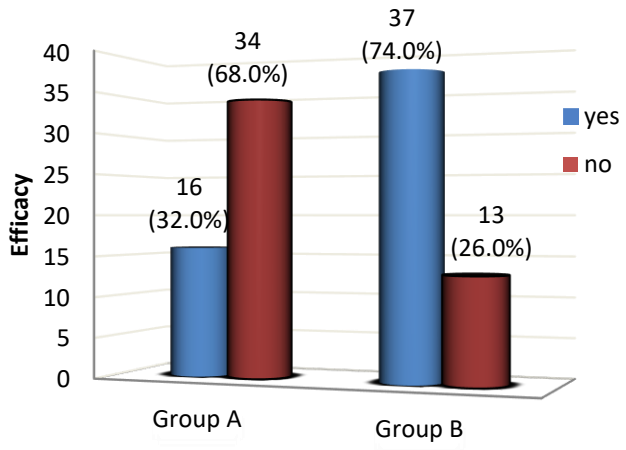
In this study, efficacy of metformin versus insulin in terms of glycemic control was 74.0% versus 32.0% respectively, p = 0.0001) as shown in Figure I. This indicate that the efficacy of metformin group is significantly higher as compared to patients treated with insulin.

The stratification with respect to age showed that efficacy of metformin treatment is significantly (p-value < 0.05) higher as compared to insulin group in age group

of 18-30 years but this difference in efficacy become insignificant (p-value > 0.05) in the age group of 31-40 years indicating same efficacy level between both treatment groups. Stratification of efficacy with respect to gestational age, parity and BMI showed that metformin treatment has significantly high efficacy independently from gestational age, parity, and BMI status of the patient as elaborated in Table II.

Table I: Distribution of Demographic characteristics of the women

Insulin Group (A) (n=50)	Metformin Group (B) (n=50)	P-value
Mean ± SD	Mean ± SD	
Age of the women		
27.86 ± 4.17	28.22 ± 3.97	0.659
Gestational age of the women		
25.04 ± 3.26	24.60 ± 3.30	0.504
Parity distribution of the women		
2.66 ± 0.87	2.76 ± 0.85	0.562
Distribution of BMI (kg/m2)		
30.60 ± 2.79	30.72 ± 2.60	0.824



P-value = 0.0001 which is statistically significant

Figure I: Comparison of efficacy in both groups.

Discussion

Gestational diabetes mellitus (GDM) is a condition where glucose intolerance is detected for the first time during the pregnancy. Its prevalence is increasing globally and it can result in multiple congenital anomalies involving both fetal and maternal health which includes pregnancy induced hypertension, pre-term labor and development of type 2 diabetes in the later life. Adequate blood sugar control is crucial for improving perinatal outcomes. Lifestyle modifications, such as diet control and exercise are considered first line of treatment for GDM. However, insulin is required if blood sugar is not optimally controlled with these measures. While historically insulin has been the only choice for establishing glycaemia, it is not appropriate in low resource settings with poor literacy and insulin storage facilities. Moreover, insulin administration carries risk of hypoglycemia and weight gain. Metformin, is a second generation biguanide, an insulin sensitizer that reduces insulin resistance and basal plasma insulin levels. It has the advantage of oral administration, low cost, and better compliance [13-15]

Table II: Comparison of Efficacy between both groups in different strata based upon age, gestational age, parity and BMI

Characteristics	Group A (n=50)		Group B (n=50)		P-value
	Efficacy		Efficacy		
	Yes	No	Yes	No	
Age of patients (years)					
18-30	7	24	24	9	0.0001
31-40	9	10	13	4	0.074
Gestational age of the women					
21-28	14	27	29	10	0.010
>28	2	7	8	3	0.025
Parity of the patients					
1-2	6	13	16	6	0.008
3-4	10	21	21	7	0.001
BMI of the women					
≤ 30	6	12	15	4	0.005
> 30	10	22	22	9	0.002

The results of this present study show that the mean age of women in insulin group was similar (27.86 ± 4.17 vs. 28.22 ± 3.97 years) to metformin group, with no statistically significant (p-value > 0.05) difference in the mean ages of both groups.

The mean gestational age of women in insulin group (25.04 ± 3.26 weeks) had no significant (p-value > 0.05) difference as compared to metformin group (24.60 ± 3.30 weeks). Similarly, there was no significant (p-value > 0.05) difference in both groups with respect to mean parity (2.66 ± 0.87 vs 2.76 ± 0.85) and mean BMI (30.60 ± 2.79 vs. 30.72 ± 2.60) kg/m^2 between the insulin and metformin groups. [16]

Metformin suppresses hepatic glucose output, increases insulin-mediated glucose uptake and utilization and improves lipid profile by decreasing triglyceridemia, fatty acid and low-density lipoprotein cholesterol levels, while slightly increasing high-density lipoprotein cholesterol and decreasing intestinal absorption of glucose.[17-18] As metformin crosses the placenta, there are health concern relating to both maternal and fetal health, but scientific data has not proven it yet.[19]

In this study, efficacy of metformin in comparison to insulin in terms of glycemic control was 74.0% versus 32.0% respectively, p = 0.0001). This indicate that the efficacy of metformin group is significantly higher as compared to patients treated with insulin. Results are very much in agreement with international studies like an Australian study by Rowan and colleagues, reported that metformin use in women with GDM is more effective with better outcome. The Metformin had a very low failure rate of 7.4%, in which a second diabetic agent was needed to maintain controlled glucose levels. Although there was no difference in mean fasting blood glucose levels between groups, those on Metformin, had lower 2-hour postprandial glucose levels. There was no difference in the rate of preeclampsia. Women in the Metformin group had less weight gain compared to women in the insulin group. [21]

Similar results were reported by local studies eg. in a study conducted in Islamabad, it was found that Fasting blood sugar level after 1 month was controlled in 64.7% patients in insulin group and in 79.4% in metformin group (p > 0.05). Comparison of post-treatment HbA1C level depicts that diabetes was controlled in 79.4% patients in insulin group as compared to 82.3% patients of metformin group. [22]

Conclusion

This study concluded that there is better glycemic control with metformin compared to regular insulin in managing gestational diabetes mellitus. So, we recommend that metformin should be used as a primary medicine for treating gestational diabetes mellitus in order to reduce the morbidity and mortality of both mother and fetus.

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