

Metformin versus Insulin Treatment in Gestational Diabetes in Pregnancy and Their Effects on Neonatal Birthweight

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ABSTRACT

Aim: To compare the maternal and neonatal outcomes (in terms of birthweight) in women treated with metformin versus insulin for the management of gestational diabetes mellitus.

Methods: This was a randomized clinical trial in nature. We included 60 women who presented with gestational diabetes mellitus. Group I patients were given metformin therapy (500-2 Grams) in intermittent doses daily for the management of GDM, and to group II patients (control group) subcutaneous NPH insulin was given. The dose of insulin and metformin was dependent upon the glycemic control of the patient.

Results: Mean gestational age of the patients at the time of enrolment in study was 28.13 ± 2.30 weeks in metformin group and 28.26 ± 2.46 weeks in insulin group (p-value 0.82). Mean weight gain was 8.96 ± 1.78 Kg in mothers taking metformin therapy and 9.36 ± 1.40 Kg in mother taking insulin therapy (p-value 0.33). The rate of cesarean section was 43.3% in metformin group and 36.7% in insulin group with a p-value of 0.59. In metformin group, the mean weight of babies at the time of birth was 3.2 ± 0.20 Kg versus 3.67 ± 0.19 Kg in insulin group (p-value < 0.001).

Conclusion: Metformin is a safe drug for the management of gestational diabetes mellitus because of its less monitoring and comparatively comparable maternal side effects. The only problem with metformin therapy is lower birthweight of neonates.

Keywords: Gestational Diabetes Mellitus, metformin, insulin, neonatal birthweight

INTRODUCTION

The incidence of gestational diabetes is increasing day by day, about 1% to 14% of all pregnancies are complicated by gestational diabetes mellitus (GDM)¹. GDM is defined as any degree of glucose intolerance with onset or first recognition during pregnancy². GDM is associated with increased risk of adverse maternal and neonatal outcomes e.g., it increases the risk of pre-eclampsia, caesarian section and type 2 diabetes after pregnancy. Regarding neonatal outcomes, it can increase the risk of still birth, neonatal death, congenital defects, macrosomia, neonatal hypoglycemia and shoulder dystocia^{3,4}. Australian carbohydrate intolerance study in pregnant women have concluded that optimal treatment of gestational diabetes mellitus reduces the risk of adverse maternal and neonatal outcomes and maintain the normal quality of life of pregnant females⁵.

Subcutaneous insulin therapy is the standard treatment of GDM^{6,7}. But insulin therapy has many disadvantages e.g. multiple daily injections, risk of maternal hypoglycemia and weight gain.⁸ So oral therapy for GDM will be accepted as much safer and easily usable by females. Metformin is a first line treatment used for the management of type 2 diabetes⁹. Metformin is now gaining access and is

regularly being used for the management of GDM in pregnant females. Reduction in neonatal weight after use of metformin has been reported by some studies¹⁰. But some studies have documented normal weight of neonates after metformin therapy^{11,12}.

In the study of Ainuddin et al., neonatal birth weight was significantly less in metformin group 3.4 ± 0.4 kg versus 3.7 ± 0.5 kg in insulin group. This study established that metformin has a significant effect on neonatal birth weight¹⁰. But in another study, the authors did not find any significant difference in mean birth weight of neonates in metformin versus insulin group. In that study, the mean birth weight was 3604 ± 488 grams in metformin group and 3589 ± 448 grams in insulin group¹².

As literature has mixed results regarding effects of metformin therapy on neonatal birth weight. So in presented study, the effects of metformin therapy versus insulin therapy for management of GDM on neonatal birth weight are compared. Because reduced birth weight is an indication of improper nutrient supply to neonates during pregnancy that can lead to serious adverse effects e.g., still birth and neonatal death.

MATERIALS AND METHODS

This was a randomized clinical trial in nature and conducted in gynecology department of Jinnah

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Hospital Lahore. We included 60 women who presented with gestational diabetes mellitus. Females with singleton pregnancy were included. We assigned individuals to two groups using randomization after taking informed consent and giving a brief introduction about study purpose and parameters. Patients who required both insulin and oral hypoglycemic agents for treatment of gestational diabetes, having renal or cardiorespiratory ailments and who were taking previously any hypoglycemic agents were excluded. Patients were said to have gestational diabetes mellitus (GDM) if she has the following results on oral glucose tolerance test (OGTT), usually undertaken after 20 weeks of gestation (Fasting Glucose ≥ 7.0 mmol/L, 2 hour Glucose ≥ 11.1 mmol/L).

Group I patients were given metformin therapy (500-2 Grams) in intermittent doses daily for the management of GDM, and to group II patients (control group) subcutaneous NPH insulin was given. The dose of insulin and metformin was dependent upon the glycemic control of the patient.

Patients were asked to measure their blood sugar levels daily and note it on a diary and after every week, their doses of metformin and insulin were adjusted according to the control of their blood sugar levels. Birth weight of the baby was calculated immediately after birth and was presented in Kilograms.

SPSS V23 was used for data analysis. Independent sample t-test was used to compare the mean birth weight of neonates and other quantitative between the groups. Chi-square test was used to compare mode of delivery between the groups.

RESULTS

Mean gestational age of the patients at the time of enrolment in study was 28.13 ± 2.30 weeks in metformin group and 28.26 ± 2.46 weeks in insulin group (p-value 0.82). 15(50%) patients had positive family history of diabetes in metformin group and 13(43.3%) in insulin group (p-value 0.61). Mean body weight of mothers at the time of enrolment was 58.90 ± 5.78 kg in metformin group and 58.10 ± 5.01 kg in insulin group (p-value 0.50) (Table 1).

Mode of delivery was vaginal in 17(56.7%) mothers in metformin group and 19(63.3%) in insulin group (p-value 0.59). We noticed a significant reduction in baby birthweight in metformin group. In metformin group, the mean weight of babies at the time of birth was 3.2 ± 0.20 Kg versus 3.67 ± 0.19 Kg in insulin group (p-value < 0.001). Maternal weight gain occurred in both groups after starting the therapy and at the time of child birth; mean weight gain was 8.96 ± 1.78 Kg in mothers taking metformin therapy and 9.36 ± 1.40 Kg in mother taking insulin therapy (p-value 0.33).

Table 1: Patients Characteristics at the time of enrolment in study.

Parameters	Metformin Group(n=30)	Insulin Group(n=30)	P-value
Age (Years)	30.26 (3.97)	29.63 (3.81)	0.53
Gestational Age (Weeks)	28.13 (2.30)	28.26 (2.46)	0.82
BMI (Kg/m ²)	22.94 (5.86)	23.43 (5.06)	0.29
Weight at the time of enrolment (Kg)	58.90 (5.78)	58.10 (5.01)	0.56
Positive Family History of Diabetes	15 (50.0%)	13 (43.3%)	0.61

Table 2. Study outcomes

Parameters	Metformin Group(n=30)	Insulin Group(n=30)	P-value
Maternal Weight Gain (Kg)	8.96 (1.78)	9.36 (1.40)	0.33
Mode of Delivery			
Vaginal (%)	17 (56.7%)	19 (63.3%)	0.59
Cesarean Section (%)	13 (43.3%)	11 (36.7%)	
Birth Weight (Kg)	3.22 (0.20)	3.67 (0.19)	< 0.001

DISCUSSION

Incidence of gestational diabetes mellitus (GDM) complicating pregnancies is increasing in developing countries like Pakistan. With optimal GDM management, the incidence of adverse events such as macrosomia, stillbirth and other adverse effects can be reduced^{8,13,14}. Improvements in dietary habits, exercise, oral and subcutaneous hypoglycemic agents are routine used methods for GDM. There is a controversy regarding oral (metformin) and

subcutaneous (insulin) therapy regarding maternal and neonatal outcomes. In this present controlled trial, we compared metformin with insulin and compared their effects on maternal and neonatal weight.

In our study, mean weight gain was 8.96 ± 1.78 Kg in mothers taking metformin therapy and 9.36 ± 1.40 Kg in mother taking insulin therapy with insignificant statistical difference. Ainuddin et al¹⁰ found significant difference in weight gain of mothers taking insulin versus metformin therapy. In their

study, mean weight gain was 9.8 ± 1.5 Kg in metformin group and 12.5 ± 1.1 Kg in insulin group. Niromanesh et al.¹¹ also found significant weight gain 13.7 ± 3.1 in insulin versus 11.3 ± 3.8 in metformin group. Other studies have also concluded that metformin has a beneficial effect on the weight of mothers and had found similar effects as of these studies^{15,16}.

In our study, mean birthweight was high in insulin group, 3.67 ± 0.19 kg versus only 3.22 ± 0.20 Kg in metformin group. Ainuddin et al¹⁰ also found lower birthweight in metformin group 3.4 ± 0.4 kg versus 3.7 ± 0.5 kg in insulin group. Niromanesh et al¹¹ also found similar results with 3.3 ± 0.4 kg in metformin group and 3.4 ± 0.4 Kg in insulin group (p-value 0.004). However, Tertti et al¹² did not found any significant difference in birthweight of neonates in metformin versus insulin groups. Marques et al¹⁷ also did not found any significant difference in birthweight of neonates in metformin versus insulin group. Their results are contrary to many published trials.

In our study, the rate of cesarean section was 43.3% in metformin group and 36.7% in insulin group with a p-value of 0.59. Similar results of cesarean section have also been found by many other studies¹⁸⁻²⁰. Rate of cesarean section in the study by Balaniet al²¹ was 48% in metformin group and 52.0% in insulin group (p-value 0.67). Rate of cesarean section was 41.9% in metformin group and 50.7% in insulin group in the study of Ainuddin et al. with p-value of 0.35¹⁰ However, Ijas et al¹⁷ have found significant difference in cesarean section rate in metformin 20% in insulin group and 38.0% in metformin group with p-value of 0.04.

In the end, we have concluded that metformin is a safe drug for the management of gestational diabetes mellitus because of its less monitoring and comparatively comparable maternal side effects. The only problem with metformin therapy is lower birthweight of neonates.

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