Original Article

Efficacy of metformin in maintaining euglycemia in patients with Gestational Diabetes Mellitus

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Objective: To determine efficacy of metformin in maintaining euglycemia in patients with GDM among women presenting in our institution.

Methodology: It was a prospective study conducted at the department of Obstetrics & Gynecology Railway teaching Hospital IIMCT, Rawalpindi from October 2014 to April 2015 and included 60 patients of 18-45 years of age at 10-32 weeks gestation in singleton pregnancy with fasting blood glucose levels > 6.1 mmol /L & 2 hours Post Prandial levels > 7.8 mml/L Metformin was started at a dose of 500mg daily and increased up to 2500mg daily. Aim was to keep fasting sugar level between 3.5 5.9 mmol/L & 2 hours post prandial < 7.8 mmol/L.

Results: The median daily dose of metformin was 1500 mg. The mean gestational age at delivery was 38.1 weeks. Neonatal hypoglycemia (glucose level < 1.6mmol/L) was less common. The only adverse effects of metformin was GI upset (13.1 %) The results of postpartum questionnaire assessing acceptability of treatment among women treated with metformin alone, 65.6 % said they would choose metformin in subsequent pregnancy. The efficacy of metformin alone was 85.7%.

Conclusion: In women with gestational diabetes mellitus, metformin (alone or with supplemental insulin) is not associated with increased prenatal complications. The women preferred metformin to insulin treatment. (Rawal Med J 201;42:299-301)

Key Words: Metformin, gestational diabetes, BMI, Insulin.

INTRODUCTION

Gestational diabetes (GDM) is a complication in 5% of pregnancies and its prevalence is increasing and is associated with pregnancy complications and risk of diabetes in neonate and mother.[1,2] Pregnancy itself is a diabetagonic state and as the pregnancy advances the insulin sensitivity decreases. This increases the chances of development GDM, especially in women with pre-existing insulin resistance and obesity.[3] Gestational diabetes increases the risk of congenital malformations, spontaneous abortion, preterm labor, eclampsia, shoulder dystocia vaginal infections and cesarean section. Advances in antenatal care, life style modification, dietary control and use of insulin significantly reduces the rate of perinatal mortality and morbidity as well as maternal morbidity.[4] The main aim of treatment is to reduce maternal glucose levels.[5]

Conventional treatment of GDM is dietary control and insulin therapy, when indicated. For insulin therapy, women need to get hospitalized, occurrence of hypoglycemia also needs to be monitored because it may be dangerous for the mother as it may cause fetal demise.[6] Metformin is cheap, easy to administer with fewer side effects and insulin therapy is costly and requires skill to administer and need special storage conditions like refrigeration. It causes hypoglycemia when not properly administered or when adequate diet is not consumed along with it. The rationale of this study was to assess the efficacy of metformin in treatment of GDM.

METHODOLOGY

This study was conducted at the Department of Obstetrics and Gynecology Islamic International Medical College Rawalpindi, Pakistan from 5th October to 5th April and included 60 subjects using non probability purposive sampling. Patient with gestational diabetes who had at least twice fasting plasma glucose level of >6.1 mmol/L and 2 hrs Post Prandial (PP) value >7.8 mmol/L at 11-32 gestational weeks were included. All those women with fasting blood glucose level >7.0 mmol/L and 1 hr PP plasma glucose >11.0 mmol and those with pre

gestational use of metformin and multiple fetuses were excluded. Data were collected after taking administrative permission from concerned authorities and ethical committee. Informed written consent was taken from all patients.

Treatment was initiated the following day, after checking results of fasting blood samples, measurement of renal and liver functions to ensure unexpected contra indications to the use of metformin. Metformin was started at a dose of 500mg daily and was increased up to 2500mg daily depending upon maternal blood glucose levels. The aim was to keep fasting sugar levels between 3.5-5.9 mmol/L and 2 hrs PP <7.8 mmol/L

Follow up of patients was planned at two weeks as outpatient during which they were evaluated for the control of blood sugar. If diabetic control was inadequate with metformin, insulin was started along with metformin. But metformin was stopped if maternal conditions like pre-eclampsia, cholestasis or IUGR developed. Tab Methyl cobalamin (Vit B12) was given daily to prevent Vit. B 12 deficiency, which is associated with metformin therapy.

RESULTS

The mean gestational age at delivery between the metformin group (38.1 weeks) and metformin with insulin group was (38.0 weeks). As compared with women who were treated with metformin alone, women requiring supplemental insulin had higher BMI (32.2±8.2 Vs 35.1±8.3) and had higher baseline glucose levels (BSR 174±37.8 Vs 169.2±37.8). (Table 1). The median daily dose of metformin was 1500 mg (range 1500-2000). For women who required supplemental insulin, the median maximum daily dose of insulin was 42 units (range 22-81). Supplemental insulin was started at a median of 20.2 days (range 12.4-27.5) after random assignment to metformin. Only 8 (85.7% Vs 14.3%) patients required insulin along with metformin (Table 2).

Table 1. Descriptive statistics.

Variables	Mean±SD
Age	29.7±3.42
Gestational Age	31.4±9.97
BMI	26.328±24.4
Dose of Metformin	1400±44.24

Table 2. Need of Insulin.

	Number	Percentage
Metformin alone	52	85.7
Metformin + insulin	8	14.3
Total	60	100

Neonatal hypoglycemia (glucose level <1.6 mmol per liter) was less common in the metformin alone than combine metformin and insulin (1.6% Vs 8.3%). The only adverse effect of metformin was GI upsets (13.1%). A postpartum questionnaire assessing acceptability of treatment showed that among women treated with metformin, 65.6% said they would choose metformin in a subsequent pregnancy. Women in the metformin group has greater weight loss between the time of enrollment and the postpartum visit and less weight gain between the time of enrollment and 36 weeks of gestation. The efficacy of metformin alone was 85.7%.

DISCUSSION

This study has revealed the efficacy of metformin in maintaining euglycemia in patients with GDM. Advances in antenatal care and strict dietary control and insulin regimen have shown to reduce the maternal morbidity and perinatal mortality and morbidity. Historically, fetal teratogenicity and hypoglycemic effects on fetus limited the use of oral hypoglycemic agents in pregnancies complicated with gestational diabetes or type II diabetes mellitus.[7] Now physicians start prescribing new generations of oral hypoglycemic agents to treat type-II Diabetes Mellitus in pregnancy and GDM. Biguanide compound, metformin, exerts its effect by increasing insulin sensitivity and reducing hepatic output of glucose. This results in a decreased glucose level without weight gain causing hypoglycemia.[8] In our study, the efficacy of metformin was 85.75%. This is in agreement with a previous study which showed that glycemic control achieved with metformin was 89.5%.[6]

We found no significant increase in neonatal complications, especially congenital defects among women with GDM. Same results have shown in a study conducted by Rowan et al, [9] Dhulkotia et al,[8] and Silva et al.[10] Gilbert et al[11] also showed that there is no evidence of an increased risk for major congenital

defects when metformin is taken during the first trimester of pregnancy. In our study, 11.53% of women taking metformin required supplemental insulin, as Rowan et al[9] showed that 46% needed insulin.

Although our study was not designed to compare the outcome of combined treatment with that of either treatment alone, the rate of neonatal complications especially congenital malformation did not differ significantly between women who required supplemental insulin and those who received metformin alone. The result of our study are comparable and study of Rowan et al,[9] Silva et al,[10] Dhulkota et al[8] and Gilbert et al.[11] Moreover, women receiving combined treatment required less dose of insulin and gained less weight than those taking insulin alone. Same results were seen in study conducted by Rowan et al.[9]

CONCLUSION

Our findings suggest that metformin, alone or with supplemental insulin, is an effective and safe treatment option for women with gestational diabetes mellitus and that metformin is more acceptable to women who meet the usual criteria for starting insulin. Further follow-up data is needed to establish long-term safety.

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