DOI: https://doi.org/10.53350/pjmhs22165242

ORIGINAL ARTICLE

Comparison of Efficacy of Metformin and Insulin in management of Gestational Diabetes. An experience in Social Security Teaching Hospital, Ferozepur Road Lahore

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ABSTRACT

Objective: To compare the feto-maternal outcomes in patients receiving metformin with those receiving standard insulin therapy for management of gestational diabetes mellitus (GDM).

Methods: This randomized control study was conducted in gynecology unit of Social security Teaching Hospital, Ferozepur Road Lahore from January-2021 to December-2021. We included patients of GDM who needed pharmacologic intervention. In group M; Metformin was administered at a dose of 500mg twice daily for the first week, followed by an increase to a maximum dose of 2500mg daily in divided doses until the goal glycemic control was reached. In group I patients, regular insulin (Humulin R) was prescribed three times a day before each meal, with a single dose of intermediate acting insulin (NPH) given at bedtime. The primary study outcomes were birth weight, APGAR score, pre-term birth and maternal HBA1c levels before birth.

Results: Maternal HbA1c levels before birth were 6.1±1.1 in group M and 6.0±1.2 in group I (p-value 0.66). The mean gestational age at birth was 37.9±1.1 weeks in group M and was 37.1±1.0 weeks in group I (p-value 0.0002). The frequency of pre-term was high in group I (16%) in comparison to only 6.0% in group M, but with insignificant p-value 0.11. The mean birth weight was 2.9±0.5 Kg in group M and 3.0±0.6 kg in group I (p-value 0.36).

Conclusion: Better maternal glycemic control has been linked to the usage of metformin during pregnancy. In terms of patient compliance, the medicine is well tolerated. Patients with gestational diabetes mellitus who took Metformin experienced fewer neonatal problems than those who used insulin.

Keywords: Gestational diabetes mellitus, metformin, insulin

INTRODUCTION

Gestational diabetes mellitus (GDM) is glucose intolerance disorder that develops during pregnancy (during 2nd or 3rd trimester) in the absence of a prior history of the condition.[1] According to the American Pregnancy Association, 1 to 14 percent of all pregnancies are complicated by this condition, with the prevalence varied based on race and ethnicity, as well as the screening method utilised.[2,3] Obesity has reached epidemic proportions, and with it, the incidence of gestational diabetes has increased proportionally.[4]

GDM is associated with both short- and long-term dangers for both the mother and the foetus. Preeclampsia, a higher probability of caesarean delivery, and an increased chance of developing type II diabetes mellitus later in life are all elevated risks for the mother throughout pregnancy.[5] Macrosomia can cause harm to the foetus, increasing the chance of congenital abnormalities, stillbirth at term, shoulder dystocia at birth, and postnatal hypoglycemia.[6] Macrosomia can also cause foetal death. A higher risk of long-term consequences on child health, such as obesity and metabolic syndrome, is also associated with this exposure.[7]

GDM is treated first with a lifestyle change that involves food therapy and physical activity.[8] Patients who do not respond to the therapy described above will need to be treated with pharmaceuticals. The goal is to reduce hyperglycemia in the mother, which will result in a significant decrease in perinatal morbidity and an increase in the mother's quality of life. Insulin injections are the gold standard for type 2 diabetes therapy.[9] Despite the development of better and safer forms of insulin, its use during pregnancy is linked to increased maternal weight or hypoglycemia. Controlling blood sugar levels with insulin needs daily dosage modifications as well as the preservation of the cold chain. Because of the higher cost of treatment and training, as well as the demand for daily insulin injections, which can create complications, some women find it to be an unappealing option.[9]

Metformin is a drug that has been in use for a long time and is used to treat type 2 diabetes in patients who have the condition. It enhances insulin sensitivity by boosting the activity of AMP kinase and lowers hepatic gluconeogenesis, which is a precursor to type 2 diabetes. According to the findings of the study, it is not associated with weight gain or hypoglycemia. The fact that there is a 10–16 percent probability of medication transfer from mother to foetal has not been shown to have any harmful effect on the foetus in subsequent investigations. Metformin is recommended as a first-line treatment for type 2 diabetes by the National Institute of Health and Care Excellence (NICE) where no contraindications exist, according to the most recent guidelines.[10,11]

In this study we compared the feto-maternal outcomes in patients receiving metformin with those receiving standard insulin therapy for management of GDM.

METHODS

This randomized control study was conducted in gynecology unit of Social security Teaching Hospital, Ferozepur Road Lahore from January-2021 to December-2021. A 75gm oral glucose tolerance test was performed on pregnant women who presented to the clinic between 22 and 34 weeks of pregnancy with a singleton pregnancy and were between 22 and 34 weeks of gestation (OGTT). In accordance with the International Association of Pregnancy Study Group (IADPSG) criteria, gestational diabetes mellitus (GDM) was defined as a fasting glucose level greater than 5.1mmol/L (92mg/dl), a 1 hour glucose level greater than 10mmol/L (180mg/dl), or a 2 hour postprandial glucose level greater than 8.5mmol/l (153mg/dl). 15. Any other systemic condition, such as type 1 or type 2 diabetes, known hypertension, or foetal abnormality detected on ultrasound, was ruled out of the study for the women who participated.

Following a diagnosis of gestational diabetes, all women were instructed on how to control their diabetes through food, exercise, and a change in lifestyle. Patients were contacted after two weeks and their blood glucose levels were tested; fasting blood glucose levels less than 95mg/dl and 1 hour postprandial glucose levels less than 140mg/dl were considered normal. If a participant's blood glucose level surpassed these limitations, they

were recruited in the study after being told of the study's purpose and providing written consent.

A lottery system was used to divide the registered patients into two groups. Metformin was administered at a dose of 500mg twice daily for the first week, followed by an increase to a maximum dose of 2500mg daily in divided doses until the goal glycemic control was reached (fasting blood glucose level 95mg/dl and 1 hour postprandial glucose level 140mg/dl). If glycemic control was not achieved despite using the maximum dose of metformin, insulin was given. Those assigned to the insulin group were hospitalised after receiving insulin dose adjustment counselling as well as education on insulin administration, insulin storage, and hypoglycemia symptoms and indications. In the second and third trimesters of pregnancy, total insulin dosages were calculated by multiplying maternal weight by 0.7 and 0.8, respectively. To manage blood glucose levels, short acting insulin (Humulin R) was prescribed three times a day before each meal, with a single dose of intermediate acting insulin (NPH) given at bedtime.

The primary study outcomes were birth weight, APGAR score, pre-term birth and maternal HBA1c levels before birth.

SPSS version 23.0 was utilised for data analysis. The independent sample t-test and the chi-square test were employed to compare quantitative and qualitative variables, respectively. A P-value of 0.05 was deemed statistically significant.

RESULTS

Baseline characteristics were similar among groups, with mean age of 30.1±4.7 years in group M and 29.9±4.9 years in group I (p-value 0.85). The parity was 2.6±1.2 in group M and 2.6±1.1 in group I (p-value 1.0). the gestational age at study recruitment was 28.4±3.0 weeks in group M and 28.7±2.9 weeks in group I (p-value 0.61) [Table 1].

Maternal HbA1c levels before birth were 6.1±1.1 in group M and 6.0±1.2 in group I (p-value 0.66). The mean gestational age at birth was 37.9±1.1 weeks in group M and was 37.1±1.0 weeks in group I (p-value 0.0002). The frequency of pre-term was high in group I (16%) in comparison to only 6.0% in group M, but with insignificant p-value 0.11. The mean birth weight was 2.9±0.5 Kg in group M and 3.0±0.6 kg in group I (p-value 0.36) [Table 2].

Table 1. Baseline Maternal Characteristics.

	Group M (N=50)	Group I (N=50)	P-value
Age	30.1±4.7	29.9±4.9	0.85
Parity	2.6±1.2	2.6±1.1	1.0
Gestational age at study enrolment	28.4±3.0	28.7±2.9	0.61

Table 2. Feto-maternal outcomes.

	Group M (N=50)	Group I (N=50)	P-value
Maternal HbA1c	6.1±1.1	6.0±1.2	0.66
Gestational age at Birth	37.9±1.1	37.1±1.0	0.0002
Pre-term Birth	3 (6.0%)	8 (16.0%)	0.11
APGAR Score	8.2±0.99	8.1±1.0	0.61
Birth Weight (Kg)	2.9±0.5	3.0±0.6	0.36

DISCUSSION

Absolute insulin deficiency develops in gestational diabetes mellitus (GDM), which leads to hyperglycemia in the mother. The incidence of gestational diabetes is alarmingly increasing. Dietary modifications, physical activity, and the ingestion of nutrient-rich foods may all aid in the prevention of GDM. The most frequent therapies for gestational diabetes are insulin therapy or oral metformin therapy. Metformin's drawback is that it rapidly crosses the placenta and reaches the foetus via organic cation transporters.[12] At 25 to 32 weeks of gestation, the placenta of the foetus begins to create organic cat-ion transports.[13] Metformin inhibits mitochondrial respiration and prevents the entry of nutrients such as glucose and amino acids into the developing foetus via the mTOR pathway.[14] This occurs when the beta subunit of insulin binds to the glycoprotein receptor (alpha subunit) on the surface of the cell, which is activated and provides a signal that stimulates insulin to act on glucose in the bloodstream.[15] The effects of subcutaneous insulin therapy and oral metformin on the outcomes of pregnant women are the subject of considerable discussion.

Numerous studies have pointed to the possibility that metabolic processes are connected to both the development of the foetus while it is still inside the uterus and the early stages of the postpartum period.[16] Terry-Adkins and colleagues conducted a meta-analysis in which they found that children who were given metformin had a lower birth weight but considerably increased their total body mass by the time they reached the middle of their childhood.[17] As a result of our findings, we noticed that the metformin-exposed group had a similar birth weight as that of insulin-exposed group. In yet another study, it was discovered by Slagjana Simeonova-Krstevska and colleagues that the rate of preterm births is significantly higher in the group that was treated with insulin as opposed to the group that was treated with metformin. In a similar manner, we found that the mean gestational age in the group that was exposed to insulin was 37.1±1.0 weeks, whereas the mean gestational age in the group that was exposed to metformin was 37.9±1.1 weeks.[18]

Despite the fact that metformin has been used in pregnancy for 40 years, the controversy over its safety and appropriate use persists, with guidelines differing from country to country.[19] Its ease of administration, low incidence of adverse effects, and lack of the need for a cold chain make it an appealing first-line therapy for the high-risk population with whom we work in Pakistan. This will also eliminate delays in the start of therapy, which will reduce morbidities caused by delays in receiving specialised care.

CONCLUSION

Better maternal glycemic control has been linked to the usage of metformin during pregnancy. In terms of patient compliance, the medicine is well tolerated. Patients with gestational diabetes mellitus who took Metformin experienced fewer neonatal problems than those who used insulin.

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