Metformin and Insulin Therapy in GDM – Comparison of Maternal and Neonatal Complications

Syed Yasir Hussain1*, Mehjabeen1, Afshan Rafeeq2, Mansoor Ahmed3

1Department of Pharmacology, Faculty of Pharmacy, Federal Urdu University of Arts, Science and Technology, Karachi, Pakistan
2Department of Pharmacology, Faculty of Pharmacy, University of Karachi, Karachi, Pakistan
3Research Institute of Pharmaceutical Science, University of Karachi, Karachi, Pakistan
*Corresponding Author: syasir_huss@hotmail.com

Received 12 February 2016 ; Accepted 16 April 2016

Abstract. Gestational diabetes mellitus (GDM) is very common medical condition of pregnancy, associated with maternal and neonatal adverse outcomes. Studies suggested that maternal and neonatal complications of gestational diabetes mellitus can be reduced by diet and life style modification, treatment with oral hypoglycemic agent and insulin. The present study was performed to compare the maternal and neonatal consequences in gestational diabetes mellitus patients, those treated with metformin with those treated with insulin. Retrospective study was performed including 31 gestational diabetes mellitus patients treated with metformin and 31 gestational diabetes mellitus patients treated with insulin. It was found that there was no difference between metformin treated patients and insulin treated patients regarding maternal outcomes (body mass index, pregnancy induced hypertension, preeclampsia, candidiasis etc.). Cesarean deliveries were significantly higher in metformin treated group than in insulin group (p<0.05). Forty eight percent GDM patients treated with metformin underwent cesarean delivery, the most of full term live birth compare with metformin. Forty eight percent GDM patients treated with metformin group underwent cesarean delivery. The frequency of full term live birth was higher in insulin group than in metformin group (p<0.01). Fifty five percent patients treated with metformin stay at hospital more than 24 hours. There was no difference between the groups in other neonatal outcomes (preterm live birth, macrosomia, still birth, miscarriage, respiratory distress syndrome etc.). The only incidence of neonatal hypoglycemia was higher in insulin group. The data of present retrospective study suggests that there was no major difference in maternal and neonatal outcomes in metformin and insulin treated GDM patients, both drugs showed good glycemic control in GDM patients which resulted in reduction of maternal and perinatal complications, furthermore insulin was not associated with the higher incidence of cesarean section, post natal stay at hospital and preterm live birth compare with metformin.

Keywords: Gestational diabetes mellitus, insulin, maternal, metformin, neonatal

1. INTRODUCTION

Gestational diabetes mellitus (GDM), the most common medical condition and associated with many adverse consequences over the short and lasting for both mother and their children (Maymone et al., 2011). Usually, women with GDM show no symptoms, but certain women may exhibit many symptoms like more thirst, more urination, lethargy, nausea, vomiting, infection in bladder, yeast infections and blurry vision (Yin et al, 2014). The aim of treatment / management is to lower the risks of GDM for mother and child. Scientific evidence is showing that managing blood glucose levels can result in lessen serious fetal complications and increased maternal quality of life (Crowther et al., 2005; Sermer et al., 1995).

Consequences of GDM faced by mother are more chance to develop excessive weight, preeclampsia, undergo cesarean delivery, development of Type 2 diabetes in later in the life (Arshad et al., 2014), hypertensive disorder (Joffe et al., 2008), pregnancy induced hypertension, recurrent vaginal infections (Tamas and Kerenyi, 2000). Difficulties of GDM run into in newborns for example, more birth weight, respiratory distress syndrome (RDS), hypoglycemia, hyperbilirubinemia, polycythemia, hypocalcaemia, congenital anomalies, intrauterine deaths, still births (Arshad et al., 2014), tetany, juandice (Tamas and Kerenyi, 2000). In pregnancy with GDM, the fetus is exposed to high level of glucose which results in excess fetal growth, impaired insulin secretion and decreased insulin sensitivity (Crowther et al., 2005), the short term complications are shoulder dystocia and
infant hypoglycemia (Ferrara et al., 2009), type 2 diabetes mellitus and obesity are the possibility for neonates whose mothers with GDM (Declercq et al., 2007).

There are many studies available to assessing Metformin safety and efficacy. The largest study is known as Metformin in Gestational Diabetes (MiG) study by Rowan et al., (2008) this study involved 751 pregnant women with GDM. Globally, the results of MiG study have been in the favor of Metformin. Study compared the women taking insulin with those taking Metformin; result showed there have no differences in following: maternal glycemic control, congenital anomalies, macrosomia and neonatal hypoglycemia. Furthermore, it has been reported that maternal hypoglycemia rates was lessen in metformin as compare to insulin regimes. However, in metformin group in Mig trial was related with increase occurrence of premature, this is unrecognized concern of the labor process (Rowan et al., 2008). Later, Balani et al. (2009) and Mesdaghinia et al. (2013) reported lower rates of prematurity with Metformin in comparison to insulin.

Other studies has shown that extent of increasing number of diabetes with associated risk of increase in perinatal mortality and morbidity lead to search of other way for safe and effective medical therapy of diabetes in pregnancy. Studies have shown that particular oral hypoglycemic agents (OHA) (Food and Drug Administration (FDA) category B: Glibenclamide and Metformin) are safe in pregnancy (Langer, 2003 and 2007; Ho et al., 2007).

This study was performed to compare the maternal and neonatal consequences in women with gestational diabetes mellitus, those treated with metformin with those treated with insulin.

2. MATERIALS AND METHODS

2.1. Search Strategy

This was a retrospective study conducted on all gestational diabetes mellitus (GDM) pregnancies, where metformin and insulin were used from 2012-2014 at Tertiary care Hospital in Karachi-Pakistan. Data was retrieved from medical record files of GDM patients, who were admitted in the hospital (Ekpebeigh et al., 2007; Tertiit et al., 2008).

2.2. Selection of Patients

The study was retrospective study, was conducted on 62 pregnant patients with gestational diabetes mellitus treated with insulin and metformin at tertiary care hospital in Karachi- Pakistan. All patients were equally divided into two groups, group 1 consisting of 31 gestational diabetes mellitus patients treated with metformin and group 2 consisting of 31 gestational diabetes mellitus patients treated with insulin (Ekpebeigh et al., 2007; Tertiit et al., 2008).

2.3. Procedures

A structured Performa was used to collect data from medical record files of all pregnant patients with GDM and treated with either insulin or metformin. Unique study numbers were assigned to all eligible patients and following data were extracted from their medical record files:

1. Demographic data:
   (a) Patient MR number (kept confidential); (b) Patient’s age; (c) Patient’s weight; (d) Name of drug was given to patient after GDM has been diagnosed; (e) Maternal outcomes; (f) Type of delivery; (g) Body mass index; (h) Pregnancy induced hypertension (PIH); (i) Preeclampsia; (j) Candidiasis; (k) Urinary tract infection; (l) Neonatal outcomes; (m) Full term delivery; (n) Preterm delivery (< 37 weeks of gestation); (o) Still birth; (p) Miscarriage; (q) Birth weight of neonates; (r) Postnatal stay at hospital; (s) Respiratory distress syndrome; (t) Hypoglycemia; (u) Hyperbiliuribinemia

2.4. Confidentiality

Patient identification was kept confidential. Unique study number was assigned to them. Only data extracted from medical records were used.

2.5. Statistical Analysis

This retrospective study was statistically analyzed by presenting result in frequency (Percentage) for qualitative variables and for quantitative variables results were presented as mean ± standard deviation. Conditional logistic regression was performed to compare the qualitative variables between groups. Linear regression was performed for compared the continuous variables between groups. All analysis was conducted by using statistical package for social sciences SPSS. P – values <0.05 were considered statistically significant.

3. RESULTS AND DISCUSSIONS

3.1. Result

Figures 1 and 2 show the effect of metformin and insulin on maternal outcomes of GDM patients. Data analyzed by binary logistic regression (df =1, 95).

Regression analysis by Wald test showed that hyperemesis is non-significantly more (14/31, 45%) in
metformin and marginal significantly lowered (10/31, 32%, p≤0.05) in insulin, however frequency of anemia was non-significantly higher (19/31, 61%) in metformin than in insulin (12/31, 39%). Pregnancy induced hypertension was much significantly more (7/31, 23%, p≤0.005) in metformin and highly significantly lowered (1/31, 3%, p≤0.001) in insulin, similarly preeclampsia was much significantly more (6/31, 19%, p≤0.005) in metformin and highly significantly lowered (1/31, 3%, p≤0.001) in insulin. Incidence of candidiasis was significantly lowered (10/31, 32%, p≤0.05) in metformin and highly significantly lowered (8/31, 26%, p≤0.05) in insulin, whereas urinary tract infection was significantly more (31, 31%, p≤0.05) in metformin and highly significantly lower (3/31, 10%, p≤0.001) in insulin.

Figures 3 and 4 showed the effect of metformin and insulin on perinatal outcomes of GDM patients. Data analyzed by binary logistic regression (df =1, 95).

Regression analysis by Wald test showed that full term live birth was highly significantly more (28/31, 90%, p≤0.001) in insulin and non-significantly lowered (18/31, 58%) in metformin whereas preterm live birth was significantly more (8/31, 26%, p≤0.05) in metformin and highly significant lowered (1/31, 3%, p≤0.001) in insulin. Incidence of still birth and miscarriage was highly significantly increased (3/31, 10%, p≤0.001), (2/31, 6.5%, p≤0.001) in metformin respectively and in insulin the both incidence was highly significantly reduced (1/31, 3%, p≤0.001). Respiratory distress syndrome was highly significantly increased (5/31, 16%, p≤0.001) in metformin and highly significantly lowered (4/31, 13%, p≤0.001) in insulin however hyperbilirubinemia was non-significantly increased (15/31, 48%) in metformin and significantly lowered (8/31, 26%, p≤0.05) in insulin. Prevalence of hypoglycemia was highly significantly lowered (2/31, 65%, p≤0.001) in metformin and significantly higher (10/31, 32%, p≤0.05) in insulin. Postnatal stay in hospital more than 24 hours was non-significantly increased (17/31, 55%) in metformin and also non-significantly decreased (4/31, 13%) in insulin.

Figures 5 and 6 showed the effect of metformin and insulin on type of delivery of GDM patients. Data analyzed by binary logistic regression (df =1, 95).

Regression analysis by Wald test showed incidence of cesarean section was non-significantly increased (15/31, 48%) in metformin and significantly lowered (9/31, 29%, p≤0.05) in insulin however vaginal delivery was non-significantly lowered (16/31, 52%) in metformin and significantly increased (22/31, 71%, p≤0.05) in insulin.

3.2. Discussion

Gestational diabetes mellitus is a metabolic disorder. Pakistani women are also considered to be at a high risk for developing gestational diabetes similarly to other members of the Asian race (Jawa et al., 2011). The present study explored that there was no significant difference in maternal outcome (preeclampsia, candidiasis, pregnancy induced hypertension, urinary tract infection) and neonatal complications (miscarriage, still birth, respiratory syndrome, macrosomia) between metformin treated group and insulin treated group. Several studies have shown same outcomes, there was no difference between the metformin and insulin group, comparing gestational hypertension, preeclampsia (Balani et al., 2009), and vaginal infection (Tamas and Kerenyi, 2011).
Hussain et al.
Metformin and Insulin Therapy in GDM – Comparison of Maternal and Neonatal Complications

Treatment of gestational diabetes mellitus by diet, exercise, oral hypoglycemic agents and insulin are also helpful in the control of the adverse consequences of maternal outcomes (Khan et al., 2013).

**Fig. 3**: Effect of metformin on perinatal outcomes of GDM patients
Values are frequency (percentage), (n=31). Significant differences by Wald test *p<0.05, **p<0.005, ***p<0.001 compared maternal outcomes to metformin and insulin in GDM patients, following Binary logistic regression df (1, 95).

**Fig. 4**: Effect of insulin on perinatal outcomes of GDM patients

Treatment of GDM resulted in significantly reduction in neonatal outcomes (Langer et al., 2010). The women with diabetes in pregnancy must be good control regardless of the type of diabetes which lessens the possibility of neonatal consequences (Kalra and Anakal, 2013). Present study was showed a minor increase in pregnancy induced hypertension, preeclampsia and urinary tract infection in metformin group.

Finding of present study was revealed that preterm live births were higher in metformin group compared with insulin group; similar result was reported by Rowan et al. (2008), but Goh et al. (2011) showed women treated with insulin had increased rate of preterm live birth (Goh et al., 2011). This increased rate of preterm live birth was not related with higher rates of other neonatal complications.

In present study rate of cesarean delivery was reduce in insulin treated group and it was similar to Turok et al study. However Balani et al. (2009) study showed there was no statistically significant difference between the insulin and metformin group. The incidence of postnatal stay at hospital more than 24 hours was higher in metformin compared with insulin; this longer in postnatal stay may be due to increased cesarean delivery rate in metformin group. Rate of neonatal hypoglycemia was reduced in metformin group (6.5%) compared with insulin group (32%), similar findings were reported in Rowan et al. (2008), Goh et al. (2011) and Tertti et al. (2008).
4. CONCLUSION

In conclusion, the result of this retrospective study shows overall there was no significant difference in maternal and neonatal outcomes between the metformin and insulin group. The initiation of insulin as a primary treatment in gestational diabetes mellitus patients may not be associated with preterm live births and cesarean section.

5. RECOMMENDATION

This work could further be extended to observe the perinatal and postnatal quality of life (QOL) of women with GDM with healthy pregnant women. This work could also be extended to observe the maternal and perinatal complication in metformin group, metformin plus life style modification group, insulin group and insulin plus life style modification group in women with GDM.

REFERENCES


