Original Research Article

Comparison of maternal and perinatal outcome among patients with gestational diabetes treated with either metformin or insulin – an observational prospective cohort study

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Abstract

Introduction: Insulin therapy is the current gold standard in the treatment of gestational diabetes. Safe and effective oral therapy would be more acceptable to the pregnant population. We did this study to compare the maternal and fetal outcomes among patients treated with insulin and metformin in gestational diabetes. **Materials and Methods:** We did an observational prospective cohort study on 123 consecutive patients diagnosed to have gestational diabetes. Patients included in the study were followed up for the rest of the antenatal period, during labour and for 6 weeks after delivery for maternal and perinatal outcomes. **Results:** There was no significant difference between the two groups in respect to all the maternal and perinatal outcomes studied. Among the 61 patients in the metformin group 55 (90%) attained glycemic target with metformin alone while 6 (10%) had to be given insulin along with metformin. **Conclusion:** Metformin appears to be an effective treatment for gestational diabetes. Metformin is more acceptable to women due to its ease of administration and lower cost as compared to insulin. A drawback which is observed with the use of metformin is the inability of metformin therapy alone to achieve good glycemic control and thereby leading to adverse consequences in the fetus.

Keywords: Gestational diabetes, Insulin, Metformin

Introduction

The prevalence of type 2 diabetes mellitus in India is on the rise and the number of women with gestational diabetes is also following the same trend. Insulin therapy is the current gold standard in the treatment of gestational diabetes [1]. The drawbacks of insulin include among others, difficulty in motivating the patients to take insulin, weight gain, risk of hypoglycaemia, practical difficulties like storage and multiple injections.

These difficulties are more among people of lower socioeconomic status. Safe and effective oral therapy would be more acceptable to the pregnant population. Oral hypoglycaemic agents were discouraged in pregnancy, mainly fearing terratogenicity. Recently it has been shown that oral agents like metformin, glibenclamide and acarbose could be safely used in pregnant patients with diabetes [2]. But the use of oral agents is not universally accepted. MIG trial studied the use of metformin in the treatment of gestational diabetes [3]. We did this study to compare the maternal and fetal outcomes among patients treated with insulin and metformin in gestational diabetes.

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Materials and Methods

Study design- We did an observational prospective cohort study.

Participants- The study population included 123 consecutive patients diagnosed to have gestational diabetes.

Setting- The study was done in the department of obstetrics and gynecology of Government Medical College Thrissur, tertiary care centre in the central part of Kerala.

Exclusion criteria- Those patients who were diagnosed with diabetes prior to pregnancy and those with fasting plasma glucose of > 126 mg% were excluded from the study.

Inclusion criteria- All patients attending the antenatal clinic were screened for diabetes with fasting blood sugar. Those who had fasting blood glucose 92 - 125 mg% were considered to have gestational diabetes mellitus (GDM) [4] and were included in the study.

For those pregnant ladies who had fasting plasma glucose of <92mg %, oral glucose tolerance test was done at 24-28 weeks gestation as per International Association of Diabetes and Pregnancy Study Group guidelines. If the fasting plasma glucose after 75 g of glucose was >92 mg% or the 1 hour value was >180 mg% or the 2 hour value was >153% they were diagnosed to have GDM. Those patients diagnosed with GDM who achieved glycemic targets (pre-prandial capillary glucose <95 mg%, 1 hour post prandial <140 mg% and 2 hour <120 mg%) by life style modifications –medical nutrition therapy and exercise were excluded from the study. If glycemic target is not achieved within 2 weeks, treatment was started with metformin or insulin. The two groups were comparable regarding their baseline characteristics like age, socioeconomic status, body mass index, past obstetric history and family history of gestational diabetes. Patients included in the study were followed up for the rest of the antenatal period, during labour and for 6 weeks after delivery for maternal and perinatal outcomes with respect to the following parameters. Ante partum parameters included threatened abortion, infections, hypertension, polyhydramnios, preterm labour, ketoacidosis, adequacy of blood sugar control, preterm premature rupture of membrane, premature rupture of membrane. Intrapartum parameters which were studied included type of delivery, genital tract injury, and shoulder dystocia. Post partum parameters were postpartum haemorrhage and post partum infections. The perinatal parameters which were analysed included congenital anomalies, prematurity, macrosomia, perinatal mortality, neonatal hypoglycaemia, hypocalcaemia, hyperbilirubinemia respiratory distress, APGAR score at birth, neonatal ICU admission, and neonatal death. Statistical methods. Statistical analysis was done using SPSS 16 soft ware. Quantitative data were expressed as mean ± standard deviation. Qualitative data was expressed as percentages. The statistical tests used included chi square test. Chi square test was applied to find out the significance of association. P value of less than 0.05 was taken as significant.

Results

Table-1: Showing the baseline characteristics of the patients in the two groups.

Characteristic	Metformin n (%)	Insulin n (%)	95%CI
Age			
<19 years	nil	nil	
20-24years	5(8)	4(7)	
25-29 years	30(49)	29(47)	
30-34years	26(43)	28(45)	
>35years	nil	1(2)	
Total	61	62	
Parity			
Primi	30(49.2)	25(40)	
Multipara	30(49.2)	36(58)	
Grand multipara	1(.8)	1(1)	
Socioeconomic status			
APL	11(18)	14(23)	
BPL	50(82)	48(77)	0.3-1.8
BMI			
Normal(19-24)	24(40)	21(34)	
Overweight(25-29)	30(50)	36(58)	0.4-1.6
Obese (>30)	6(10)	5(8)	
Previous birth weight			
>4.5 kg	2(3)	4(7)	
3.5-4.4 kg	16(26)	17(27)	0.08-3
2.5-3.4 kg	4(7)	3(5)	
<2.5 kg	1(2)	1(2)	
Past history of GDM	7(44%)	9(56%)	0.3-2.1
Past history of HT	5(39%)	8(61%)	0.2-2
History-anomalous baby	1(25%)	3(75%)	0.03-3.2
Family history of GDM	28(45%)	34(55%)	0.3-1.4

There were 61 patients in the metformin group and 62 patients in the insulin group. Majority of the patients in both the groups belonged to the age group of 25-34 years. The two groups were similar with regards their base line characteristics.

Table-2: Comparing the maternal outcome in the metformin and insulin groups.

Parameter	Metformin n (%)	Insulin n (%)	95% CI
History of threatened abortion	5(56%)	4(44%)	0.3-5
Infections	20(50%)	20(50%)	0.5-2.1
Hypertension			
Gestational hypertension	5(42%)	7(58%)	0.2-2.3
Mild preeclampsia	6(60%)	4(40%)	0.4-6
Severe preeclampsia	4(57%)	3(43%)	0.3-6.4
Preterm PROM	8(57%)	6(43%)	0.5-4.3
PROM	8(47%)	9(53%)	0.4-3
Polyhydramnios	3(38%)	5(62%)	0.1-2.6
Preterm labour	10(56%)	8(44%)	0.5-3.7
Ketoacidosis	nil	nil	
Blood sugar control	55(90%)	62(100%)	0.38-0.57
Abdominal circumference	9(43%)	12(57%)	0.3-1.9
Induced labour	34(49%)	36(51%)	0.5-2.2
Assisted delivery	24(51%)	23(49%)	0.5-2.3
Genital tract injury	1(33%)	2(67%)	0.04-5.6
Shoulder dystocia	1(50%)	1(50%)	0.06-16
Postpartum haemorrhage	5(46%)	6(54%)	0.2-2.9
Postpartum infection	4(57%)	3(43%)	0.3-6.4
GTT after 6 weeks	5(33%)	10(67%)	0.2-2.4

Of the 40(33%) patients who had infection in the antenatal period the commonest was vulvovaginitis in 19(15%) followed by urinary tract infection 13(11%), respiratory infection 8(7%). 12(10%) of the study population had gestational hypertension, 10(8%) had mild preeclampsia, 7(6%) had severe preeclampsia.

There was no significant difference between the two groups in respect to all the maternal and perinatal outcomes studied. Among the 61 patients in the metformin group 55 (90%) attained glycemic target with metformin alone while 6(10%) had to be given insulin along with metformin. All the 62 patients who were started on insulin achieved glycemic target. GTT was done in 66 patients at 6 weeks post partum and was abnormal in 15(23%)

Table-3: Showing the neonatal outcome in the metformin and insulin groups.

Parameter	Metformin n(%)	Insulin n(%)	95%CI
Congenital anomalies	4(40%)	6(60%)	0.18-2.4
Prematurity	10(56%)	8(44%)	0.5-3.6
Macrosomia	4(40%)	6(60%)	0.18-2.4
IUD	nil	nil	
Neonatal hypoglycaemia	10(42%)	14(58%)	0.3-1.7
Hypocalcaemia	1(20%)	4(80%)	0.02-2.2
Respiratory distress	2(33%)	4(67%)	0.08-2.8
Hyperbilirubinemia	11(44%)	14(56%)	0.3-1.8
Birth trauma	1(50%)	1(50%)	0.06-16
Polycythemia	4(40%)	6(60%)	0.18-2.4
APGAR <7 at 5 minutes	1(50%)	1(50%)	0.06-16
NICU admission	22(44%)	22(44%)	0.5-2.1

Congenital anomalies were seen in 10(8%) which include one each of ventricular septal defect and meningomyelocele and 2 each of hydronephrosis, cleft lip, preauricular skin tag and congenital talipes equino varus.

Discussion

Diabetes mellitus is one of the most important medical problems encountered in pregnancy. Gestational Diabetes Mellitus (GDM) is characterised by glucose intolerance with onset or first recognition in pregnancy [5]. Pregnancy is associated with a state of insulin resistance because of the effect of placental hormones. In normal pregnancy this state of insulin resistance is overcome by pancreatic beta cell hyperplasia and increased insulin levels. GDM results when the beta cells are unable to overcome this insulin resistance [6]. In India GDM has been estimated to affect nearly 5 million women. GDM is associated with adverse outcomes for both mother and child. There is increased risk for macrosomia and other complications in the fetus. A person with GDM is more likely to develop diabetes in later life. Treatment of GDM has been shown to reduce the adverse events. [7].

Nearly 80% of the patients with GDM can be managed with life style modification alone [8]. The pregnant women with higher blood sugar levels will need pharmacological interventions.Insulin is the drug of choice for the treatment of GDM. According to a recent study from India[9] insulin was used by 50.4% of the clinicians resorted to insulin in GDM, which was not controlled by life style modifications.Among the oral hypoglycaemic agents Metformin was used by the majority (53.8%) [8]. Metformin which is a category B drug in pregnancy is now considered an easier alternative to insulin in the management of gestational diabetes mellitus [3]. There are randomised controlled trials which show that there are no differences in the maternal and neonatal outcomes with the use of metformin and insulin [10,11]. At the same time there are also observational studies which show increased risk of pre eclampsia and worse perinatal outcome with the use of metformin [12,13].

Some studies also have shown added advantages with metformin therapy like lesser maternal weight gain [14,15] and lesser fetal macrosomia and neonatal hypoglycaemia [15]. We have observed in this study that there are no significant differences in both the maternal and neonatal outcomes with the use of metformin or insulin. But the main drawback of metformin appears to be the inability to achieve good glycemic control when used as monotherapy and the subsequent inadvertent risk of hyperglycemia to the fetus [1]. In the MIG trial 46.3% of the patients in the metformin group needed additional insulin to maintain glycemic target [3]. Our observation is that only 10% of the patients who were started on metformin monotherapy had to be given additional insulin in order to achieve glycemic target.

Conclusion

Metformin appears to be an effective treatment for gestational diabetes. Metformin is more acceptable to women due to its ease of administration and lower cost as compared to insulin. A drawback which is observed with the use of metformin is the inability of metformin therapy alone to achieve good glycemic control and thereby leading to adverse consequences in the fetus.

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