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Original Research Article

Metformin as a safe and cost effective alternative to insulin in women with Diabetes in pregnancy

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Abstract

There is a substantial rise in diabetes complicating pregnancies in south Asian countries especially India. Until many decades, insulin eras thought to be the only management option to maintain euglycemia in these cases. But metformin can be a safe and convenient alternative in such cases. In this background we have conducted a study I 40 women with diabetes complicating pregnancies and studied the outcome of the mother and neonate in important parameters. Metformin was found to be a safe, effective and cheap alternative to insulin therapy in pregnant diabetic women.

Key words

Gestational diabetes, Insulin, Metformin, Type 2 diabetes, Glycemic status, Hypoglycemia.

Introduction

Diabetes complicating pregnancies are becoming very common in present day obstetric units. Earlier diet or medical nutritional therapy with or without insulin was the only choices for these cases. Oral hypoglycemic agents for diabetic pregnancies like metformin or glybruride have been tried with success by many workers. However insulin therapy was considered the best because of its safety, effectiveness in controlling blood glucose, inability to cross the placenta and fetal safety .But frequent injections, hypoglycemic attacks, cost and hospital admissions to titrate insulin doses are the main disadvantages which stimulated many obstetricians to try metformin in pregnant diabetic women [1, 2, 3, 4].

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Objectives

To compare the usefulness of Metformin over insulin in pregnancies with diabetes and non responding to diet management alone. The outcomes measured were maternal glycemic control, antenatal complications, perinatal outcome and cost of the treatment.

Material and methods

This was a prospective observational study done over 1 year period from January to December 2014.

Inclusion criteria

Antenatal woman with Type 2 DM and GDM complicating not responding to diet alone was included.

Exclusion criteria

Type 1 DM, BOH, twins and other obstetric high risk conditions.

Patients were diagnosed as GDM after 100 gm GTT following positive glucose challenge with 50 gm glucose load. If 2 or more glucose values in a 3 hr GTT were abnormal, GDM was diagnosed. Women with known Type 2 DM and those GDM cases who failed to respond to diet alone in 2 weeks were included for the study. 40 women with diabetes complicating their pregnancies and non responding to diet alone were categorized into 2 groups. Group 1 received Metformin 500 mg to 1500 mg in divided doses as per the requirement and group 2 received Insulin intermediate acting (mixtard) and short acting (actrapid) whenever needed in doses according to their glycemic control. Both groups were matched for age, parity, BMI and pre-treatment glycemic levels.

Glycemic profile FBS, 2HR PP were done weekly for all cases. The goal of therapy was to maintain FBS at <100 mg/dl and PPBS at << 120 mg/dl. USG was done at regular intervals for birth weight, amniotic fluid index and fetal well being. All babies were monitored for asphyxia, hypoglycemia, hyperbilirubinemia and hypocalcemia.

Maternal glycemic control was the primary outcome measure.USG for any macrosomia or fetal compromise and neonatal outcome were secondary outcome measures.

Results

Glycemic control was achieved faster and reached the expected target values earlier in metformin group than with insulin group as per **Table - 1**. Moreover stabilization for adequate glycemic control needed hospitalization with insulin also demanding multiple endocrinologist consultations. In insulin group, there was increased in and around 36th week in 40% cases but not in metformin group.

Table – 1: Maternal parameters.

	Metformin group	**Insulin group**
Glycemic control		
good	19	18
poor	1	2
Cost in Rs (average/day)	20	50 – 100

Maternal weight gain was significantly less in metformin group as compared to insulin group. The incidence of maternal complications generally encountered with diabetes in pregnancy was almost comparable in both the groups as per **Table - 2**.

There were no macrosomic babies in metformin group and 2 babies in insulin group showed macrosomia on USG as per **Table - 3**. Polyhydramnois was significantly higher in

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insulin users in our study. LSCS was done only for obstetric indications and no difference in either of the groups.

Table – 2: Maternal complications in either group.

	Metformin group	Insulin group
Preeclampsia	4	3
UTI	2	1
Preterm labour	nil	1
Vaginitis	nil	nil

Table – 3: USG parameters.

	Metformin group	Insulin group
Estimated birth weight (EBW) in kg		
<4	20	18
>4	--	2
Amniotic fluid index AFI (>20 as abnormal)		
normal	20	15
abnormal	--	5
Fetal compromise	nil	nil

Shoulder dystocia was encountered in 2 babies one in each group. Neonatal Intensive Care Unit (NICU) admission rate was higher in babies whose mothers received insulin as compared to metformin mothers in the present study. More over hypoglycemia and hypocalcemia were not encountered in metformin baby group while the insulin group babies showed these complications as per **Table - 4**. There were no perinatal deaths in either group.

Discussion

In this prospective observational study, we observed metformin is an effective, safe and convenient alternative to insulin in gestational diabetes mellitus (GDM) or Type 2 DM complicating pregnancies who failed to respond to medical nutrition therapy (MNT) alone.

Table – 4: Neonatal outcome.

	Metformin group	Insulin group
APGAR 8-10	20	20
Hypoglycemia	nil	4
Hyperbilirubinemia	nil	2
NICU admission	nil	4

Insulin improves the glycemic profile by way of substituting the deficiency while metformin corrects the underlying insulin resistance. Maternal glycemic control and complications are comparable or even slightly better in metformin users than in insulin group [5]. Further patients need not have to take multiple injections or admissions to dose adjustments as is the case with insulin. This is the most attracting feature to the woman from their perspective [6, 7, 8].

The outcomes measured in terms of maternal complications, perinatal outcome, glycemic control were almost same in either group. Neonatal hypoglycemia, Hyperbilirubinemia and NICU admission rates were slightly higher in insulin group as compared to Metformin group. The cost also is much lower in Metformin users than with Insulin users [9, 10]**.**

The present study was comparable to the studies by Coetzee, et al. [3], Hellmuth, et al. [5] and Lavanya Rai, et al. [10] from India as per **Table - 5**. Though our study group is small, it brought out significant conclusions.

Conclusion

- Metformin is a safe, effective and cheap alternative in pregnant diabetic women.

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- Metformin targets insulin resistance unlike Insulin.
- Frequent dose adjustments not required with Metformin, unlike insulin.
- Patient compliance better with Metformin.
- Glycemic control of Metformin comparable with and faster than with insulin.
- Metformin therapy more practical and convenient first line modality than insulin, especially in India and must be tried as first line in pregnant diabetic women.
- Milder forms of GDM respond well to Metformin and severe forms only require insulin as add on therapy which is less cheap than insulin alone as primary therapy.
- No major maternal problems in either group except polyhydramnios in 2 cases on insulin.
- Neonatal hypoglycemia higher and hyperbilirubinemia slightly more in insulin group.

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Table – 5: Other studies.

	Maternal	**Neonatal**
Coetzee, et al. [3]	Glycemic control better in insulin users	Hyperbilirubinemia more in metformin group
Hellmuth, et al. [5]	Glycemic control same in both groups but preeclampsia more in metformin users	No difference in perinatal outcome in either group
Lavanya, et al. [10]	Maternal glycemic control better and complications less in metformin group	Neonatal hypoglycemia, hyper bilirubinemia and NICU admissions are less in metformin group