Oral Hypoglycemic Glibenclamide: Can it be a Substitute to Insulin in the Management of Gestational Diabetes Mellitus? A Comparative Study

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INTRODUCTION

Gestational diabetes mellitus is one of the most common medical complications of pregnancy and is associated with adverse maternal and fetal outcome. Gestational diabetes is increasing globally and India is not an exception. Study conducted by V Seshiah et al in 2004 concluded that there is an overall prevalence of 17.7% of gestational diabetes mellitus (GDM) in our country. They also concluded that this high prevalence of GDM necessitates a universal screening for glucose intolerance in pregnancy in Indian women. The principal approach to treatment of GDM is diet control with addition of insulin when diet alone is not sufficient. Over the years, insulin was the only option and oral hypoglycemic agents were avoided due to the fear of teratogenicity as well as fetal hyperinsulinemia and hypoglycemia. Insulin therapy is effective in achieving appropriate levels of glycemia, but it involves multiple daily injections and patient compliance is often suboptimal as women prefer to take tablets rather than multiple injections. The use of oral agents is a pragmatic alternative to insulin therapy because of easy administration and patient satisfaction due to noninvasive treatment. Glyburide (micronized form of glibenclamide) belonging to sulfonylurea group has been studied in many randomized control trials and has shown to achieve similar levels of glycemic control as insulin. It was also shown that this drug does not cross the placenta and hence can be safely administered in the second trimester of pregnancy as an alternative to insulin. Hence, we undertook a study to compare insulin and glibenclamide for treatment of GDM.

MATERIALS AND METHODS

The study was conducted at Department of Gynecology and Obstetrics, Medical College and Hospital, Kolkata, from 1st January 2010 to 31st December 2010, after taking clearance from all the women participating in the study. Any patient with diabetes mellitus during pregnancy was excluded. All women with gestational diabetes mellitus were randomized into two groups. The first group (group A) was treated with glibenclamide with a starting dose of 2.5 mg subcutaneously three times daily and increased weekly by 2.5 mg up to a maximum of 20 mg (group A, n = 30) or insulin (group B, n = 30). In group A, glibenclamide was given 2.5 mg orally in morning and doses were increased weekly by 2.5 mg up to a maximum of 20 mg and doses >7.5 mg were given in two divided doses. In group B, insulin 0.7 units per kilogram of body weight at admission was given subcutaneously three times daily and increased weekly as necessary. Self monitoring of blood glucose with glucometer was done. Blood glucose was also measured from the laboratory every week. Glycosylated hemoglobin (HbA1c) was measured before initiation of therapy and repeated in the third trimester before confinement. Terminations of pregnancy in both the groups were done between 37 and 38 weeks. The infant birth weight, blood glucose and serum bilirubin were also recorded in all cases.

POSSIBLE PLAGIARISM:

1. They also concluded that this high prevalence of GDM necessitates a universal screening for glucose intolerance in pregnancy in Indian women. The principal approach to treatment of GDM is diet control with addition of insulin when diet alone is not sufficient. Over the years, insulin was the only option and oral hypoglycemic agents were avoided due to the fear of teratogenicity as well as fetal hyperinsulinemia and hypoglycemia. Insulin therapy is effective in achieving appropriate levels of glycemia, but it involves multiple daily injections and patient compliance is often suboptimal as women prefer to take tablets rather than multiple injections. The use of oral agents is a pragmatic alternative to insulin therapy because of easy administration and patient satisfaction due to noninvasive treatment. Glyburide (micronized form of glibenclamide) belonging to sulfonylurea group has been studied in many randomized control trials and has shown to achieve similar levels of glycemic control as insulin. It was also shown that this drug does not cross the placenta and hence can be safely administered in the second trimester of pregnancy as an alternative to insulin. Hence, we undertook a study to compare insulin and glibenclamide for treatment of GDM.

2. The present study showed that the two groups had similar glycaemic status (fasting blood sugar in group A was 103.5 ± 14.62 mg/dl whereas in group B it was 109.3 ± 19.63 mg/dl and 194.3 ± 18.47 mg/dl) at the time of entry into the study. The two groups also showed similar levels of glycaemic control just before confinement (fasting blood sugar in group A was 88.23 ± 6.55 mg/dl and postprandial blood sugar was 122.7 ± 10.3 mg/dl whereas in group B it was 88.17 ± 12.38 mg/dl) and there was no significant statistical difference in the two groups (p > 0.05). The perinatal outcomes in both the groups were also nearly same. There was no significant difference in birth weight, blood sugar level of neonates and complications between the two groups. There was no case of macrosomia in the two groups and the number of infants large for gestational age (LGA) was four in group A and two in group B. Hypoglycemia in newborn was slightly higher in the group A compared to group B (4 and 3 respectively).

Conclusion: From our study, it is evident that the use of oral agents is a pragmatic alternative to insulin therapy in cases of gestational diabetes because of similar glycemic control, ease of administration and better patient compliance due to noninvasive treatment.

KEYWORDS: Gestational diabetes mellitus (GDM), Glibenclamide, Insulin, Glycemic, Hypoglycemia, Macrosomia.
Oral Hypoglycemic Glibenclamide: Can it be a Substitute to Insulin in the Management of Gestational Diabetes Mellitus?

A total of 60 women with GDM were randomly divided into two groups: Group A (n = 30, received glibenclamide) and group B (n = 30, received insulin). The two groups were similar in terms of mean age, BMI and gestational age at the initiation of treatment (Table 1). The present study showed that the two groups had similar glycemic status (fasting blood sugar in group A was 103.5 ± 14.62 mg/dl and postprandial blood sugar was 184.1 ± 20.46 mg/dl whereas in group B it was 109.3 ± 19.63 mg/dl and 194.3 ± 18.47 mg/dl) at the time of entry into the study (Table 2). There was no statistical difference in the two groups in their screening blood glucose (p > 0.05). The two groups also showed similar levels of glycemic control (fasting blood sugar in group A was 88.23 ± 6.55 mg/dl and postprandial blood sugar was 122.7 ± 10.3 mg/dl whereas in group B it was 88.17 mg/dl and 128 ± 12.38 mg/dl) before confinement (Table 3). Glycosylated hemoglobin (HbA1c) at the time of entry into the study (HbA1c in group A was 6.25 ± 0.60% and in group B was 6.46 ± 0.77%) and before confinement (HbA1c in group A was 6.08 ± 0.55% and in group B was 6.24 ± 0.57%) was also similar in both groups with no significant statistical difference (p > 0.05) between the two groups. Group B receiving insulin required more frequent dose titration compared to group A receiving glibenclamide. There were no documented episodes of hypoglycemia in the two groups; however, two patients in the glibenclamide group had occasional symptoms suggestive of hypoglycemia in the morning before breakfast. The majority of the patients in the two groups had delivered by elective cesarian section at 37 to 38 weeks. The perinatal outcomes in both the groups were also nearly same. There was no significant difference in birth weight, blood sugar and complications between the two groups (Table 4). There was no case of macrosomia in both groups and the number of infants large for gestational age (LGA) was four in group A and two in group B. It was found that these LGA infants were born to those women who initiated their treatment late at 30 to 33 weeks. Hypoglycemia in newborn was slightly higher in the group A compared to group B (4 and 3 respectively, Table 4). Two infants in the group A had hyperbilirubinemia requiring phototherapy. One infant in the group A had congenital anomaly in the form of spina bifida occulta. There was one incident of sudden intrauterine fetal death in the group B. One infant in group B was admitted in NICU due to acute respiratory distress syndrome (ARDS).

DISCUSSION

The present clinical study was done to compare insulin and glibenclamide for treatment of GDM. In our study 60 women with GDM were divided into two groups—group A (n = 30,
received glibenclamide) and group B (n = 30, received insulin). The two groups had similar glycemic status (fasting blood sugar in group A was 103.5 ± 14.62 mg/dl and postprandial blood sugar was 184.1 ± 20.46 mg/dl, whereas in group B, it was 109.3 ± 19.63 mg/dl and 194.3 ± 18.47 mg/dl) at the time of entry into the study. The fasting blood sugar (FBS) in group A (treated with glibenclamide) just before confinement was 88.23 ± 6.55 mg/dl and postprandial blood sugar (PPBS) after 75 gm oral glucose was 122.7 ± 10.3 mg/dl whereas in group B (treated with insulin) it was 88.17 ± 8.44 mg/dl and 128 ± 12.38 mg/dl. Therefore, the two groups showed similar levels of glycemic control before confinement with no significant statistical difference (p > 0.05) between the two groups. This study showed that the glycemic control in GDM treated with insulin and glibenclamide was essentially the same. Similar findings were also reported by Langer O et al 2004.

Glyburide (micronized form of glibenclamide) has been studied in many randomized control trials and has shown to achieve similar levels of glycemic control before confinement with no significant statistical difference (p > 0.05) between the two groups. This study showed that the glycemic control in GDM treated with insulin and glibenclamide was essentially the same. Similar findings were also reported by Langer O et al 2004.

The perinatal outcomes in both the groups were also nearly same. There was no significant difference in birth weight, blood sugar and complications between the two groups. There was no case of macrosomia in the two groups and the number of infants large for gestational age (LGA) was four in group A and two in group B. Hypoglycemia in newborn was slightly higher in the group A compared to group B (4 and 3 respectively). A cost analytic study conducted by L. Goetzl et al, comparing glyburide and insulin in treatment of GDM showed an average cost saving per pregnant women of US$ 165.84 in favor of glyburide. A cost analysis was not done in our study as both the drugs were freely available through government supply.

**CONCLUSION**

From our study, it is evident that the use of oral glibenclamide for the treatment of gestational diabetes is an alternative to insulin therapy because of similar glycemic control, ease of administration and better patient compliance due to noninvasive treatment.

**REFERENCES**

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