Original Article

EFFICANCY OF GLIBENCLAMIDE FOR THE CONTROL OF GESTATIONAL DIABETES MELLITUS

Quddsia Tanveer[*], Anees Faima[**], Mubashra Naz[***]
[*]Senior registrar Gynae Department Jinnah Hospital, Lahore,
[**]Senior registrar Gynae Department, Madina Teaching Hospital, UMDC, Faisalabad.
[***]Associate Professor, HOD Gynae, Madina Teaching Hospital, UMDC, Faisalabad.

ABSTRACT

OBJECTIVE:

To evaluate the efficacy of glibenclamide for control of gestational diabetes mellitus.

STUDY DESIGN:

An interventional: Quasi-experimental

PLACE AND DURATION OF STUDY:

Study was carried out at Obstetrics & Gynaecology department of Punjab Medical College and affiliated hospital, Faisalabad. The study duration was six months from Apr 2008 to Sep 2008.

MATERIAL AND METHOD:

Total of 50 Patients with gestational diabetes mellitus (GDM) were treated with oral glibenclamide. Achievement of satisfactory glycemic control, maternal hypoglycemia, complications like macrosomia, neonatal hypoglycemia, hypocalcaemia, neonatal polycythemia, gross neonatal congenital anomalies, transient tachypnea of new born (TTN) and need for admission in neonatal intensive care unit were main outcome measures.

RESULTS:

Of the 50 patients treated with glibenclamide, 40 (80%) achieved satisfactory glucose control. Maternal hypoglycemic events were found in 1 (2%), macrosomia in 07(14%), neonatal hypoglycemia in 05(10%), transient tachypnea of newborn in 4(8%) and need for admission to neonatology in 09 (18%) of cases. No case of gross congenital abnormality, neonatal hypocalcaemia and neonatal polycythemia observed.

SCONCLUSION:

In treatment of GDM, glibenclamide is successful in achieving good glycemic control.

KEY WORDS: Glibenclamide (glyburide), GDM, pregnancy.

INTRODUCTION:

Gestational diabetes mellitus (GDM) is one of the common medical disorders complicating the pregnancy [1]. It is defined as glucose intolerance with onset or first recognition during pregnancy [2]. During pregnancy, 5-14% of women are diagnosed with gestational diabetes mellitus (GDM) and the incidence has been increasing [3,4].

Corresponding Author:
Dr. Quddsia Tanveer
Senior Registrar, Gynae Department,
Jinnah Hospital, Lahore.
E-Mail: drqudsia@live.com

The condition is associated with various poor pregnancy outcomes including miscarriages, congenital malformations, pre-eclampsia, preterm labor, shoulder dystocia, cesarean section, neonatal metabolic complications and increased risk of developing type-2 DM in later life both in the mother and the offspring[5,6]. Treatment reduces serious perinatal morbidity and improves mother's quality of life. While insulin treatment is still the "gold standard" therapy for controlling maternal blood sugar levels, the increasing use of oral anti-diabetic agents such as glyburide and metformin has begun to change standard care[7,8].

Glibenclamide (Glyburide) is a second generation oral sulfonylurea. Considerable data in the literature suggest that glyburide may be a safe alternative to insulin for the treatment of GDM due to its similar efficacy to insulin and its low fetal distribution[9,10]. Insulin therapy has several disadvantages including patient's discomfort, pain, inconvenience of injections and the increased cost. Therefore, finding of an effective alternative is desirable for pregnant patients and their doctors. The rationale of this study was to control the GDM effectively in a convenient way. The option of using glibenclamide is particularly attractive in countries like Pakistan where insulin is not accessible to all who need it because of high cost, administration and storage issues.

MATERIAL AND METHOD:

50 patients attending the antenatal clinic of Punjab Medical College & affiliated hospital Faisalabad, diagnosed as having gestational diabetes mellitus (GDM) on the basis of 75 g oral glucose tolerance test(OGTT) carrying singleton fetuses (confirmed on obstetric ultrasound) between 11-33 weeks of gestation were included in the study. A patient was considered to be having GDM if her fasting blood glucose level is 126mg/dl or 2hours post glucose load blood glucose level is > 140mg/dl as according to WHO criteria. Patients with severe chronic hypertension (history and examination, chronic liver disease (abnormal liver function tests), chronic renal disease (raised blood urea & serum creatinine), patients with pre-existing diabetes mellitus (history), women having complicated gestational diabetes mellitus(GDM) like that associated with congenital abnormalities, polyhydramnios and large for gestational age fetus were excluded from the study (all diagnosed on the basis of ultrasound) to control the confounding variable. Non probability purposive sampling technique was used. Risks i.e. sometimes maternal hypoglycemia, occasionally nausea, vomiting, rarely reversible thrombocytopenia and allergic reactions and benefits i.e; good glycemic control, less cost, less frequent doses, no need of frequent needle pricks as it has oral route of administration were explained to the patients and informed consent was taken. Study was started after taking approval from hospital ethical committee. At the initial visit, they were admitted in antenatal ward and evaluated by taking detailed history including age and socio economic status. Detailed clinical examination was carried out. Serial blood sugar levels monitored (fasting, preprandial and 2 hour post prandial). Patients failing to achieve target blood glucose levels on dietary therapy for at least 3-4 days (as assessed by their blood glucose monitoring in antenatal ward) were assigned to receive glibenclamide.

Glibenclamide was administered as oral drug starting from a dose of 2.5 mg/day with morning meal and the patients were sent home after being taught about home glucose monitoring by glucometer or laboratory. Patients were taught about target blood glucose levels which were; fasting blood sugar level (FBS) 60-108 mg/dl and 2hr post prandial level not more than 126mg/dl. They were recalled weekly, were admitted for 24 hours and dose adjustment was done. Dose was increased weekly by 5mg up to a total of 20mg/ day when necessary after reviewing home glucose monitoring record. Patients were inquired about adverse effects already explained to them. If target values for blood glucose not achieved despite of one week treatment with maximal dose of glibenclamide, treatment was switched to insulin therapy. Time and mode of delivery was decided according to obstetric indications. At delivery, cord blood was taken and sent to look for evidence of hypoglycemia (blood sugar $\leq$40mg/dl), hypocalcaemia (serum calcium

≤7mg/dl), polycythemia (hematocrit>60%). New born was examined for macrosomia (birth weight ≥4kg), gross congenital anomalies, Transient tachypnea of new born (TTN), and need for admission in neonatal intensive care unit (NICU) . Patients were advised to repeat 75-g OGTT 6 weeks after delivery. Data was analyzed with SPSS-10. Percentages were calculated for variables like age groups, socio economic status, achievement of maternal euglyc- emia (target blood sugar levels), maternal hypoglycemia, macrosomia (birth weight of ≥4kg), neonatal metabolic complications (hypocalcemia, hypoglycemia, polycythemia), gross congenital anomalies, TTN and need of neonate to be admitted in NICU.

RESULTS:

In this interventional study of evaluation for efficacy of glibenclamide for the control of gestational diabetes mellitus conducted at PMC & affiliated hospital, Faisalabad, 50 patients were recruited in 6 months period. All the patients were between 11-33 weeks of gestation. Out of 50 patients, 35 (70%) women were between 20-30 years of age and 15 (30%) women were between 31-40 years.

Satisfactory maternal glycemic control was achieved in 40 (80%) of patients. 10 (20%) women failed to achieve target blood sugar levels.

Among those who achieved target blood sugar levels (n=40), 28 (70%) patients required a dose of ≤ 5mg per day, 10 (25%) needed glibenclamide dose of 6-10 mg per day while 02 (5%) required a dose of > 10 mg per day.

Maternal hypoglycaemic symptoms were found in 01 (2%) patients treated with glibenclamide for control of gestational diabetes mellitus which were managed by dose adjustment.

Regarding the neonatal outcomes, macrosomia was found in 07 (14%) neonates. No anomalies identified in the neonate of patients treated with glibenclamide. Neonatal hypoglycaemia was found among 05 (10%) cases in this study. No case of neonatal polycythemia was found in the study. TTN was found in 4(8%) of cases. 9 (18%) of neonates needed admission in neonatology.

DISCUSSION:

The aim of diabetes management in pregnancy is to achieve normoglycaemia and meeting this goal is more important than the means by which it is achieved. However, with the exception of metformin and glibenclamide, there are insufficient data to recommend treatment with any other currently available oral hypoglycaemic agent during pregnancy. This interventional study was carried out to evaluate the efficacy of glibendamide for control of gestational diabetes mellitus. The study was designed at Allied Hospital Faisalabad which is affiliated with Punjab Medical College. The hospital is a major referral center for the population of 3rd largest city of Pakistan. The study highlights the effect of glibenclamide therapy in achieving normoglycaemia which is a key to manage the gestational diabetes mellitus. The study had special interest in maternal glycaemic control and neonatal complications. Fifty patients with gestational diabetes mellitus were recruited in the study. 38 (76%) women had low socio-economic status, 10 (20%) belong to middle while 02 (4%) were from good socioeconomic status reflecting the overall socioeconomic status as well as trends of selecting center for antenatal care in different socioeconomic groups. 80% (n = 40) of patient achieved satisfactory glycaemic control. The results are supported by the study conducted by Moore LE et al [11]. Regarding the dose of glibenclamide needed to use in achieving euglycemia, 70% (n = 28) of patients who achieved target blood sugar levels (n=40), required a dose of ≤ 5mg/day, 25% (n=10) needed a dose of 6-10 mg/day while 5% (n=02) of them needed a dose of > 10 mg/day. Regarding side effects of therapy, maternal hypoglycemic symptoms were found in 02% (n=01) of patients using glibenclamide and are comparable to the study performed by Moore LE [11]. Regarding the neonatal outcomes, Macrosomia i.e; neonatal weight ≥ 4 kg was seen in 14% (n=7) of neonates. These results are consistent with the study conducted by Cheng YW et al [12]. Results of my study are different from those conducted by Moore LE [11] and Tempe A[13] which had

percentage of macrosomia 5.4 and 3.3% respectively. Lain KY[14] et al observed 22% incidence of macrosomia in their study which is higher than observed in our study. A different set of population can be the explanation for these differences. Neonatal metabolic complications are major participants of perinatal morbidity and mortality. These include hypoglycemia, hypcalcaemia and polycythemia. Neonatal hypoglycaemia was seen among 10% (n=5) of cases in our study. The results of this study are consistent with those conducted by Tempe A and Mayanglambam RD[13]. Results of the study are also comparable to that conducted by Lain KY et al[14]No gross congenital anomaly was identified among infants of diabetic mother treated with glibenclamide. Results of current study are supported by the one conducted by Tempe A[13]. Infants of diabetic mothers visit the NICU (neonatal intensive care unit) more frequently than those of background population. Lain KY[14] and Tempe A[13] reported the NICU admission rates of 12% and 13% respectively. In this study, the percentage of neonates who visited NICU was 18% (n=9). 4 cases (8%) of TTN observed in the current study. Neonatal hypocalcaemia is another contributor to neonatal morbidity and mortality. No case of neonatal hypocalcaemia was found in our study. Similarly, no case of neonatal polycythemia was found in our study. Literature search was made for local studies conducted in Pakistan to compare the results of this study but no such study was found using the glibenclamide for control of gestational diabetes mellitus.

In the context of Pakistani population with significant prevalence of diabetes mellitus,

Table-1: Maternal Socioeconomic status

Socioeconomic status	No of cases	%
Low	38	76
Middle	10	20
Good	02	04

there is a need to identify the women with gestational diabetes mellitus along with their proper treatment. Although insulin therapy during pregnancy is recommended worldwide but research is going on to evaluate and establish the efficacy of oral hypoglycemic agents in GDM and among these, glibenclamide is widely studied drug. In third world countries, there are problems with insulin use like high cost, difficulty in storage, administration, increased risk of needle induced infection and high level of anxiety among patients using it due to their ignorance and local customs. There is growing need of treating the gestational diabetes mellitus with certain drug which can be stored, purchased and administered easily without fetomaternal compromise and up-till-now, glibenclamide has proved itself effective in treating GDM in most of the patients treated for. Going forward, several issues regarding use of glibenclamide (glyburide) in management of GDM remain to be considered like the need for larger randomized controlled trials to detect the actual rate of neonatal problems in GDM, its safety in first trimester of pregnancy and the optimum dosing regimen for glibenclamide.

CONCLUSION:

In the treatment of gestational diabetes mellitus, glibenclamide is successful in achieving good glycaemic control in most women in our study. In countries like Pakistan where the use of insulin may not always be possible, the option of using glibenclamide for the control of GDM may be particularly attractive. However, it would be reassuring to have more of such studies on a large scale to confirm these findings further.

Table-2: Complications of glibenclamide therapy

COMPLICATION	N	%
MATERNAL HYPOGLYCEMIA	1	2
NEONATAL HYPOGLYCEMIA	5	10
NEONATAL HYPOCALCEMIA	0	00
NEONATAL POLYCYTHEMIA	0	00
GROSS CONGENITAL ANOMALY	00	00
TRANSIENT TACHYPNEA	04	8
ADMISSION IN NEONATOLOGY	09	18
MACROSOMIA	7	14

Table-3: Glibenclamide dose requirement among patients achieving target blood sugar levels (n=40).

DOSE(mg/dl)	No of cases	%
<5	28	70
6-10	10	25
>10	2	5

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Submitted for publication: 10-11-14
Accepted for publication: 10-02-15

Do not feel ashamed if the amount of charity is small because to refuse the needy is an act of greater shame.

Hazrat Ali (Karmulha Wajhay)