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COMPARATIVE STUDY OF METFORMIN AND GLIBENCLAMIDE IN THE MANAGEMENT OF GESTATIONAL DIABETES MELLITUS AND PRE GESTATIONAL DIABETES MELLITUS

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Abstract
This prospective observational comparative study aimed to compare the efficacy of metformin and glibenclamide, both individually and in combination with insulin, in managing gestational diabetes mellitus (GDM) and pre-gestational diabetes mellitus (pre-GDM). Our results showed that although glibenclamide had better glycemic control than metformin, it was associated with a greater incidence of adverse effects. Therefore, metformin should be considered as the safe first-line drug or drug of choice in patients with GDM and pre-GDM.
Keywords: Metformin; Glibenclamide; Insulin; Gestational Diabetes Mellitus; Pre-gestational Diabetes Mellitus; Glycemic control; Maternal hypoglycemia; Neonatal hypoglycemia; Birth weight; N.I.C.U. admissions; APGAR score of newborn.

Introduction

Gestational diabetes mellitus (GDM) and pre-gestational diabetes mellitus (pre-GDM) are significant health concerns during pregnancy. The management of GDM and pre-GDM involves lifestyle modifications and pharmacological interventions. Metformin and glibenclamide are commonly used oral hypoglycemic agents in the management of GDM and pre-GDM. According to the American Diabetes Association Workshop Conference on Gestational Diabetes[1], the management of GDM requires a multidisciplinary approach. Several studies have compared the efficacy of oral hypoglycemic agents and insulin in the management of GDM[2,3,4].

Methods

This prospective observational comparative study was conducted at the Department of Obstetrics and Gynecology, Medical College, Kolkata. Census method of sampling was used and all GDM and preGDM patients visiting antenatal outdoor clinic of Medical College, Kolkata or getting admitted in indoor antenatal ward of Medical College, Kolkata and being put on antidiabetic drug therapy there, in a limited time period , were counted in the sample population. Following this, the study included 100 pregnant women with GDM or pre-GDM, who were randomly assigned to receive either metformin or glibenclamide. This study focused on pregnant women with gestational or pre-existing diabetes. To be included, women must have had a 2-hour plasma glucose level of 140 mg/dl or higher following a 75g oral glucose load, or a fasting plasma glucose level above 126 mg/dl or an HbA1c of 6.5% or higher if they have pre-existing diabetes. Women were excluded if they had COVID-19, allergies to the study medication, kidney or liver disease, diabetic ketoacidosis, certain blood disorders, chronic alcoholism, adrenal dysfunction or fetal congenital anomalies.

The study tracked various outcomes, including demographic and clinical data such as age, gestational age, blood glucose levels, renal function, and treatment outcomes. Pregnancy and delivery outcomes, such as birth weight, mode of delivery, and neonatal outcomes like APGAR scores and NICU admission, were also monitored. The goal was to gather comprehensive data on the management and outcomes of diabetes in pregnancy. The patients were followed up till delivery, and the outcomes were

measured in terms of glycemic control, maternal hypoglycemia, and neonatal outcomes.

Results

For statistical analysis, data was entered into a Microsoft excel spreadsheet and then analyzed by SPSS (version 27.0; SPSS Inc., Chicago, IL, USA) and Graph Pad Prism version 5. Data was summarized as mean and standard deviation for numerical variables and count and percentages for categorical variables. Two-sample t-test, paired t-test, chi-squared test ($\chi 2$ test), Fischer's exact test were used. Once a *t* value was determined, a *p*-value was found using a table of values from Student's t-distribution. If the calculated *p*-value was below the threshold chosen for statistical significance (usually the 0.10, the 0.05, or 0.01 level), then the null hypothesis was rejected in favour of the alternative hypothesis. p-value ≤ 0.05 was considered for being statistically significant.

The results showed that glibenclamide had better glycemic control than metformin, but was associated with a greater incidence of adverse effects, including maternal hypoglycemia and neonatal outcomes[5,6,7]. The combination of metformin and insulin was more effective than metformin alone in controlling blood sugar levels[8,9,10].

Table 1: -Distribution of maternal parameters between Metformin and Glibenclamide

Parameters	**Metformin**	**Glibenclamide**	**p-value**
Post-treatment FBS (mean±S.D.) (mg/dl)	97.039±11.141	90.039±2.315	<0.0001 (statistically significant)
Post-treatment 2-hour PPBS (mean±S.D.) (mg/dl)	121.70±6.680	116.16±2.411	<0.0001 (statistically significant)
Maternal hypoglycemia (%)	25.8	58.0	0.0060 (statistically significant)

Table 2: -Distribution of neonatal parameters between Metformin and Glibenclamide

Parameters	**Metformin**	**Glibenclamide**	**p-value**
Birth weight (mean±S.D.) (kg)	3.055±0.1786	3.148±0.2393	0.0455 (statistically significant)
N.I.C.U. admission (%)	32.3	54.0	0.0489 (statistically significant)
APGAR score at 1 minute <7 (%)	16.1	38.0	0.0463 (statistically significant)
APGAR score at 5 minutes <8 (%)	6.5	34	0.0060 (statistically significant)
Neonatal hypoglycemia (%)	19.3	46.0	0.0180 (statistically significant)

Table 3: -Distribution of maternal parameters between Metformin and Metformin combined with Insulin

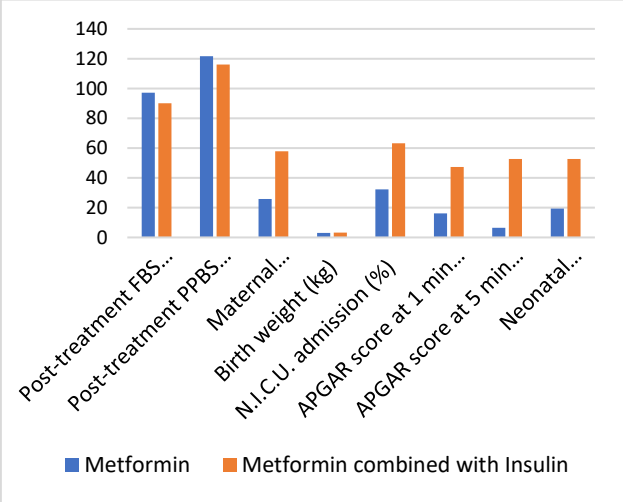
Parameters	**Metformin**	**Metformin combined with Insulin**	**p-value**
Post-treatment FBS (mean±S.D.) (mg/dl)	97.160±11.220	90.105±1.629	0.0084 (statistically significant)
Post-treatment 2-hour PPBS (mean±S.D.) (mg/dl)	121.70±6.680	116.05±2.677	0.0007 (statistically significant)
Maternal hypoglycemia (%)	25.8	57.9	0.0359 (statistically significant)

Table 4: -Distribution of neonatal parameters between Metformin and Metformin combined with Insulin

Parameters	**Metformin**	**Metformin combined with Insulin**	**p-value**
Birth weight (mean±S.D.) (kg)	3.055±0.1786	3.200±0.2261	0.0151 (statistically significant)
N.I.C.U.	32.3	63.1	0.0432

admission (%)			(statistically significant)
APGAR score at 1 minute <7 (%)	16.1	47.4	0.0247 (statistically significant)
APGAR score at 5 minutes <8 (%)	6.5	52.6	0.0004 (statistically significant)
Neonatal hypoglycemia (%)	19.3	52.6	0.0272 (statistically significant)

Figure 1



Distribution of various parameters between Metformin and Metformin combined with insulin

Discussion

Our study suggests that metformin may be a better option than glibenclamide for managing GDM and pre-GDM, especially when used in combination with insulin. The results are consistent with previous studies that have shown metformin as the safe first-line drug for glycemic control in patients with GDM and pre-GDM[4,5,6,11,12].

Conclusion

In conclusion, although glibenclamide had better glycemic control than metformin, it was associated with a greater incidence of adverse effects. Therefore, metformin should be considered as the safe first-line drug or drug of choice in patients with GDM and pre-GDM. The combination of metformin and insulin may be considered for patients who require more intensive glycemic control.

References

1. Freinkel N, Josimovich J. Conference planning committee: American Diabetes Association Workshop Conference on Gestational Diabetes. Diabetes Care. 1980;3: 499–501.
2. Dhulkotia JS, Ola B, Fraser R, Tom F, et al. Oral hypoglycemic agents vs insulin in management of gestational diabetes: a systematic review and meta-analysis. Am J Obstet Gynecol. 2010;203(4): 457.e1-9.
3. Bertini AM, Silva JC, Taborda W, Becker F, Bebber FRL, Viesi JMZ, et al. Perinatal outcomes and the use of oral hypoglycaemic agents. J Perinat Med. 2005;33(6):519–23.
4. Blumer I, Hadar E, Hadden DR, Jovanovič L, Mestman JH, Murad MH, et al. Diabetes and pregnancy: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2013;98(11):4227–49.
5. Kalra B, Gupta Y, Singla R, Kalra S. Use of oral anti-diabetic agents in pregnancy: a pragmatic approach. N Am J Med Sci. 2015;7(6):6–12.
6. Nachum Z, Zafran N, Salim R, Hissin N, Hasanein J, Gam Ze Letova Y, et al. Glyburide versus metformin and their combination for the treatment of gestational diabetes mellitus: a randomized controlled study. Diabetes Care. 2017;40(2):332-9.
7. Balsells M, García-Patterson A, Solà I, Roqué M, Gich I, Corcoy R. Glibenclamide, metformin, and insulin for the treatment of gestational diabetes: a systematic review and meta-analysis. BMJ. 2015;350:h102.
8. Reynolds RM, Denison FC, Juszczak E, et al. Randomized controlled trial of metformin versus insulin for gestational diabetes: effects on pregnancy outcomes. BMC Pregnancy Childbirth. 2017;17(1):316.
9. Rowan JA, Hague WM, Gao W, Battin MR, Moore MP. Metformin versus insulin for the treatment of gestational diabetes. N Engl J Med. 2008; 358(19):2003-15.
10. Faraji A, Tahamtani L, Maharlouei N, Asadi N. Comparison of metformin and glibenclamide in the treatment of gestational diabetes: a randomized clinical trial. Obstet Med. 2023;16(2):98-103.
11. de Oliveira Martins M, de Oliveira Andrade KF, Lima GHS, Rocha TC. Metformin versus glibenclamide in the treatment of gestational diabetes: a systematic review and meta-analysis. Einstein (Sao Paulo). 2022;20: eRW6155.
12. Balsells M, García-Patterson A, Solà I, Roqué M, Gich I, Corcoy R. Glibenclamide,

metformin, and insulin for the treatment of gestational diabetes: a systematic review and meta-analysis. BMJ. 2015;350:h102