

Pharmacological treatment in diabetic patients during pregnancy in the Gynecology-Pediatrics and Family Medicine Hospital No. 31 of the Mexican institute of social security (hospital gineco-pediátrica y Medicina familiar no. 31 Del instituto mexicano Del seguro social, IMSS)

Abstract

Pharmacological treatment in diabetic patients during pregnancy in the Gynecology-Pediatrics and Family Medicine Hospital No. 31 of the Mexican Institute of Social Security (Hospital Gineco-Pediátrica y Medicina Familiar No. 31 del Instituto Mexicano del Seguro Social, HGP/MF No.31 of IMSS)

Objective: To describe the pharmacological treatment of Gestational Diabetes Mellitus (GDM) and Pregestational Diabetes Mellitus (PGDM) in the HGP / MF No. 31 of IMSS, Mexicali B.C., from 2014 to 2015.

Design: Observational, descriptive and longitudinal study.

Setting: Gyneco-Pediatrics and Family Medicine Hospital No. 31 of the Mexican Institute of Social Security (HGP / MF of IMSS), Mexicali B.C, in the high-risk pregnancy consultation.

Participants: Records of pregnant women diagnosed with Gestational Diabetes Mellitus and Pregestational Diabetes Mellitus without any other comorbidity, for the 2014-2015 period.

Main measurements: Data on age, gestational age, capillary blood glucose, serum glucose, pharmacological treatment and perinatal complications were collected. It was analyzed with descriptive statistics with the statistical program SPSS version 21.

Results: The study population was 123 patients, 52% received metformin, 21.9% with Isophane Insulin (NPH) and 26% with both. The majority of patients was treated with metformin and had good glycemic control.

Conclusions: The highest number of patients treated pharmacologically in the second level was metformin.

Keywords: gestational diabetes, pharmacological treatment, metformin, insulin, isophane insulin, pregnancy

Abbreviations: HGP/MF, gynecology-pediatrics and family medicine hospital; IMSS, Mexican Institute of social security

Introduction

Diabetes mellitus during pregnancy can be classified into gestational diabetes and pregestational diabetes; the first is a carbohydrate intolerance that is identified for the first time before or during the first trimester of pregnancy and the second is the carbohydrate intolerance that is diagnosed in the second or third trimester of pregnancy, both as a result of defects in the secretion or action of insulin, or both.¹⁻³ The worldwide prevalence of Diabetes during pregnancy is 5%-20%, and its variation depends on the population, type of screening and diagnostic criteria. In Mexico, a prevalence ranging from 3% -19.6% is reported, increasing in recent years due to the fact that there are more cases of obesity and type 2 diabetes in increasingly younger

patients.¹ The first choice treatment for pregestational and gestational diabetes mellitus is diet and moderate exercise, which can control up to 70% -85% of patients.^{1,2} The first line pharmacological treatment for gestational diabetes mellitus is insulin, however, recent studies suggest that the use of metformin could be the first line treatment. Pathophysiologically, in these cases there is an alteration in the insulin receptors at the cellular level and not an alteration in their secretion. This causes resistance to insulin, and this drug allows improvement in the quality of the receptors and thus diminishes serum glucose levels.^{4,5} On the other hand, recent studies in which metformin was used as first-line treatment from the first trimester, did not find alterations in the newborn and good glycemic control was obtained. However, international and national guidelines still mention insulin as a first line treatment, which suggests that although clinically it is prescribed, there is still insufficient evidence for the use of metformin

as the first choice.¹⁻⁸ According to this background, the objective of the present study is to determine and analyze the pharmacological treatment (insulin, metformin and insulin plus metformin) in women with gestational and pregestational diabetes.

Material and methods

An observational, descriptive and longitudinal study was carried out, which included the records of pregnant women who developed pregestational and gestational diabetes mellitus, who received pharmacological treatment in the HGP / MF No.31 of IMSS, during the 2014-2015 period; files with lack of information were excluded. Data on age, capillary blood glucose, gestational age, preprandial and postprandial serum glucose, pharmacological treatment and perinatal complications was collected. Descriptive statistics were used, with measures of central tendency, percentages and frequencies. The analysis was carried out on SPSS version 21. Ethical considerations: The study was carried out in accordance with the ethical standards of

the General Health Law on Research and the Declaration of Helsinki, as well as the Health Research guidelines of IMSS. The project also had the authorization of the Research Committee of IMSS. In accordance with the above, the confidentiality of patient information was ensured. Due to the characteristics of the study, no letter of informed consent was required.

Results

Of 140 records, 123 met the inclusion criteria and 17 were excluded due to incomplete information. The average age of pregnant women was 34.41 ± 6.04 years. 69.9% (86/123) had a diagnosis of gestational diabetes mellitus and 30.1% (37/123) were diagnosed with pregestational diabetes mellitus. The average gestational age in which pharmacological treatment was initiated was 16.3 ± 12.6 weeks of gestation (SDG). The general characteristics of the population are defined in Table 1.

Table 1 Descriptive statistics of the population under study and by diagnosis

Generalities	Media	SD	Minimum	Maximum
Age (years)	34.41	6.04	17	48
Weeks of gestation at the beginning of treatment	16.3	12.6	0	35
Number of pregnancies	3	2	1	6
Capillary blood glucose (mg / dl)	112.65	14.83	90	140
Serum glycemia (mg / dl)	101.62	16.01	70	140
Postprandial glucose (mg/dl)	118.78	16.97	90	150
GDM				
Age (years)	34.5	6	17	48
Weeks of gestation at the beginning of treatment	26.1	2.70	24	35
Number of pregnancies	3	1	1	6
Capillary blood glucose (mg / dl)	111.19	14.08	90	139
Serum glycemia (mg / dl)	99.92	13.36	70	135
Postprandial glucose (mg/dl)	116.84	15.88	90	140
PGDM				
Age (years)	34.05	6.14	22	42
Weeks of gestation at the beginning of treatment	4.69	5.53	0	20
Number of pregnancies	3	1	1	6
Capillary blood glucose (mg / dl)	116.05	16.11	90	140
Serum glycemia (mg / dl)	105.59	20.59	70	140
Postprandial glucose (mg/dl)	123.29	18.73	90	150

SD: Standard Deviation

Treatment

The first choice of treatment was metformin in 78% (96/123) of the patients; of these patients, 33.33% (32/96) also used insulin to achieve glycemic control. Table 2 describes the way in which treatments were administered. 52% (64/123) of total patients were managed with metformin and 21.9% (27/123) were managed with NPH insulin as monotherapy. In addition, according to the diagnosis, it is observed that within the group of GDM, 67.44% (54/86) were managed with metformin and in the group of DMPG, 48.64% (18/37) were managed with NPH insulin. On the other hand, regarding the most frequent complications associated with the treatment, it was observed that polyhydramnios were the most frequent in this population, both for patients with GDM and with PGDM. Table 3 In addition, of the patients treated with metformin, 17.18% had preterm birth as a complication and of those treated with NPH insulin, 14.81% were

polyhydramnios. Table 4 Out of the total of patients who had preterm birth as the main complication, 100% were treated with metformin, all having good glycemic control.

Table 2 Pharmacological treatment

Treatment	GDM n (%)	PGDM n (%)	Total of the population n (%)
NPH insulin	9 (10.46%)	18 (48.64%)	27 (21.9%)
Metformin	58 (67.44%)	6 (16.21%)	64 (52%)
NPH Insulin / Metformin	19 (22.09%)	13 (35.13%)	32 (26%)
Total	86 (100%)	37 (100%)	123 (100%)

N: 123 GDM, gestational diabetes mellitus; PGDM, pregestational diabetes mellitus.

Table 3 Complications in relation to GDM or PGDM

Complications	Diagnosis	
	GDM n: 86 (%)	PGDM n: 37 (%)
Polyhydramnios	12 (13.95%)	8 (21.62%)
Preterm delivery	11 (12.79%)	1 (2.70%)
Macrosomic newborn	6 (6.97%)	5 (13.51%)
Preeclampsia	1 (1.16%)	2 (5.40%)
PIH	1 (1.16%)	2 (5.40%)
None	55 (63.95%)	19 (51.35%)

PIH, pregnancy induced hypertension; GDM, gestational diabetes mellitus; PGDM, pregestational diabetes mellitus

Table 4 Complications in relation to treatment

Complications	Treatment		
	NPH Insulin n: 27 (%)	Metformin n: 64 (%)	NPH Insulin / Metformin n: 32 (%)
Polyhydramnios	4 (14.81%)	8 (12.5%)	8 (25%)
Preterm delivery	0	11 (17.18%)	1 (3.12%)
Macrosomic newborn	3 (11.11%)	4 (6.25%)	4 (12.5%)
Preeclampsia	3 (11.11%)	0	0
PIH	3 (11.11%)	0	0
None	14 (51.8%)	41 (64.06%)	19 (59.37%)

PIH, pregnancy induced hypertension; GDM, gestational diabetes mellitus; PGDM, pregestational diabetes mellitus

Glycemic control

Regarding glycemic control and treatment, 84.37% (54/64) of the patients were controlled with metformin; On the other hand, 70.37% (19/27) of those treated with insulin alone had good metabolic control. The data is shown in Table 5. Regarding diagnosis and glycemic control, 81.39% (70/86) of the patients with GDM and 67.56% (25/36) of the patients diagnosed with PGDM achieved good glycemic control. Of the total of patients diagnosed with GDM who were in good glycemic control, 68.57% (48/70) were treated with metformin, and of the total with diagnosis of PGDM, 44% (11/25) were managed with NPH Insulin. These results are seen in Table 6. No teratogenic effect was documented within the clinical record by the medications used for glycemic control of patients under prenatal control during the course of the study. It should be noted that 15 patients were treated with metformin from the first trimester of pregnancy.

Table 5 Glycemic control

Treatment	Controlled n (%)	Not controlled n (%)
Metformin	54 (84.37%)	10 (15.62%)
NPH Insulin	19 (70.37%)	8 (29.62%)
NPH Insulin / Metformin	22 (68.75%)	10 (31.25%)

Table 6 Glycemic control in relation to treatment and diagnosis

Treatment	Controlled (95/123)		Not controlled (28/123)	
	GDM (70/95) (%)	PGDM (25/95) (%)	GDM (16/28) (%)	PGDM (12/28) (%)
NPH Insulin	8 (11.42%)	11 (44%)	1 (6.25%)	7 (58.33%)
Metformina	48 (68.57%)	6 (24%)	10 (62.5%)	0
NPH Insulin/ Metformin	14 (20%)	8 (32%)	5 (31.25%)	5 (41.66%)
Total	100%	100%	100%	100%

GDM, gestational diabetes mellitus; PGDM, pregestational diabetes mellitus

Discussion

In this study, 69.9% of the total population was diagnosed with gestational diabetes mellitus and the rest with pregestational diabetes mellitus; these figures are lower than those reported in the 2016 Clinical Practice Guideline, which reports that 90% of women in prenatal care are diagnosed with gestational diabetes mellitus. This suggests an increase in the diagnosis of pregestational diabetes mellitus, which agrees with the increase in patients diagnosed with type 2 diabetes mellitus.¹ The main pharmacological management that the patients received was metformin and in addition, 33.33% required insulin for better glycemic control; these results are similar to those reported in Brazil in 2010, where of 94 women treated with metformin during pregnancy, 21% required insulin to reach the therapeutic goal. With this we can suggest that metformin as monotherapy represents good glycemic control in patients.⁹ The treatment started from week 16.3 of gestation in the average of the population, similar to what most of the previous studies report; however, onset varies according to the diagnosis, since patients diagnosed with WMD would be treated earlier than patients diagnosed with GDM.^{10,11}

The main complications of diabetic patients during pregnancy (polyhydramnios and preterm delivery), differs from what has been mentioned by other authors, that is, that the macrosomic newborns and preterm deliveries are most frequent; this could be due to the fact that in this study there were more patients diagnosed with GDM that recorded the aforementioned complications.¹⁻⁶

On the other hand, patients treated with metformin had preterm labor as the main complication, which coincides with that reported in other studies where they relate preterm delivery with the use of metformin.⁹ Although no significant differences were found in the glycemic control of patients treated with metformin as monotherapy with respect to those treated with insulin, a greater number of the former registered good glycemic control. These results coincide with those reported by a study conducted in Australia and New Zealand in 2013.⁶⁻¹⁵ As in most of the studies reviewed, the patients who had better glycemic control were those diagnosed with gestational diabetes mellitus compared with those diagnosed with pregestational diabetes mellitus. This may be due to the physiopathological mechanism, or to external factors such as diet and lifestyle of the patient.⁵⁻¹²

Conclusion

With this study we can conclude that the use of metformin during pregnancy can generate good glycemic control in patients diagnosed with gestational diabetes who did not improve with diet and exercise

as first choice treatment; this suggests that international guidelines should probably consider it; however, additional studies are needed in different sociocultural contexts that support the external validity of our research. Although the results presented here suggest that the main complication related to the use of metformin in patients is preterm delivery, more evidence is required in this regard.

Recommendations

This study may recommend the use of metformin in patients diagnosed with gestational diabetes who do not improve with diet and exercise, however, more evidence is needed to confirm this recommendation evaluating perinatal complications.

Key points

What is known?

- I. Insulin is the first choice in Pharmacological treatment.
- II. More studies are needed on the use of metformin during pregnancy.

What this study contributes

- I. Metformin demonstrated good glycemic control.
- II. The use of metformin is more frequent in patients diagnosed with gestational diabetes mellitus
- III. Metformin may be the treatment of choice in patients with gestational and pregestational diabetes.

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Conflict of interests

The author declares that there is no conflict of interest.

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