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Glycemic control and maternal and fetal outcomes in pregnant women with type 1 diabetes according to the type of basal insulin

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Abbreviations: T1DM, type 1 diabetes; CSII, continuous subcutaneous insulin infusion; HbA_{1c}, glycated haemoglobin A_{1c}; SGA, small-for-gestational age; MDI, multiple daily injections of insulin; RCT, randomized control trials; PIH, pregnancy-induced hypertension; SD, standard deviations; DCCT, Diabetes Complications Control Trial; LGA, large-for-gestational age; OR, odds ratio.

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ABSTRACT

Objective: To examine the potential role of the type of basal insulin on glycemic control and maternal and foetal outcomes in pregnant women with type 1 diabetes (T1DM).
Study design: Retrospective cohort study of pregnancies attended at 18 Spanish tertiary hospitals.
Inclusion criteria: T1DM, singleton pregnancies, delivery between 2002–2010, and use of the same basal and prandial insulin from before pregnancy until delivery.
Results: A total of 1534 pregnancies were included. The basal insulin most commonly used was Neutral Protamine Hagedorn (NPH) (51.7%), followed by glargine (23.2%) and continuous subcutaneous insulin infusion (CSII) (21.1%). CSII users had longer diabetes duration. Multiple logistic regression analysis showed that CSII was independently associated with lower doses of insulin, higher glycated haemoglobin (HbA_{1c}) in all trimesters, and higher rates of miscarriage, preterm birth and neonatal hypoglycemia. Glargine was related to a higher risk of preterm birth and a small-for-gestational age infant (SGA). The odds ratios (OR) of the associations between insulin type and clinical outcomes (from 0.642 to 4.894) have a relevant magnitude.
Conclusions: In this observational study of pregnant women with T1DM, the type of basal insulin was independently associated with metabolic variables and foetal outcomes.

Introduction

A strict glycaemic control from before pregnancy until delivery is essential to reduce the risk of maternal and foetal complications in women with type 1 diabetes (T1DM) [1]. The type of basal insulin could play a role in both the glycaemic control and in pregnancy outcomes.

Outside pregnancy, continuous subcutaneous insulin infusion therapy (CSII) has proven to be superior to multiple daily injections (MDI) in terms of glycaemic control and hypoglycaemia [2] but randomized control trials (RCT) have shown no clear benefit of CSII in pregnancy. However, these trials included a limited number of patients and compared old CSII systems with human insulins [3]. Despite lack of evidence, this treatment is still used as a last option when glycaemic goals are not achieved with MDI in women who are pregnant or in pre-pregnancy care.

MDI is the standard treatment for T1DM subjects and consequently for women in childbearing age. The introduction of new long-acting insulin analogues such as insulin detemir and glargine with its characteristic non-peaking action profile could reduce the CSII indications. Nevertheless, little information is available on safety and efficacy of these analogues compared to other types of basal insulin in pregnancy. Glargine was the first marketed long-acting analogue, and no increase in adverse events in pregnancy has been reported in case reports, case-series and meta-analyses published to date [4,5]. The safety of insulin detemir in pregnancy has been demonstrated in a RCT [6], but no RCT addressing the use of glargine has been performed. Further information is therefore needed on glycaemic control and pregnancy outcomes achieved with different basal insulins in pregnancy.

The objective of the present study was to compare three basal insulin regimens in pregnant women with T1DM in terms of glycaemic control and maternal and foetal outcomes.

Patients and methods

We performed an observational, retrospective, multicentre cohort study in women with T1DM attended at 18 tertiary university hospitals in Spain between 2002 and 2010. Inclusion criteria were: (1) T1DM; (2) singleton pregnancy; (3) MDI or CSII; (4) entire pregnancy followed at the same hospital; and (5) the same basal and prandial insulin from before pregnancy until delivery. Use of detemir and glulisine was not considered due to infrequent use and lack of authorization for pregnancy respectively in the study period. No additional exclusion criteria were used. The study was approved by the ethics committee at each participating centre. Information was obtained from medical records or databases in place. Most of these databases had a prospective design.

Variable definitions

We assessed baseline demographic (age at time of delivery, self-reported prepregnancy weight and body mass index (BMI), height at booking), and diabetes characteristics (diabetes duration at booking), smoking habit (none, ≥1 cigarette/day at the beginning of pregnancy and discontinued, ≥1 cigarette/day at the beginning of pregnancy and continued) and additional treatment (folic acid supplementation, metformin, statins, angiotensin converter enzyme inhibitors/angiotensin receptor antagonists).

Maternal outcomes were: glycaemic control (glycated haemoglobin (HbA_{1c}), insulin dose and severe hypoglycaemia (events requiring third party assistance)), weight gain (difference between prepregnancy weight and weight at the end of pregnancy), pregnancy-induced hypertension (PIH, blood pressure ≥ 140/90 mmHg [7]), preeclampsia (blood pressure ≥ 140/90 mmHg plus proteinuria ≥ 300 mg/day [7]) and caesarean section.

Gestational age at delivery was defined as the number of completed weeks based on the last menstrual period or on the earliest ultrasound assessment if discordant. Foetal outcomes were: miscarriage (foetal death < 22 weeks [8]), preterm birth (delivery < 37 weeks [8]), small-for-gestational age infant (SGA, birth weight <10th centile according to Spanish foetal growth charts that take into account sex and gestational age [9]), large-for-gestational age infant (LGA, birth weight >90th centile), macrosomia (birth weight ≥ 4000 g [8]), stillbirth (foetal death ≥ 22 weeks [8]), perinatal mortality (foetal and infant death from 22 weeks of gestation to 4 weeks after birth [8]), neonatal hypoglycaemia (glycemia < 40 mg/dl in the first 24 h after delivery requiring treatment [10]), respiratory distress (any distress requiring treatment [8]), neonatal sepsis (confirmed or suspected systemic infection treated with antibiotics), umbilical cord blood