CASE REPORT

ARE CONVENTIONAL TARGETS FOR METABOLIC CONTROL SUFFICIENT TO PREVENT FETAL MACROsomia DURING DIABETIC PREGNANCY?

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SUMMARY - We report the case of a 26 year-old woman, with an uncomplicated type 1 IDDM of 17 yr duration followed for her first pregnancy. At conception, HbA1c (measured by HPLC) was 6.5 % and fructosamine was 280 u.mol.l (normal range below 285). During the follow-up, 15-days-interval fructosamine never exceeded the normal range and HbA1c values were under 6.5 % excepted in the third trimester (7.0 + - 0.8 %) coinciding with a bad control of the 2 hours post-prandial blood glucose. A fetal macrosomy was discovered at 34 weeks of gestation and a heavy-for-date 4680 g baby was delivered by caesarean section at 38 weeks of gestation. Our case report outlines again the need to achieve the recommended target of metabolic control for the diabetic pregnant woman (blood preprandial glucose: 3.9-5.6 mM; post-prandial 2h < 6.7 mM) specially during the third trimester of pregnancy. The use of computer databases might be helpful for precise monitoring during this narrow window period.

Key-words: diabetes, pregnancy, HbA1c.

RÉSUMÉ - Les objectifs métaboliques conventionnels sont-ils suffisants pour prévenir la macrosomie fœtale durant la grossesse de femmes diabétiques ? Nous rapportons le cas d’une patiente diabétique non compliquée, âgée de 26 ans, insulino-dépendante (type 1) depuis 17 ans, suivie pour sa première grossesse. À la conception, l’HbA1c (mesurée par HPLC) était à 6.5 % et la fructosamine à 280 umol.l (normale < 285). Pendant le suivi, la fructosamine (dosée tous les 15 jours) n’a jamais dépassé la normale et l’HbA1c est restée en dessous de 6.5 % excepté au troisième trimestre (7.0 + - 0.8 %), ce qui coïncidait avec un mauvais contrôle des glycémies post-prandiales. Une macrosomie fœtale a été découverte à la 34e semaine de gestation et la patiente a accouché à la 38e semaine par césarienne d’un enfant pesant 4680g. Notre observation souligne de nouveau la nécessité d’atteindre les valeurs recommandées pour un équilibre métabolique optimal de la femme enceinte diabétique (glycémie à jeun: 3.9-5.6 mM ; post-prandiale 2 heures < 6.7 mM ) en particulier dans le 3e trimestre. L’analyse régulière des glycémies adressées par les patientes via les réseaux informatiques pourrait être d’une grande utilité dans cette période critique.

Mots-clés : diabète, grossesse, HbA1c.

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Previous reports have noted the risk of foetal macrosomia during pregnancy in diabetic women whose glycosylated haemoglobin (HbA1c) levels exceed the mean control value by $+7 \pm 0.2$ or more at conception [1]. Poor metabolic control at the beginning of pregnancy is also associated with a high risk of teratogenesis. For all these reasons, clinicians are quite well aware of the need for intensive follow-up programmes during diabetic pregnancy. We report the case of a Type 1 diabetic patient whose pregnancy was complicated by macrosomia despite normal HbA1c and fructosamine levels from conception to delivery.

A 26-year-old woman with uncomplicated Type 1 insulin-dependent diabetes mellitus (IDDM) of 17 years’ duration and a body mass index of 24 kg/m$^2$ was followed-up during her first pregnancy. At conception, HbA1c (measured by high-performance liquid chromatography) was 6.5 % (normal range: 3.9-5.8 %). Visits were monthly from the diagnosis of pregnancy to the second trimester and every 15 days from the third trimester until hospital admission at the 34th week of gestation. Insulin therapy consisted of rapid-acting Actrapid® (Novo Nordisk) alone before breakfast and lunch and mixed with NPH (Mixtard 30°, Novo Nordisk) before dinner. The patient was instructed in insulin adjustment algorithms to reach the goal of blood capillary values recommended in diabetic pregnancy (preprandial: 3.9-5.6 mM; 2 h postprandial <6.7 mM). Throughout pregnancy, recommended self-monitoring of blood glucose consisted of capillary controls before and 2 h after each meal (n = 6/day), with additional controls if hypoglycaemic symptoms occurred. Compliance with this recommendation was good (mean number of controls about 5/day). Biological evaluation of metabolic control, which was repeated at 8-week intervals, consisted of analysis of HbA1c, fructosamine and venous blood glucose levels. The difference between blood venous glucose and self-monitored blood glucose at the same time never exceeded 2.2 mM.

The results of the metabolic follow-up are summarised in Table I. The patient’s weight increased by 14 kg during pregnancy. Throughout pregnancy, mean $\pm$ SD HbA1c and fructosamine values were in the normal range. Mean capillary blood glucose values obtained by glucose self-monitoring were 7.7 $\pm$ 0.3 mmol/l (n = 210) during the third trimester, but higher 2 h postprandial glucose values were recorded (9.2 $\pm$ 1.2 mmol/l, n = 160). No episodes of symptomatic hypoglycaemia were observed. The patient was admitted to the hospital at 34 weeks of gestation after the discovery of foetal macrosomia by ultrasonography. A heavy-for-date 4,680 g baby delivered by caesarean section at 38 weeks of gestation had the typical appearance of a baby born after a poorly controlled diabetic pregnancy. No hypoglycaemic symptoms or neonatal jaundice were observed during the first weeks of life.

Knight et al. [2] reported a similar case of macrosomia in the first pregnancy of a 25-year-old IDDM woman whose diabetes was well-controlled by continuous subcutaneous insulin infusion (capillary preprandial blood glucose: 4.3 $\pm$ 1.6 mM in the first trimester [n = 215], 4.3 $\pm$ 1.7 mM in the second trimester [n = 197] and 5.0 $\pm$ 1.9 mM in the third trimester [n = 151]). This case report as well as ours confirms the need to reduce target blood glucose levels and HbA1c values in pregnant diabetic women. Thus, at the beginning of pregnancy it is necessary to advise the patient of the pre- and 2 h postprandial blood glucose values to be achieved during the pre-
pregnancy and provide an insulin algorithm. The algorithm can be modified, if necessary, at each follow-up visit. In the third trimester, visits should be more frequent because of the known increase in insulin resistance during this period. The biological evaluation of metabolic control during diabetic pregnancy includes HbA1c and fructosamine. Nevertheless, HbA1c levels may be lowered by haemodilution during normal or diabetic pregnancy, by an increase of erythropoiesis or by contamination of maternal samples with foetal blood. Late development of insulin resistance and resulting hyperglycaemia may not be taken into account. For these reasons, HbA1c values for a diabetic pregnant patient should be lower than for a non-pregnant one, and values < 7% need to be achieved [3]. The fructosamine assay, which reflects shorter periods of follow-up than HbA1c, has been proposed for metabolic follow-up during diabetic pregnancy. However, this correlation is less significant during the third trimester, which suggests that neither HbA1c nor fructosamine is a precise parameter for blood glucose levels [4]. Some authors have also reported preliminary studies about other serum glycated proteins than HbA1c. Koskinen et al. [5] found a progressive rise in glycated albumin levels in IDDM women during pregnancy (despite the usual decrease of serum albumin secondary to haemodilution), which suggests that glycated albumin levels are correlated with the decreased glucose tolerance observed throughout pregnancy.

It cannot be excluded that other growth factors than foetal hyperinsulinism [6] are involved in the development of foetal macrosomia during diabetic pregnancy. In fact, macrosomia can also occur in non-diabetic pregnant women.

In conclusion, our case emphasises once again the need for careful obstetric and metabolic monitoring of diabetic women during the third trimester of pregnancy. Other glycosylated serum proteins than HbA1c and blood glucose control with computer databases might be helpful for precise monitoring during this narrow window period.

REFERENCES