A standardized protocol to achieve normoglycaemia during labour and delivery in women with type 1 diabetes

J. Lepercq a,*, H. Abbou a, C. Agostini a, F. Toubas a, C. Francoual a, G. Velho b, D. Dubois-Laforgue c, J. Timsit c, d

a Department of obstetrics and gynecology, AP–HP, hospital Cochin Saint-Vincent-de-Paul, Paris-5 University, 82, avenue Denfert-Rochereau, 75674 Paris cedex 14, France
b Inserm U695, Paris-7 University, 16, rue Henri-Huchard, 75018 Paris, France
c Department of Diabetology, Hospital Cochin Saint-Vincent-de-Paul, Paris-5 University, 24, rue du faubourg Saint-Jacques, 75014 Paris, France
d Inserm U561, Hospital Cochin Saint-Vincent-de-Paul, Paris-5 University, 82, avenue Denfert-Rochereau, 75674 Paris cedex 14, France

Received 29 May 2007; received in revised form 8 August 2007; accepted 16 August 2007

Abstract

Aim. – To evaluate a standardized protocol for maintaining near-normoglycaemia during labour and delivery in women with type 1 diabetes.

Methods. – Over a nine-year period (1997–2005), 229 pregnancies in 174 women with type 1 diabetes were delivered at one centre. The same regimen was used for the induction of labour (group 1) and in women admitted in spontaneous labour (group 2): 10% dextrose (80 ml/h) intravenous was given along with short-acting insulin, starting at 1 IU/h intravenous via an infusion pump. Capillary blood glucose (CBG) was determined hourly, and the insulin infusion rate was modified accordingly.

Results. – Labour was induced in 85 cases (37%) and spontaneous in 23 cases (10%), and an elective C-section was performed in 121 cases (53%). Maternal glycaemia during labour was 6.1 ± 1.6 (range: 3.9–9.2) mmol/l in group 1, and 6.9 ± 2.0 (range: 4.7–12.0) mmol/l in group 2. Maternal glycaemia at delivery was 5.8 ± 1.5 (range: 3.4–9.4) and 6.3 ± 1.9 (range: 4.1–11.4) mmol/l in groups 1 and 2, respectively. Women who underwent an elective C-section were not included in the standardized protocol and had higher glycaemia at delivery 7.1 ± 2.0 (range: 2.7–13.5) mmol/l. Neonatal hypoglycaemia occurred in 30 infants (13%), and was only associated with preterm delivery.

Conclusion. – Using a standardized simple protocol during labour, maternal glycaemia was maintained within a near-normal range in 80–85% of cases.

© 2007 Elsevier Masson SAS. All rights reserved.

Résumé

Protocole standardisé destiné à maintenir la normoglycémie pendant le travail et l’accouchement des femmes atteintes de diabète de type 1.

But. – Évaluer un protocole standardisé pour maintenir un contrôle glycémique proche de la normale pendant le travail et l’accouchement des femmes ayant un diabète de type 1 (DT1).

Méthodes. – En neuf ans (1997–2005), 229 grossesses chez 174 femmes ayant un DT1 ont été prises en charge dans un seul centre. Le même protocole a été appliqué pour le déclenchement du travail (groupe 1) et chez les femmes admises en travail spontané (groupe 2) : une perfusion de glucose à 10 % (80 ml par heure) était associée à une perfusion intraveineuse d’insuline ordinaire débutée à 1 UI par heure. La glycémie capillaire était mesurée toutes les heures et le débit de la perfusion d’insuline adapté selon les résultats.

Résultats. – Le travail a été déclenché dans 85 cas (37 %), spontané dans 23 cas (10 %) et une césarienne a été effectuée d’emblée dans 121 cas (53 %). La glycémie maternelle pendant le travail était de 6.1 ± 1.6 (extrêmes : 3.9–9.2) mmol/l dans le groupe 1 et 6.9 ± 2.0 (extrêmes : 4.7–12.0) mmol/l dans le groupe 2. La glycémie maternelle à l’accouchement était de 5.8 ± 1.5 (extrêmes : 3.4–9.4) et 6.3 ± 1.9 (extrêmes : 4.1–11.4) mmol/l respectivement dans les groupes 1 et 2. Les femmes ayant eu une césarienne d’emblée n’étaient pas incluses dans ce protocole standardisé et ont eu une glycémie plus élevée lors de l’accouchement (7.1 ± 2.0 ; extrêmes : 2.7–13.5 mmol/l). Une hypoglycémie néonatale est survenue chez 30 enfants (13 %) et était associée exclusivement avec la prématurité.

* Corresponding author.
E-mail address: j.lepercq@svp.aphp.fr (J. Lepercq).

1262-3636/$ – see front matter © 2007 Elsevier Masson SAS. All rights reserved.
doi:10.1016/j.diabet.2007.08.003
Conclusion

Un protocole standardisé simple au cours du travail permet de maintenir la glycémie maternelle dans des valeurs quasi-normales dans 80 à 85 % des cas.

© 2007 Elsevier Masson SAS. All rights reserved.

Keywords: Type 1 diabetes; Pregnancy; Delivery

Mots clés : Diabète de type 1 ; Grossesse ; Accouchement

1. Introduction

In women with type 1 diabetes mellitus, perinatal outcome is closely related to glycaemic control throughout pregnancy [1]. However, there are few published reports on the management of diabetes during labour in women with type 1 diabetes [2,3], and on the level of maternal glycaemic control that should be achieved during labour and delivery, which remains a matter of debate. Recommended targets for blood glucose control during labour range from 3.9–6.7 [4] to 4.0–8.0 mmol/l [5]. Algorithms have been published and usually include simultaneous adjustment of both dextrose and insulin infusion rates during labour.

We have performed a prospective study to evaluate the efficacy of a standardized protocol for maintaining near-normoglycaemia during labour and at delivery in women with type 1 diabetes. To set up a simple algorithm that can be implemented by non-specialized nurses or midwives, our protocol uses a constant infusion of 10% dextrose and a sliding scale for insulin infusion. In addition, we evaluated the impact of maternal glycaemic control on the occurrence of neonatal hypoglycaemia.

2. Methods

Over a nine-year period (1997–2005), 229 pregnancies in 174 women with type 1 diabetes were delivered in the same centre. Management of diabetes during pregnancy was standardized as described [6]. In brief, insulin therapy was given as three to four daily injections or by continuous subcutaneous infusion using an external pump. Capillary blood glucose (CBG) target values were below 5.3 mmol/l before meals and below 6.7 mmol/l two hours after meals. Glycaemic control was assessed by HbA1c level, as measured by HPLC (normal: 4.3–5.5%), during the first and second trimesters and at delivery. During pregnancy, women were seen every other week at the diabetes clinic. All women were followed monthly at the obstetrics clinic [6], and delivery was planned at 38–39 weeks of gestation.

Maternal baseline characteristics included age, parity and pre-pregnancy body mass index. Diabetes characteristics included duration of diabetes, and the presence of retinopathy, nephropathy and chronic hypertension [6]. Three groups were considered: induced labour (group 1); spontaneous labour (group 2); elective caesarean or C-section (group 3). Gestational age at delivery was determined from the date of the last menstrual period and confirmed by first-trimester ultrasonography. Preterm delivery was defined as birth before 37 weeks of gestation. Birth weight according to gestational age was used to define macrosomia as “large for gestational age” (LGA), according to the French growth standard curves [7].

Women whose delivery was planned (either by induction of labour or elective C-section) were advised to maintain their usual insulin and meal regimen on the preceding day. All women fasted on the morning of delivery, when the protocol was started. In women admitted in spontaneous labour, the procedure began from the time of admission. A 10% dextrose solution was given intravenously at a constant flow (80 ml/h). Short-acting insulin was administered intravenously using an infusion pump, starting at 1 IU/h. Capillary blood glucose (CBG) was measured hourly until delivery. Target values were 3.4–7.8 mmol/l and the insulin infusion rate was adapted as follows:

- maintained at 1 IU/h if CBG was 3.4–7.8 mmol/l;
- increased to 1.5 IU/h if CBG was 7.8–10.0 mmol/l;
- increased to 2 IU/h if CBG was 10.0–12.2 mmol/l;
- increased to 3 IU/h if CBG was above 12.2 mmol/l.

In cases of hypoglycaemia (CBG ≤ 3.3 mmol/l), insulin infusion was stopped for 30 min, and 30% dextrose intravenous was given if CBG remained low. In group 3, the C-section was performed in the early morning, while the women were still on the long-acting insulin injected the previous evening. The protocol was started at administration of epidural anaesthesia. For all three groups, 500 ml of Ringer’s lactate was given before administration of the epidural anaesthesia.

At birth, to prevent neonatal hypoglycaemia, a combination of glucagon and medium-chain triglycerides was routinely used: all infants received glucagon 0.3 mg/kg intramuscularly and were fed for three hours by continuous nasogastric gavage with a term formula (67 kcal/100 ml) enriched with glucose polymers and medium-chain triglycerides (Caloreen® 3 g and Liprocil® 2 g, per 100 ml of formula, respectively) providing a total of 97 kcal/100 ml. CBG was measured at 0.5 and at three hours of life and plasma glucose was measured at three hours of life. Neonatal hypoglycaemia was defined as a capillary or plasma glucose level below 2.0 mmol/l at three hours of life despite preventative treatment, regardless of clinical symptoms [8].

Data are presented as mean ± S.D. Comparisons among groups were performed with parametric or non-parametric tests when appropriate. Correlations were calculated by using Pearson’s test. Statistical significance was defined as \( P < 0.05 \). Statistical analysis was performed using Graphpad InStat (GraphPad Software Inc., USA).
3. Results

We analyzed 229 consecutive single pregnancies, occurring in 174 women with type 1 diabetes. The main characteristics at enrollment and during pregnancy are shown in Table 1. Labour was induced in 85 cases (37%) and spontaneous in 23 cases (10%) and an elective C-section was performed in 121 cases (53%). Among the 108 induced and spontaneous labours, 37 (34%) C-sections were eventually performed. The rate of preterm delivery was 21%. The length of labour was significantly longer in group 1 compared with group 2 (559 vs 378 min; P = 0.006).

One woman was excluded from the analysis because of diabetic ketoacidosis at 34 weeks of gestation (maternal glycaemia was 21.6 mmol/l). She was immediately delivered by C-section because the fetal heart-rate pattern was abnormal; the protocol was also not implemented.

Maternal CBG values at admission were 6.6 ± 2.3 and 6.8 ± 2.5 mmol/l in women from groups 1 and 2, respectively (P = 0.75) and were above 7.8 mmol/l in 21 (25%) cases from group 1, and in six (26%) from group 2. During labour, the insulin infusion rate was modified 2.2 times on average (range 0–7) and less than four times in 68% of the cases. As shown in Fig. 1, the proportion of cases with a CBG above 7.8 mmol/l decreased regularly during the first four hours of treatment in both groups. Hourly maternal CBG was not different in the two groups, except at three hours of labour (Table 2).

The mean maternal CBG calculated over the entire labour was 6.1 ± 1.6 (range: 3.9–9.2) mmol/l in group 1 and 6.9 ± 2.0 (range: 4.7–12.0) mmol/l in group 2 (P = 0.03). It was above the 7.8 mmol/l target in 15% and 22% of cases from groups 1 and 2, respectively. At delivery, maternal CBG was 5.8 ± 1.5 (range: 3.4–9.4) and 6.3 ± 1.9 (range: 4.1–11.4) mmol/l in groups 1 and 2, respectively (P = 0.17). At delivery, maternal blood glucose was above the 7.8 mmol/l target in 8% and 17% of cases from groups 1 and 2, respectively (P = 0.24). Maternal hypoglycaemia (CBG < 3.3 mmol/l) occurred in 16 cases. No value below 2.2 mmol/l was recorded and no woman experienced severe hypoglycaemia.

In women who underwent elective C-section, the mean CBG at delivery was 7.1 ± 2.0 (range: 2.7–13.5) mmol/l and above 7.8 mmol/l in 33%, both values being significantly higher than in those of groups 1 and 2 (P = 0.002).

At three hours of life, neonatal hypoglycaemia was observed in 30 (13%) infants, despite preventative treatment. The occurrence of neonatal hypoglycaemia was similar across the three groups and did not differ according to route of delivery (vaginally or abdominally). Forty-two term infants (23%) were transferred into Neonatology and 12 stayed for more than five days. In the univariate analysis (Table 3), the occurrence of neonatal hypoglycaemia was associated with the maternal second-trimester HbA1c value, but not with maternal blood-glucose values during labour or at delivery. Accordingly, we found no correlation between neonatal glycaemia at three hours of life and maternal glycaemia during labour (r = −0.12, P = 0.29) or at delivery (r = −0.3, P = 0.71). Neonatal hypoglycaemia was more fre-

Table 1
Main characteristics of 229 pregnancies in 174 women with type 1 diabetes

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (N=85)</th>
<th>Group 2 (N=23)</th>
<th>Group 3 (N=121)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at pregnancy (years)</td>
<td>30.9 ± 5.2</td>
<td>30.5 ± 4.9</td>
<td>31.4 ± 4.2</td>
<td>0.59</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>23.3 ± 3.8</td>
<td>22.6 ± 2.6</td>
<td>23.4 ± 3.1</td>
<td>0.14</td>
</tr>
<tr>
<td>Nulliparous</td>
<td>56 (66%)</td>
<td>17 (74%)</td>
<td>61 (50%)</td>
<td>0.02</td>
</tr>
<tr>
<td>Duration of diabetes (years)</td>
<td>14.2 ± 8.1</td>
<td>14.4 ± 6.7</td>
<td>15.7 ± 6.2</td>
<td>0.47</td>
</tr>
<tr>
<td>Retinopathy</td>
<td>27 (32%)</td>
<td>14 (61%)</td>
<td>69 (57%)</td>
<td>0.03</td>
</tr>
<tr>
<td>Nephropathy</td>
<td>12 (14%)</td>
<td>1 (4%)</td>
<td>26 (22%)</td>
<td>0.09</td>
</tr>
<tr>
<td>Preconception care</td>
<td>58 (68%)</td>
<td>11 (48%)</td>
<td>67 (55%)</td>
<td>0.15</td>
</tr>
<tr>
<td>First trimester HbA1c (%)</td>
<td>6.5 ± 0.9</td>
<td>6.6 ± 1.0</td>
<td>6.6 ± 0.6</td>
<td>0.49</td>
</tr>
<tr>
<td>Second trimester HbA1c (%)</td>
<td>6.0 ± 0.8</td>
<td>6.1 ± 0.9</td>
<td>5.9 ± 0.6</td>
<td>0.78</td>
</tr>
<tr>
<td>HbA1c at delivery (%)</td>
<td>6.0 ± 0.8</td>
<td>6.0 ± 0.9</td>
<td>6.0 ± 0.6</td>
<td>0.85</td>
</tr>
</tbody>
</table>

Group 1: induced labour; group 2: spontaneous labour; group 3: elective caesarean section. Data are presented as mean ± S.D. or N with percentage in parentheses.

Table 2
Mean (±S.D.) capillary blood glucose (mmol/l) during the seven first hours of labour (hour 1 to hour 7) in women with type 1 diabetes

<table>
<thead>
<tr>
<th>Hour of labour</th>
<th>Group 1 (N=85)</th>
<th>Group 2 (N=23)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>6.7 ± 2.4</td>
<td>6.9 ± 2.6</td>
<td>0.65</td>
</tr>
<tr>
<td>2</td>
<td>7.0 ± 2.6</td>
<td>8.1 ± 2.1</td>
<td>0.13</td>
</tr>
<tr>
<td>3</td>
<td>6.2 ± 2.1</td>
<td>7.8 ± 2.0</td>
<td>0.01</td>
</tr>
<tr>
<td>4</td>
<td>6.1 ± 2.2</td>
<td>7.1 ± 2.0</td>
<td>0.23</td>
</tr>
<tr>
<td>5</td>
<td>5.8 ± 2.0</td>
<td>6.1 ± 1.6</td>
<td>0.67</td>
</tr>
<tr>
<td>6</td>
<td>5.9 ± 1.9</td>
<td>5.3 ± 1.9</td>
<td>0.38</td>
</tr>
<tr>
<td>7</td>
<td>5.7 ± 1.9</td>
<td>4.7 ± 0.6</td>
<td>0.17</td>
</tr>
</tbody>
</table>

Group 1: induced labour; group 2: spontaneous labour

Fig. 1. Capillary blood glucose values (mmol/l) during labour and at delivery, according to the modality of delivery: induced labour (black square = group 1), spontaneous labour (black circle = group 2). Dotted lines indicate the target capillary blood glucose values.
Maternal CBG during labour (mmol/l) 6.7

Data are presented as mean ± S.D. or N with percentage in parentheses. CBG, capillary blood glucose.

4. Conclusion

We found that, during labour, maternal blood glucose can be maintained within a near-normal range in the majority of women with type 1 diabetes. Moreover, the proposed protocol is safe, as limited numbers of women experienced significant hypoglycaemia.

The management of type 1 diabetes during labour and delivery has not received much attention in the literature. The standard regimen for glycaemic control during labour most often uses intravenous administration of glucose and insulin, with adjustments of both insulin and glucose infusion rates. Recently, it has been claimed that intrapartum glycaemic control in insulin-requiring diabetes may be comparable to a standard insulin infusion or administration of intravenous glucose and non-glucose-containing fluids [9]. However, the study included 36 women, of whom only seven had prediabetic states. Thus, the protocol used in that study might be more appropriate for the management of gestational diabetes during delivery.

As shown in Fig. 1, maternal blood-glucose values appeared to be more stable in spontaneous labour when it was induced rather than spontaneous. This might be due to the fact that women in spontaneous labour were heterogeneous in terms of time of their last meal and insulin injection, when the protocol was started. However, as shown in Fig. 2, most women who were above target values at admission were controlled within a few hours without significant hypoglycaemia. Overall, diabetes was well controlled in 80–85% of the women in whom the protocol was applied. In comparison, glycaemic control at delivery was significantly poorer in women who underwent elective C-section. An explanation might be that these women were on their usual insulin regimen and did not receive the intensified intravenous protocol at the time of delivery.

Previous reports have shown that marked maternal hyperglycaemia during labour is associated with the occurrence of neonatal hypoglycaemia [3,4]. In contrast, the present study and others [4,7] found no association between glycaemic control during labour and at delivery, and the occurrence of neonatal hypoglycaemia. This is probably due to the maintenance of maternal blood glucose within a near-normal range. Neonatal hypoglycaemia still occurs in 8–40% of infants of diabetic mothers in recent European studies [5,10,11]. In the present study, it was seen in 13% of the infants, mostly preterm. Preterm delivery is a known risk factor for neonatal hypoglycaemia [12] and this was confirmed by our multivariate analysis.

In conclusion, a simple protocol that is easily implemented by care providers who are not specialized in diabetology offers good glycaemic control during labour and delivery in women with type 1 diabetes.

References

[7] Mamelle N, Munoz F, Martin JL, Laumon B, Grandjean H. Fetal growth from the AUDIPOG study II. Application for the diagnosis of...


