



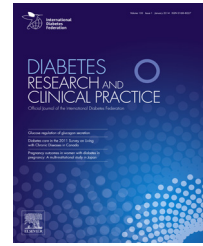
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Effects of uncomplicated vaginal delivery and epidural analgesia on fetal arterial acid–base parameters at birth in gestational diabetes

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ABSTRACT

Aim: To investigate the effects of uncomplicated vaginal delivery and epidural analgesia on fetal acid–base parameters in women with gestational diabetes (GDM) compared with controls.

Methods: A retrospective case–control study of 142 women with gestational diabetes and 284 controls. To evaluate the effect of diabetes and analgesia on acid–base status correcting for potential confounders we used ordered logistic equations including quartiles of fetal arterial acid–base parameters collected at birth as outcomes and categories of diabetes and epidural analgesia as explanatory variables.

Results: In the GDM group cord base deficit (-2.63 mmol/l, interquartile range [IQR] = 4.2 to -0.65 mmol/l vs. -1.9 mmol/l, IQR = -3.3 to -0.2 mmol/l, $p = 0.009$, odds ratio (OR) = 1.51 , 95% confidence interval (CI) = 1.04 – 2.18) was lower and concentration of calcium higher (1.49 mmol/l, IQR = 1.42 – 1.56 mmol/l vs. 1.47 mmol/l, IQR = 1.41 – 1.51 mmol/l, $p = 0.009$, OR = 1.69 , 95% CI = 1.12 – 2.56) compared with controls. Epidural analgesia in the GDM group was associated with reduced cord concentration of glucose (84.0 mg/dl [4.7 mmol/l], IQR = 70 – 103.3 mg/dl vs. 92.5 mg/dl [5.1 mmol/l], IQR = 76.5 – 121.8 mg/dl, $p = 0.004$), lactate (2.65 mmol/l (IQR = 1.80 – 4.20) vs. 3.70 mmol/l (IQR = 2.90 – 5.55 mmol/l), $p = 0.002$) and less pronounced base deficit (-2.05 mmol/l, IQR = -3.90 to -0.17 mmol/l vs. -2.8 , IQR = -5.57 to -1.05 mmol/l, $p = 0.01$, OR = 0.7 , 95% CI = 0.49 – 0.99).

Conclusions: In uncomplicated pregnancies and deliveries, well-controlled gestational diabetes mellitus has potentially significant detrimental effects on fetal acid–base status at birth. Epidural analgesia reduces cord arterial glucose and lactates.

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1. Introduction

Gestational diabetes mellitus (GDM) has been associated with macrosomia and a higher risk of perinatal and postnatal complications [1]. Since glucose rapidly crosses placenta, maternal hyperglycemia associated with gestational diabetes mellitus induces fetal hyperglycemia and hyperinsulinemia [1]. Fetal oxygen consumption rises in direct proportion to the insulin level, increasing the risk of fetal hypoxia, acidosis and neonatal hypoglycemia [1]. During labor, several other factors influence the acid–base status of the fetus at birth. Intrapartum factors, such as the length of labor and epidural analgesia, are known to affect fetal oxygen saturation and umbilical cord blood gas values at birth [2]. Among women with gestational diabetes mellitus, several studies have shown a raised oxidative stress during labor with an overproduction of reactive oxygen species and a deficiency of the antioxidant defense mechanisms [3–5].

Peripartum maternal glycemic balance is related both to the quality of the glycemic control during pregnancy and to glycosylated hemoglobin (HbA1c) value in the third trimester [6]. Labor is associated with a reduction in the need for insulin and intrapartum factors such as length of labor, pain and type of analgesia could also influence maternal glycemic control [7].

Epidural analgesia increases the risk of short term side effects such as maternal hypotension, fever and longer second stage of labor [8]. However, several studies [9–11] have shown that epidural analgesia is associated with better neonatal acid–base status compared to both systemic opioid or no analgesia [12]. These data suggest that hemodynamic, metabolic and hormonal changes associated with epidural analgesia could reduce, at least partially, the risk of fetal hypoxia during normal labor [9–11]. Little is known about the effect of epidural analgesia on the neonatal acid–base status at birth among women with gestational diabetes mellitus. The purpose of this study was to investigate how vaginal delivery and epidural analgesia can influence fetal arterial acid–base parameters at birth in well-controlled gestational diabetes mellitus pregnancies as compared to unaffected controls.

2. Materials and methods

The study was designed as a retrospective case–control study of women who had prenatal care and who were delivered at the Department of Obstetrics and Gynecology of the University Hospital of Pavia in the period 2010–2012. Cases were women affected by gestational diabetes mellitus with an otherwise uncomplicated pregnancy and labor and who had a vaginal delivery after 35 weeks of gestational age. To evaluate the effect of diabetes and epidural analgesia on the neonatal acid–base status at birth in physiological conditions, we included in the study only women with an uncomplicated pregnancy, with a normal fetal growth and with reassuring fetal heart rate tracings pre- and intra-partum. Control subjects were selected among women without gestational diabetes mellitus, sharing the same obstetric characteristics as cases and matched by gestational age and number of previous vaginal deliveries. For statistical reasons, the two subsequent women meeting

inclusion/exclusion criteria and delivering after each index case were recruited as potential controls. Exclusion criteria were gestational complications (such as preeclampsia), restriction of fetal growth, and/or a non-reassuring fetal heart rate tracing during labor requiring prompt delivery. The study was approved by the Ethical Committee of our hospital and women recruited signed a consent form.

Demographic and clinical data were collected at delivery and stored in a computer database.

During the study period, all pregnant women who had prenatal care at our institution underwent routine second trimester screening for gestational diabetes mellitus (24–28 weeks). Women with gestational diabetes mellitus were diagnosed after a 75 g oral glucose tolerance test (OGTT) according to standard criteria [13].

Women with gestational diabetes mellitus were referred to a diabetologist for subsequent management of diabetes up to delivery. After the diagnosis of gestational diabetes mellitus, all women were placed on trial of a personalized dietary regimen and were encouraged to modify life-style including nutrition and physical activity. They were also asked to self-monitoring blood glucose initially at least four times a day (fasting and after each meal). Inadequate control of blood glucose requiring insulin was diagnosed when the mean blood glucose values during the previous week were as followed; fasting ≥ 90 mg/dl or 1 h postprandial ≥ 120 mg/dl. In all the women with gestational diabetes mellitus follow-up visits were scheduled every 2–4 weeks as necessary.

Subjects on insulin treatment were treated with rapid analogs of insulin before the three meals and one basal insulin at bed time. During labor, capillary glucose was checked every 2 h among women only on diet and initially every hour among those taking insulin. During the course of labor, we administered insulin as required with the goal of attaining glucose levels < 120 mg/dl.

At birth, umbilical artery was doubly clamped, fetal blood samples were collected into heparinized syringes that were immediately sealed to determine acid–base parameters as pH, oxygen saturation (Sat O₂, %), glycemia (mg/dl), hemoglobin (Hb, g/dl), calcium (Ca, mmol/l), potassium (K, mmol/l), sodium (Na, mmol/l), chloride (Cl, mmol/l), base deficit (BE, mmol/l), bicarbonate (HCO₃⁻, mmol/l), lactates (mmol/l), anion gap (AG, mmol/l), arterial oxygen partial pressure (PaO₂, mmHg), partial arterial pressure of carbon dioxide (PaCO₂, mmHg). Acid–base parameters were analyzed by ABL800FLEX blood gas analyzer (radiometer mediatecAps 2011).

Epidural analgesia was administered during the active phase of labor (at least 2 cm of cervical dilatation and 3 uterine contractions every 10 min) in women who chose it. To maintain pain relief up to delivery, after the placement of epidural catheter, boluses (20–25 ml) of ropivacaine 0.10% (20 mg) and sufentanyl (10 mcg) were administered every 2–3 h with intermittent bolusing by an anesthetist, in according to epidural analgesia guidelines.

Categorical variables were analyzed with chi-square or Fisher's exact test. Partitioning of chi-square analysis with Bonferroni correction for multiple comparisons was used to compare rates of variables in multiway tables. Normality assumptions were tested by Shapiro–Wilks test. Skewed data

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