Исходы индуцированных родов у пациенток с гестационным сахарным диабетом

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Цель. Оценить исходы индуцированного родоразрешения у пациенток с гестационным сахарным диабетом (ГСД).

Материалы и методы. В когортном ретроспективном исследовании приняла участие 251 женщина, родоразрешен- ная в 2014 году. Выделены 2 подгруппы: 210 женщин с ГСД, получавших диетотерапию, и 41 женщина, получавшая инсулинотерапию. Оценыны исходы родов в каждой подгруппе.

Результаты. Осложнения родов, такие как дискоординация и слабость родовой деятельности, встречались досто- верно чаще (p<0,05) в ходе индуцированных родов, чем при спонтанном их течении: 7 из 43 (16,3%) и 6 из 188 (3,2%), 3 из 43 (7%) и 0 из 188 (0%) соответственно. Гипоксия плода встречалась в 10,6% (20 из 188) и в 9,3% (4 из 43) случаев при спонтанном и индуцированном течении родов соответственно. Частота экстремного оперативного родоразре- шения после индуцирования родов достоверно не превышала таковую при спонтанном течении родовой деятельности.

Заключение. Родоразрешение беременных с ГСД в сроки 38—39 недель привело к повышению частоты осложнений родов, таких как слабость (16,3%) и дискоординация родовой деятельности (7%). Срок беременности, вероятно, не может рассматриваться как изолированное показание для родовозбуждения до доношенного срока при отсутствии признаков стратания плода или плохого контроля гликемии у матери.

Ключевые слова: гестационный сахарный диабет; аномалии родовой деятельности; фетопатия; сроки родоразре- шения; способы разрешения

A comparison of the clinical outcomes of induced and spontaneous labour in patients with gestational diabetes

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Aim. To evaluate the clinical outcomes of induced and spontaneous labour in patients with gestational diabetes (GD).

Materials and methods. This retrospective cohort study conducted at the Federal Almazov North-West Medical Research Centre included 251 patients with GD who had given birth during 2014. The patients were divided into the following two groups: one included 210 patients who were treated with diet and the other included 41 patients who were treated with insulin. Clinical outcomes were compared between patients who had induced (n = 43) or spontaneous (n = 188) labour.

Results. Complications of labour, such as dysthyroidism and uterine inertia, were significantly more common (p < 0.05) in induced labour patients than in those who had spontaneous labour (16.3 vs. 3.2% and 7% vs. 0%, respectively). Fetal distress occurred in 10.6% and 9.3% of patients during spontaneous and induced labour, respectively. The frequency of caesarean section after induced labour was not significantly greater than that among patients who had spontaneous labour.

Conclusion. Delivery at 38 to 39 weeks in women with GD has led to an increase in the rate of birth complications, such as uterine inertia and dysthyroidism. Gestational age cannot be considered as a sufficient indicator of labour induction at full-term in the absence of foetus distress or poor maternal glycemic control.

Keywords: gestational diabetes; embryopathy; dysthyroidism; uterine inertia; delivery time

Background

Gestational diabetes mellitus (GDM) is one of the most common metabolic disorders found in pregnant women. The worldwide incidence of GDM ranges from 1.5% to 13% of all pregnancies, significantly depending on the population studied and diagnostic criteria used [1].

According to the literature, 20%—50% of women with a history of GDM have a higher risk of developing GDM in subsequent pregnancies, whereas 25%—50% of women aged 16—20 years develop diabetes after giving birth. [1]

The high prevalence of GDM in Russia is probably caused by both a general increase in the frequency of carbohydrate metabolism disorders among the general population as well as the introduction of new, more stringent criteria for the diagnosis of GDM, as described in the Gestational Diabetes: Diagnosis, Treatment, Postnatal Care guidelines issued by the Russian Ministry of Health in 2013 [2].
One major GDM-related problem involves the timing and indications for the induction of labour. Current Gestational Diabetes: Diagnosis, Treatment, Postnatal Care guidelines as well as recommendations from the American Diabetes Association provide the following recommendations for delivery.

In the presence of GDM, it is desirable for delivery to occur at no later than 38–39 weeks of gestation, and the obstetrician should determine the indications for the delivery method. Generally accepted obstetric indications for elective caesarean section (CS) in women with GDM are contained in the existing guidelines. In cases where the foetus has pronounced signs of diabetic fetopathy, it is advisable to perform elective CS to avoid birth trauma (shoulder dystocia) [3].

These guidelines, however, do not account for an assessment of the readiness of a woman’s body (birth canal training may even be ineffective) for induced delivery, which explains why direct implementation of these guidelines may not necessarily lead to desired results.

**Aim**

This study evaluated the results of induced labour in patients with GDM.

**Materials and methods**

A retrospective cohort study was conducted at the Perinatal Centre (PC) of the Federal Almazov North-West Medical Research Centre.

The cohort consisted of 251 pregnant women with GDM who underwent delivery at PC in 2014. A diagnosis of GDM was established at 12–32 weeks using an oral glucose tolerance test (OGTT) with 75 g of glucose. In 35.8% (n = 90) of patients, GDM was determined during the 24th and 32nd weeks of pregnancy, and 64.5% of women were diagnosed based on fasting glucose levels ranging from 5.1 to 6.9 mmol/L.

Group 1 included 210 women aged 33.0 ± 5.8 years with GDM treated with diet therapy. GDM diagnosis was established at 24–32 gestational weeks. Group 2 included 41 women aged 34.5 ± 5.8 years with GDM treated with insulin therapy. Insulin therapy was prescribed for pregnant women with poor glycaemic control (1-h postprandial glucose levels > 7.0 mmol/L, two or more times during a 2-week period of self-control) who were previously treated with diet therapy for 2 weeks after early GDM detection. The following insulin therapy modes were used: 1) basal in 41.5% (n = 17) of cases, 2) basal–bolus in 19.5% (n = 8) of cases and 3) an insulin bolus in 39% (n = 16) of cases.

The degree of glycaemic control varied among patients. Seventeen out of 251 (6.8%) patients had poorly controlled GDM (target ranges of glycemia was not achieved during treatment). The criteria for poorly controlled GDM, clearly indicated by signs of diabetic fetopathy, were present in four (1.6%) foetuses.

It should be noted that the diagnosis of the following diabetic fetopathies was excluded in the absence of ultrasound confirmation.

- large foetus (over 90th percentile for gestational age or weight (>4,000 g));
- increased subcutaneous thickness of the foetal fat layer and increased buccal coefficient;
- cardiomegaly, cardiomyopathy, cardiothoracic index > 25% and thickening of the interventricular septum;
- hepatomegaly and splenomegaly;
- foetal adrenal cortex hyperplasia (adrenal coefficient > 1.2) and
- foetal pancreatic hyperplasia [4, 5, 6].

The following diagnostic criteria for GDM correspond to those mentioned in the above protocol and were applied to all patients by an endocrinologist.

**OGTT Protocol**

An OGTT using 75 g of glucose was administered between the 24th and 28th weeks in patients who did not have any carbohydrate metabolism disorder in the early stages of pregnancy (35.8%, n = 90). Patients followed a regular diet containing no less than 150 g of carbohydrates daily for no less than 3 days preceding the test. The last meal before the OGTT contained between 30 and 50g of carbohydrates. Smoking was prohibited until completion of the test. Medications that could affect blood glucose levels (multivitamins, iron preparations containing carbohydrates, steroids, β-blockers and β-agonists) were taken after test completion, if possible [3].

The following conditions contraindicated the administration of an OGTT: 1) early toxicosis (nausea, vomiting); 2) strict bed rest (OGTT was administered after increased mobility was permitted); 3) presence of acute inflammatory or infectious disease; 4) cases of exacerbated chronic pancreatitis or 5) presence of dumping syndrome (resected stomach syndrome) [3].

Venous blood plasma glucose levels were tested in the laboratory using biochemical or glucose analysers. Use of portable glucometers was prohibited [3].

Blood samples were drawn into cold vacuum test tubes containing a sodium fluoride preservative (6 mg/1 mL of whole blood) as an enolase inhibitor to prevent spontaneous glycosylation, with EDTA (ethylenediaminetetraacetic acid) and sodium citrate anticoagulants. Blood samples were immediately centrifuged (±30 min) to separate plasma from cellular components, followed by the transfer of plasma into clean plastic test tubes to determine glucose levels [3].

The OGTT consisted of the following: 1) first fasting blood sample immediately tested for glucose levels (in cases of manifested DM or GDM the 75-g glucose drink was not given, and further testing was cancelled). If prompt testing was impossible, the test was continued; 2) if the OGTT was continued, the patient was given a glucose solution [75 g of dry glucose (anhydrous or anhydride) dissolved in 250–300 mL of warm (potable or distilled) water] to drink within 5 min. The test was started immediately after the
glucose solution was ingested; and 3) blood samples for determining glucose levels were obtained 1 and 2 h after the administration of the glucose solution. Completion of the OGTT occurred if results of the second blood sample suggested GDM [3].

All patients were evaluated for the following somatic pathologies: 1) obesity; 2) various forms of hypertension; 3) thyroid disease; 4) preeclampsia and 5) pregnancy oedema. The following course and outcome of labour were analysed: planned and emergency surgical delivery as well as the results of induced labour, depending on the time of labour induction. Evaluation of the frequency of delivery complications, such as uterine inertia, uncoordinated contractions and foetal distress were examined. Indications for each type of delivery and the anthropometric status of infants were assessed.

Data are presented as mean (M) ± standard deviation (SD) using SPSS 21.0 statistical software (SPSS Inc., USA). Student’s t test was used for evaluating the distribution of qualitative indicators between groups. The 2 test was used for the comparison of qualitative attributes. Differences were considered significant at p < 0.05.

Results

Data defining the association between GDM and somatic pathology for pregnant women with the accompanying conditions of obesity, various forms of hypertension, thyroid disease and pregnancy complications, such as oedema and preeclampsia, are summarized for the diet and insulin therapy groups in Table 1 below.

Patients experienced the following types of delivery: 1) spontaneous delivery; 2) induced labour and 3) elective CS, as displayed in Table 2. No significant difference in the frequency of induced labour and elective CS between the groups.

Table 3 presents the terms at which labour was induced in GDM patients treated with diet and insulin therapies. The frequency of macrosomia and diabetic fetopathy was the same for both groups (p <0.05). Foetal macrosomia was present in 37 infants: 29 (13.4%) delivered by patients who received diet therapy (n = 217) and eight (19.5%) delivered by patients who received insulin therapy (n = 41). Signs of diabetic fetopathy were present in four infants: two (0.9%) delivered by patients who received diet therapy and two (4.9%) delivered by patients treated with insulin therapy.

In the case described below, diabetic fetopathy served as an indicator for elective surgical delivery. The patient had poorly controlled GDM that was treated with insulin according to the following protocol: Humulin NPH insulin [12 IU 38 IU at 10:00 (10 am)] and [+38 IU at 23:00 (11 pm)] and Humalog (12 + 10 + 10). Targets for glycemic control in GDM, however, was not achieved. Fasting glucose levels were 4.5—5.4 mmol/L; postprandial glucose levels ranged from 6.8 to 8.4 mmol/L. Ultrasound imaging revealed double contours around the foetal abdominal area, polyhydramnios and macrosomia at...
30–31 weeks. Macrosomia and polyhydramnios presented at 34 weeks, and signs of diabetic fetopathy presented at 38 2/7 weeks. Surgical delivery, performed at 39 0/7 weeks (weight, 4,200 g; height, 53 cm; head circumference, 39 cm and chest circumference, 36 cm) according to the recommendations of an endocrinologist, produced a male infant with signs of diabetic fetopathy that were postnatally unconfirmed.

Other cases with indications for elective CS, not immediately related to GDM, are presented in Table 4 below.

The incidence of complications due to uterine inertia or uncoordinated labour was significantly higher (p < 0.05) in patients experiencing induced labour than in those experiencing spontaneous labour. Births were physiological in 89.4% (168 of 188) and 67.4% (29 of 43) of cases with spontaneous and induced courses of delivery, respectively. No cases of uncoordinated labour in patients with spontaneous delivery occurred; however, this complication was present in 7% (3 cases out of 43) of patients with induced labour. Uterine inertia was present in 3.2% (6 out of 188) and 16.3% (7 out of 43) and foetal distress in 10.6% (20 out of 188) and 9.3% (4 out of 43) of patients with spontaneous and induced labour, respectively.

The incidence of emergency surgical delivery after the induction of labour was not significantly higher in patients with induced labour than in those with spontaneous labour, i.e., 14.4% (6 out of 43) and 20.2% (38 out of 188), respectively.

Out of all infants delivered, 192 (74%) had high Apgar scores of 8/9 at 1 and 5 min after birth, respectively. Fifty (19.4%) infants were born with Apgar scores of 7/8. Only 16 (6.2%) infants had an Apgar score < 7/8 points. Causes of foetal distress (Apgar score < 7/8) are presented in the Table 5.

The frequency of foetal macrosomia was 14.3% (37 foetuses), including 29 foetuses from patients treated with diet therapy and eight foetuses from patients treated with insulin (indicating poorly controlled GDM in these mothers).

**Discussion**

Despite a strong interest in GDM among researchers, obstetricians and endocrinologists, no consensus on the management of pregnant women with this pathology exists. A large amount of data concerning the pathogenesis of insulin resistance during pregnancy, hormone sharing, metabolites and cytokines in patients with GDM, as well as endocrine features surrounding the management of these women, have been published. However, no standard tactical recommendations regarding the methods and time of infant delivery in pregnant women with GDM exist [7].

Global guidelines concerning pregnancy management and delivery in women with GDM are ambiguous and require further research. Russian clinical guidelines and those from the International Associations of Obstetricians often contradict each other. All researchers, however, agree that delivery should be early (at a term of 37–38 weeks) when dealing with cases of poorly controlled GDM. According to the authors of this guidelines, this tactic will reduce stillbirth and childbirth complications rates. However, this tactic will also cause expected increases in the incidence of neonatal respiratory distress syndrome (RDS), a condition that requires intensive care. According to
research, no isolated tactic, with regard to the gestational term or estimated foetal weight, is considered optimal for patients with GDM [7].

According to this study, childbirth complications, such as uncoordinated labour or uterine inertia, are significantly more frequent (p < 0.05) in cases of induced labour than in cases of spontaneous delivery.

The article titled ‘Modern Concepts of Delivery Tactics in Pregnant Women with Gestational Diabetes Mellitus’ by Kapustin et al. discusses the insufficiency and ambiguity of accumulated global data intended to reduce the risk of possible antenatal foetal death while forcing planned delivery in patients with gestational diabetes mellitus [7]. The absence of such evidence contributes to disagreements between obstetric organizations regarding delivery strategies in patients with GDM. It is obvious that planned delivery in such patients requires an individual approach that considers 1) gestational age; 2) clinical and ultrasound data; 3) anticipated foetal weight; 4) level of glycaemic control; 5) availability and effectiveness of insulin; 6) obstetric history, gravidity and parity and 7) birth canal status [7].

To summarize our findings and relevant literature data, we believe that in the presence of poorly controlled GDM and signs of diabetic fetopathy, delivery by caesarean section at 37/38 weeks should be promoted. However, there is no evidence proving that early delivery (frequently accompanied by labour complications and foetal distress) is necessary in cases of well-controlled GDM and absence of foetal complications [7].

**Conclusion**

The findings of the study suggest the following:

1. Delivery in pregnant women with GDM according to the terms specified in the guidelines resulted in an increased frequency of birth complications such as uterine inertia (16.3%) and uncoordinated labour (7%), as well as foetal distress that occurred in 10.6% (20 of 188) and 9.3% (4 of 43) of cases with spontaneous and induced labour, respectively. The frequency of emergency surgical delivery after induced labour was not significantly higher than that after spontaneous labour.

2. The term of gestation probably cannot be regarded as an isolated indication for the induction of labour prior to full term gestation, in the absence of foetal ‘suffering’ or in poorly controlled cases of maternal GDM.

3. If the condition of the foetus is satisfactory, if there are no signs of macrosomia and especially if there are no signs of diabetic fetopathy, we consider it possible to discuss the continuation of prenatal care on a weekly basis, pending spontaneous labour up to 41 weeks of gestation.

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**Conflict of interest**

The authors declare no duality (conflicts) of interest in writing this manuscript.

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