Thieme

Diabetes and Pregnancy

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Bibliography
Exp Clin Endocrinol Diabetes
DOI 10.1055/a-1946-3648
ISSN 0947-7349

Georg Thieme Verlag, Rüdigerstraße 14,
70469 Stuttgart, Germany

German Diabetes Association: Clinical Practice Guidelines
This is a translation of the DDG clinical practice guideline published in Diabetologie 2022; 17 (Suppl 2): S205–S214.
DOI 10.1055/a-1901-0499

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BACKGROUND KNOWLEDGE

Notice of update
The DDG practice recommendations are updated regularly during the second half of the calendar year. Please ensure that you read and cite the respective current version.

Preliminary note

This practice recommendation addresses only type 1 and type 2 diabetes known prior to conceiving. These are high-risk pregnancies and require joint care by specialized diabetologists, obstetricians, and neonatologists in close cooperation with other areas of specialization. The practice recommendation does not present the topic comprehensively, but in a focused manner.

Epidemiology

In 2019, there were 7580 cases of preexisting diabetes mellitus (type 1, type 2 diabetes) during pregnancy. This corresponds to a relative frequency of 1.0 %. The proportion of pregnant women with type 2 diabetes among all pregnant women with preexisting diabetes is estimated to be at least 10–30 % in Germany.

Children of diabetic mothers have an average 1.5- to 3-fold increased risk of congenital malformations, prematurity, hypertrophy, respiratory failure, plexus palsy, and asphyxia. The risk of stillbirth and death in the first seven days of life is increased in pre-pregnancy diabetes. By far the most common complication in newborns of diabetic mothers is postnatal hypoglycemia, which is approximately 200- to 400-fold more common among them than in children of nondiabetic mothers.

Pre-conception care

Inadequately treated diabetes mellitus at conception – both in terms of metabolic control and treatment of concomitant diseases – carries an increased risk of congenital malformations, intrauterine fetal death, pregnancy complications, but also the risk of progression of diabetes-associated secondary diseases such as retinopathy or nephropathy and cardiovascular pre-existing conditions.

In a UK cohort study of 747 women with type 1 diabetes, 39 % of pregnancies were unplanned. Women with unplanned vs. planned pregnancies were younger, more likely to be smokers, had lower social status and education levels, and were less likely to be in pre-conception counseling. Unplanned vs. planned pregnancy showed higher HbA1c levels both pre-conception and during pregnancy. Neonates in unplanned pregnancy more often showed birth weight < 5th percentile and more often required treatment in a neonatal intensive care unit and more often required hospitalization for 10 days. Women with pre-conceptional treatment were less likely to show intrauterine amniotic death and preterm birth.

Hyperglycemia

Data supports an association between elevated maternal HbA1c/hyperglycemia pre-conceptionally and during embryogenesis, and an increased rate of malformations. Congenital malformations are 2 to 3 times less frequent with sufficient therapy pre-conception. Comprehensive diabetic-specific counseling regarding contraception, pregnancy planning and pre-conceptional therapy goals, which should regularly be aligned in fertile women, is a crucial preventative measure. Contraception should be maintained until the HbA1c therapy goal is reached.

BACKGROUND KNOWLEDGE

Recommendations

Women of fertile age **should** be counselled regarding the risk potential of unplanned pregnancy. As part of diabetes treatment, counseling **should** already be provided to adolescents regarding contraceptive methods and family planning.

Concomitant diseases

Diabetes-associated concomitant diseases are independent risk factors for pregnancy complications and adverse fetal outcome.

Obesity

Maternal obesity is an independent maternal and fetal risk factor. Women with a BMI greater than 25 kg/m^2 have an increased risk of miscarriage and perinatal mortality and as of a BMI of 30 kg/m^2 also have a lower chance of becoming pregnant [1–4]. A meta-analysis demonstrated an association between the BMI of pregnant women and the risk of preeclampsia. In cases of obesity, pre-conceptional lifestyle intervention should be sought. A lifestyle with increased exercise and adequate nutrition pre-conception shows positive effects on pregnancy and delivery [5].

Autoimmune diseases

Population studies show that approximately one in three people with type 1 diabetes has another autoimmune disease, with autoimmune thyreopathy being the most common secondary disease [6–9].

BACKGROUND KNOWLEDGE

Recommendations

- Women with type 1 diabetes **should** be screened for thyroid peroxidase (TPO) antibodies either before conceiving or once having become pregnant. In untreated euthyroid pregnant women who are TPO antibody positive, serum TSH concentration **should** be measured every 4 to 8 weeks.
- In women with TPO antibody detection, therapy with levothyroxine **should** already be started at TSH > 2.5 µU/ml due to the possible limited thyroid hormone reserve.
- If latent hypothyroidism is present, therapy with levothyroxine **should** be initiated immediately.

Metabolic targets

Pre-conception blood glucose targets

Numerous studies have demonstrated an association between pre-conception HbA1c levels and the risk of embryonic malformations and other adverse fetal and maternal events [10–14]. The risk is only slightly higher than that of the general population at HbA1c levels in the near-normal range but increases linearly with higher HbA1c levels. Accordingly, an HbA1c value < 7.0 % should be aimed for pre-conception. If there is a tendency to hypoglycemia or an unstable metabolic situation, the lowest value that is safe for the mother should be aimed for. The use of a continous glucose monitoring (CGM) system should also be considered, although a randomized trial failed to show an advantage of tissue glucose measurement across all pregnant women with type 1 diabetes in pre-conception preparation [15] In selected situations with an unstable metabolic situation, there may nevertheless be a relevant advantage here.

Blood glucose targets during pregnancy

Blood glucose control during pregnancy has also shown a clear association of higher values with adverse fetal and maternal events [11, 16, 17]. Furthermore, superiority of treatment using CGM dur-

ing pregnancy over conventional blood glucose measurement has been demonstrated [15]. Tissue glucose measurement was accompanied by slightly lower average blood glucose values, which was likely responsible for the better results observed in this group. Accordingly, this study supports the goal of achieving blood glucose levels as close to normal as possible during pregnancy. During the course of pregnancy, an HbA1c value in the upper normal range – while taking the risk of hypoglycemia into account – should be aimed for. Severe maternal hypoglycemia is, of course, also dangerous during pregnancy and must be avoided. In contrast, a negative influence of mild maternal hypoglycemia on fetal development has not been proven in humans [18–21].

BACKGROUND KNOWLEDGE

Recommendations

- Pre-conception, metabolic control close to normal (HbA1c < 7 %) **should** be aimed for. If a near-normal setting is possible without risk of hypoglycemia, then an HbA1c < 6.5 % should be aimed for before conception.
- The following target blood glucose values should be aimed for during pregnancy (capillary self-measurements):
  - Fasting and preprandial: 65–95 mg/dl (3.8–5.2 mmol/l).
  - 1 hour after the start of the meal: ≤ 140 mg/dl (≤ 7.7 mmol/l)
  - 2 hours after the start of meal: ≤ 120 mg/dl (≤ 6.6 mmol/l)
- The HbA1c value **should** be in the upper normal range during the course of pregnancy, taking into account the risk of hypoglycemia.
- When using a CGMS, a TIR (time-in-range: 63–140 mg/dl (3.5–7.7 mmol/l)) of sensor glucose of at least > 70 % **should** be aimed for in pregnant women with type 1 diabetes. When using a CGMS, a TIR (time-in-range: 63–140 mg/dl (3.5–7.7 mmol/l)) of sensor glucose of > 90 % **can** be targeted in pregnant women with type 2 diabetes.

Counseling for patients wanting to have children

Abortion and risk of malformation

Women with diabetes have an increased risk of early spontaneous abortion [22], which correlates with the quality of periconceptional metabolic control [23–25]. Similarly, malformations occur more frequently in fetuses of diabetic pregnant women in correlation with the quality of metabolic control at the time of conception. The risk is 1.7- to 11-fold (on average about 4-fold) higher than that of metabolically-healthy women [26, 27].

A meta-analysis concludes a 2.4-fold increased relative risk for relevant congenital malformations in maternal pre-conceptional diabetes [28]. In absolute terms, the risk in studies ranges from 5.0 to 9.8 %. However, an increased malformation rate is no longer found for type 1 diabetes in all studies, which is seen as a reflection of better metabolic control periconceptually and during pregnancy [29]. The risk of fetal malformations for pregnant women with known type 2 diabetes is not lower than that of women with type 1 diabetes [26, 30]. In particular, inadequate pre-conception care may also decisively contribute to the high risk in mothers with type 2 diabetes [30]. Since periconceptional metabolic control is crucial for the malformation rate, the malformation rate is lower in planned pregnancies than in unplanned pregnancies [31].

The spectrum of malformations associated with maternal diabetes (type 1 diabetes/type 2 diabetes) includes, in particular, congenital heart defects (2.3–4 %, approximately 4-fold increased compared to women without diabetes), neural tube defects (1.2–2.5 %, 2- to 3-fold increased), skeletal anomalies, omphaloceles, malformations of the urinary tract, and biliary atresia with splenic anomalies [32–35]. The risk of congenital heart defect ranges from 2.6 to 6.5 % for the offspring of patients with type 2 diabetes [36].

Multiple malformations are often present [34, 36] without a clear phenotype of diabetic embryopathy being definable. Previously, it was assumed that the risk of numerical chromosomal aberrations was not increased by preexisting maternal diabetes mellitus, but according to new findings from a large population-based study from the USA in 2020, there is an increased risk of Down syndrome and chromosomal disorders of approximately 40 % [37, 38]. This new finding, which is contrary to previous data, must first be confirmed by further studies. The fetal malformation rate in women with diabetes seems to be reduced by periconceptional administration of water-soluble vitamins, especially folic acid [39].

Risk of offspring developing type 1 diabetes

Offspring of women with type 1 diabetes have an approximate 2–5 % lifetime risk of also developing type 1 diabetes.

BACKGROUND KNOWLEDGE

Recommendations

- Women with diabetes and desire to have children **should** be advised to take oral folic acid (at least 0.4 mg/day).
- Iodine supplementation in women with type 1 diabetes who have a desire to have children **should** be the same as in metabolically healthy women (100–200 µg/day) in the pre-conceptional phase and during pregnancy.
- Every patient **should** be advised about the administration of acetylsalicylic acid (ASA), which should be administered in consensus with the patient. The indication for the administration of aspirin for the prophylaxis of preeclampsia **can** also be risk-adapted in women with diabetes via preeclampsia screening or a general recommendation can be made. However, in the presence of diabetes and nephropathy, ASA **should** be recommended to all pregnant women.
- If women with diabetes are given aspirin for prophylaxis of preeclampsia, it **should** be started before 16 + 0 weeks gestation, continued at 150 mg/day until 35 + 0 weeks gestation, and then discontinued.

Insulin therapy

Choice of insulin preparation

Analog insulins have become the insulins of choice. Due to their product characteristics, short-acting analogs lead to faster absorption and long-acting analogs to longer efficacy and more consistent absorption than human insulins. In a meta-analysis of randomized trials of short-acting insulin analogs, no differences were found in HbA1c levels in pregnant women with type 1 diabetes compared with human insulin. For the short-acting insulin analogs aspart and lispro, new formulations are available with faster absorption and onset of action and a shorter duration of action profile. Both FIASP and Lyumjev are approved for use in pregnancy. Insulin glulisine currently has insufficient data for pregnancy and should not be used in pregnancy.

BACKGROUND KNOWLEDGE

Recommendations

- Intensified conventional insulin therapy (ICT) or continuous subcutaneous insulin infusion (CSII) are considered the optimal therapy. Both forms of therapy are considered equivalent with regard to pregnancy outcomes; perfect management and blood glucose values within the target range are essential.
- Human insulins or insulin analogs **should** be used to treat pregnant women with preexisting type 1 or type 2 diabetes. If stringent therapy goals are targeted, the use of short-acting and long-acting insulin analogs **should** be considered, as advantages in terms of HbA1c reduction and a lower risk of hypoglycemia can be expected compared with normal insulins.
- Pregnant women on short-acting insulin analogs or long-acting insulin analogs insulin **should** continue to use them after appropriate instruction on metabolic goals, as no disadvantages have been reported compared with human insulins.
- In women with type 1 diabetes and a desire to have children or pregnant women with type 1 diabetes, insulin pump therapy **can** be considered in the following constellations: a. if individual therapy goals have not been achieved, b. if there is insufficient glycemic control of the metabolic state with ICT, c. if the daily routine is irregular, d. if there is a low insulin demand.

Continuous glucose monitoring

A first large randomized controlled trial (n = 325) of real time continuous glucose monitoring (rtCGM) in pregnancy [15] showed significant benefits in neonatal outcomes for rtCGM use in pregnant women with type 1 diabetes (neonatal hypoglycemia, length of intensive care unit (ICU) stay, birth weight, length of hospital stay). Glycemic testing provided significant benefits in time-in-range (68 vs. 61 %), rate of hyperglycemia (27 vs. 32 %), and HbA1c (−0.19 %); small, nonsignificant benefits in hypoglycemia frequency and severe hypoglycemia (18 CGM and 21 controls). Currently, a hybrid closed loop (HCL) system is being evaluated in pregnancy in type 1 diabetes (AiDAPT trial) [40].

Hypoglycemia

Severe hypoglycemia in pregnant women with the need for glucose or glucagon administration must be avoided mostly with regard to the mother. Pre-conceptional (overly) strict blood glucose control can result in hypoglycemic adrenergic warning signs increasingly being suppressed and eventually becoming absent due to insufficient hormonal counter-regulation. Low target blood glucose levels during pregnancy may further exacerbate hypoglycemic rates in pregnant women at risk, which in turn worsens hypoglycemia perception. Very low mean blood glucose levels increase the risk of preterm birth compared with intermediate control levels (OR 3.0; [41]). Adverse fetal effects from single, severe hypoglycemias have not been reported; however, follow-up of children regarding their psychomotor development is lacking. The risk of fetal growth restriction with persistent very low blood glucose control below the target range should be considered.

BACKGROUND KNOWLEDGE

Recommendation

- Self-management using rtCGM in pregnancy **should** be offered.
- Pregnant women with type 1 diabetes **should** be given good instruction regarding hypoglycemia risks, and the partner or another relative should be informed about hypoglycemia risks and hypoglycemia symptoms and instructed in the use of the emergency glucagon kit (injection or nasal powder).
- The most important risk factor for severe hypoglycemia in the 1st trimester of pregnancy is a positive pre-conceptional history for this in the last four months. These pregnant women **should** be fitted with a CGM system before or during pregnancy.

Complications in pregnancy due to diabetes-associated concomitant diseases

The presence of diabetic microangiopathy in early pregnancy increases the risk of complications during pregnancy. A meta-analysis in type 1 diabetes shows an increased risk of preeclampsia compared with diabetic women without microangiopathy (OR 3.0 in the presence of diabetic retinopathy and 7.2 in the presence of diabetic nephropathy). The presence of nephropathy is associated with an increased risk of preterm delivery (PTD) (OR 4.1) and small for gestational age (SGA) (OR 6.2), and the presence of retinopathy increases the risk of PTD (OR 1.6) [42].

BACKGROUND KNOWLEDGE

Recommendations

- If severe non-proliferative or proliferative retinopathy exists prior to conception, complete pan-retinal laser therapy **should** be sought first.
- Ophthalmologic checks **should** be performed:
- Before the planned pregnancy;
  - After diagnosis of pregnancy and at the 28th week;
  - In case of initial manifestation and/or progression of diabetic retinopathy during pregnancy, controls in consultation with the ophthalmologist;
  - In the first year postpartum.
- Both non-proliferative and proliferative retinopathy **should** not be an indication for a C-section birth per se.
- After diagnosis of pregnancy, albumin excretion **should** be determined to detect/control diabetic nephropathy. In case of nephropathy as of chronic kidney disease (CKD) stage 3 or already-impaired renal function according to Kidney Disease Outcomes Quality Initiative (KDOQI) (glomerular filtration rate [GFR] < 60 ml/min), renal function **should** be monitored closely due to the high maternal risks.

Pre-existing type 2 diabetes at the time of planning pregnancy and in pregnancy

In principle, type 2 diabetes mellitus is associated with the same fetal risks as type 1 diabetes mellitus. In addition to diabetes mellitus as a risk factor for pregnancy, women with type 2 diabetes mellitus have a higher risk profile compared with women with type 1 diabetes mellitus in terms of age > 30 years, high obesity prevalence, chronic hypertension, and asymptomatic concomitant vascular disease and also ethnicity [34, 43–48]. Increasingly, obesity and/or other diabetes risk factors affect women of reproductive age [49]. In such cases, diabetes screening is recommended already at the time of planning pregnancy and definitely in early pregnancy to exclude diabetes in pregnancy (DIP)/type 2 diabetes [50]. In the DALI study, 0.5 % of European obese pregnant women already had DIP at the 15th week of pregnancy [51].

Pre-conception care

Unplanned pregnancy, lack of near-normal metabolic control or even unawareness of metabolic control pre-conception, and the too-late initial consultation at a center play a crucial role in congenital malformations and increased perinatal mortality and morbidity [52]. However, up to 95 % of women with type 2 diabetes mellitus become pregnant unplanned. Up to 76 % are not under diabetological care either pre-conceptionally or during the period of organogenesis, and up to 29 % did not have a documented HbA1c value in the last six months pre-conception. Pre-conceptional folic acid supplementation occurs even less frequently than in type 1 diabetes. A switch from oral antidiabetic drugs to an intensive form of insulin therapy as well as diabetological complementary treatment should already take place at the planning stages of pregnancy, i. e., always pre-conception [53, 54]. In the case of suboptimal metabolic control, women must be informed about the possible risk of congenital malformation.

Oral antidiabetics

Data on the use of oral antidiabetic drugs during pregnancy in type 2 diabetes is sparse. Conception while on oral antidiabetic drugs (OAD) is not an indication for pregnancy termination. However, sulfonylurea preparations and metformin are placenta-permeable and potential long-term effects in the offspring are insufficiently documented [55, 56]. Study data is available mainly on glibenclamide and metformin in pregnancy, whereas publications on DPP4 or SGLT2 inhibitors is still lacking. Glibenclamide therapy showed higher maternal weight gain compared to metformin in pregnancy and also more frequent macrosomia and neonatal hypoglycemia compared to metformin or insulin [57]. Neonates from glibenclamide-treated pregnancies have a higher risk of birth complications [58].

In very insulin-resistant and severely overweight women with type 2 diabetes, therapy with metformin may also be considered in addition to insulin to improve metabolism and attenuate insulin resistance [59]. Vitamin B12 monitoring is recommended for long-term use of metformin and pregnancy [56].

Although there are now several studies of metformin compared or in addition to insulin in the treatment of type 2 diabetes in pregnancy that at least confirm the safety of the medication and fewer hypoglycemias in pregnancy, the quality and case size of the studies are still insufficient for evidence-based recommendations. A small parallel-group study from Pakistan that included women with type 2 diabetes from the 1st trimester onward with metformin therapy alone versus insulin administration alone versus a combination of metformin and insulin showed that 85 % of women required additional insulin and that metformin patients gained less weight, were less likely to develop gestational hypertension and neonatal hypoglycemia, and neonates required intensive care unit care less often, although they were more often small for their gestational age (SGA) [60] A Cochrane meta-analysis of 3 RCTs of 241 pre-conceptional type 2 diabetes or impaied glucose tolerance (IGT) and post-gestational diabetes mellitus (GDM) pregnancies, all of whom had type 2 diabetes in pregnancy, found that metformin had a potential reduction in rates of C-section, gestational hypertension, and neonatal hypoglycemia compared with insulin [61]. Rates of preeclampsia, preterm birth, and large for gestational age (LGA) were not different. However, the quality of evidence was low. Possible long-term effects of metformin therapy in pregnancy on later fetal development cannot be excluded [56] and currently argue for individualized mindful use: in the MIG TOFU study, children whose mothers received metformin therapy showed increased subcutaneous fat mass and, after 7 to 9 years, higher body weight and abdominal circumference compared with the insulin group [62, 63]. A follow-up of 4-year-old children of women with polycystic ovary syndrome (PCOS) on metformin therapy during pregnancy showed a significantly increased risk of overweight/obesity compared with placebo [64]. Currently, metformin therapy in pregnant women with type 2 diabetes is being studied in 2 trials (MiTy and MOMPOD) [65]. In the MiTy trial, 502 women with type 2 diabetes and insulin ther-

apy were randomized to additional metformin (2 × 1 g) or placebo between 6th and 22nd weeks of gestation [66].While the primary neonatal composite outcome was not different and some benefits such as better glycemic control with lower insulin requirements and fewer LGA infants and C-sections were determined with metformin, growth retardation (small for gestational age [SGA] infants) was seen almost twice as often with metformin (13 vs. 7 %). Similarly, a recent meta-analysis found that metformin exposure in utero was associated with smaller neonates and accelerated postnatal growth [67].

If women with type 2 diabetes who are already pregnant are taking metformin and these women have normoglycemic metabolic control, they can be reassured in the absence of evidence of a teratogenic effect of metformin. However, once pregnancy has been determined, it is required to switch to insulin therapy [68]. In general, for OADs, switching to insulin therapy before conceiving is indicated because of diaplacental passage, insufficient evidence for successful therapy, insufficient data regarding long-term consequences for the offspring, and the contraindication of OAD in Germany for therapy of type 2 diabetes during pregnancy. Women with type 2 diabetes who wish to have children should therefore be switched to insulin therapy before conceiving. Appropriate training of patients for self-adjustment of the insulin dose and information about possible risks, as well as the expected metabolic changes during pregnancy, should be provided by the physicians in charge of pregnancy planning/desire to have children.

The EMA approved metformin (Glucophage) 2022 for treatment in preexisting diabetes: Thus, treatment with metformin can be continued in individual cases of marked insulin resistance – in addition to insulin therapy. With regard to **insulin therapy** before and during pregnancy as well as postpartum, the same criteria and recommendations apply as for type 1 diabetes.

Lifestyle

Accompanying drug therapy in type 2 diabetes and pregnancy, the lifestyle recommendations generally applicable to diabetes, as well as the general recommendations for weight gain in pregnancy dependent on pre-conceptional weight, should also be followed. An individualized treatment plan consisting of lifestyle modification with dietary recommendations, exercise, supported and monitored by blood glucose self-monitoring, must be created. The diet plan must be based on body weight and physical activity, consisting of approximately 40–50 % carbohydrates (fiber approx. 30 g/day), 30–35 % mainly vegetable fat and 20 % protein, as well as sufficient minerals and vitamins (iron, folic acid, vitamin D, calcium, vitamin B, magnesium, iodine). Unfortunately, data is lacking for optimal specific caloric intake in pregnant women with type 2 diabetes, so reference must be made to general dietary reference values. In any case, fast absorbing carbohydrates should be avoided. A meta-analysis on low glycemic index diets in pregnancy showed lower fasting blood glucose levels and LGA rates under this dietary regimen [69]. The Endocrine Society recommends caloric restriction by about one-third in obesity; no significant weight reduction (up to a maximum of 5 kg) or catabolism occurs. Daily intake should be at least 1600 kcal [70]. Data for optimal weight gain versus weight maintenance in women with BMI > 35 kg/m^2 is lacking [65]. Body weight must be documented by the patient at each follow-up visit and on their own every week. Evidence for specific dietary recommendations for pregnant women with type 2 diabetes is low, and randomized controlled trials of different dietary approaches are not available. A pilot study from Denmark, which also included 43 women with type 2 diabetes, points to the possibility of using special apps such as “Schwanger mit Diabetes” (Pregnant with Diabetes) and the information needs of those affected, especially for topics such as diet and carbohydrates [71].

Evidence-based recommendations for physical activity in pregnant women with type 2 diabetes are lacking, and a planned systematic Cochrane review could not be performed due to the lack of available randomized controlled trials (RCTs) as sources [72]. Medical societies recommend regular moderate physical activity (at least 150 min per week) integrated into everyday life as part of the therapeutic concept in unproblematic pregnancies [72]. The types of sport must be compatible with pregnancy and adapted to the individual training status (no contact sports or martial arts, or sports with a high risk of falling or injury).

BACKGROUND KNOWLEDGE

Recommendations

- There are insufficient studies on metformin in pregnancy in type 2 diabetes. Metformin **should not** be routinely used in pregnancy in type 2 diabetes. Metformin **may** be considered in individual cases of marked insulin resistance.
- Pre-conceptional instruction and switching from oral antidiabetics to insulin, as well as diabetological complementary treatment, **should** be provided. Treatment with metformin can be continued in individual cases with pronounced insulin resistance in addition to insulin therapy.

Obstetric management

Type of birth

In perinatal statistics, the rate of C-sections is still significantly increased in women with diabetes compared to the general population. While the C-section rate is about 30 % in Germany, the C-section rates in women with diabetes are still twice as high. Infantile macrosomia per se or maternal retinopathy should no longer be a primary indication for a C-section, [73]. However, delivery by vacuum extraction or using forceps to facilitate the pushing phase may be considered if laser therapy was performed less than 6 weeks ago for actively proliferative retinopathy. The indication for secondary C-section in case of obstructed labor or abnormal cardiotocography (CTG), possibly in combination with marginal findings in fetal blood analysis, should be given generously; there is more risk of subpartum asphyxia because of the increased oxygen demand of fetuses with hyperinsulinism and diabetic fetopathy.

BACKGROUND KNOWLEDGE

Recommendations

- Pregnant women with preexisting diabetes **should** be referred to a level I or II perinatal center for delivery.
- The same induction indications apply to pregnant women with preexisting diabetes as to nondiabetic pregnant women. In addition, for pregnant women with diabetes, if the expected delivery date is reached and labor does not begin, induction of labor **should** occur.
- In the last trimester of pregnancy (30–32 weeks), the pregnant woman with preexisting diabetes **should** be presented to the maternity hospital.

Metabolic control during labor

Evidence-based findings on how to approach the intrapartum are not available. Therefore, the setting targets are based on the targets applicable during pregnancy and take into account that even short-term hyperglycemia of the mother can lead to increased insulin secretion in fetuses with an increased risk of postnatal hypoglycemia. Therefore, during induction and delivery, blood glucose levels between 90 and 126 mg/dl (5.0–7.0 mmol/l) should be aimed for. It should be noted that maternal hypoglycemia can lead to a decrease in contractions.

With the onset of labor, insulin requirements drop rapidly to 50 %. The pregnant woman should be informed about this in advance and as well about the appropriate measures to take at the onset of labor in the home environment and at induction. In the case of pump therapy, she should be able to reduce the basal rate to 50 %, and after application of basal insulin in the evening, blood glucose should be checked, and a supply of carbohydrates given at the onset of labor at night.

If a C-section is planned, the usual amount of basal insulin for the night should be injected the evening, possibly reduced to 75 % if fasting blood glucose values tend to be low. Insulin pumps can be attached to the upper arm and continue to run at a basal rate reduced to 50 % with the onset of a C-section.

At induction, 50 % of the basal insulin of the day should be injected in the morning with intensified insulin therapy. Blood glucose should be monitored in the short term and corrected with short-acting insulin. With insulin pump therapy, the basal rate should be left until the onset of contractions and, from the onset of regular contractions, lowered to 50 % of the previous insulin dose.

During labor, blood glucose should be monitored every hour [74]. Immediate consequences must be drawn from the results. The obstetric team should be responsible for managing metabolism intrapartum. There should be an in-clinic, binding standard to guide the staff. In this context, it is also important that the pregnant woman is instructed, in detail, from the diabetological side in preparation for birth with regard to the importance of keeping the glucose values stable in the target range.

After the placenta is delivered, insulin requirements drop abruptly and there is an increased risk of hypoglycemia. Insulin delivery must therefore be adapted at shorter intervals. To avoid catabolism and ketoacidosis, the insulin dose is continued at a low level (approx. 30–50 % of the pre-birth dose) and continuously adjusted to the current blood glucose values.

BACKGROUND KNOWLEDGE

Recommendations

- As part of the delivery counseling, the pregnant woman with diabetes **should** be informed about the abrupt drop in insulin requirement at the onset of labor and the appropriate measures to take.
- Each delivery center **should** have an interdisciplinary treatment regimen for diabetes therapy during and immediately after delivery.
- Glucose/blood glucose checks **should** be performed every hour for metabolic monitoring during delivery.
- Target values between 90–126 mg/dl (5.0–7.0 mmol/l) **should** be achieved during delivery. Major metabolic fluctuations, sudden blood glucose spikes, or hypoglycemic episodes should be avoided.
- After delivery, insulin therapy **should** be adjusted individually on a short-term basis because of the increased risk of hypoglycemia in the first postpartum hours.
- To prevent hypoglycemia, 40 % glucose gel **can** be applied orally to newborns of diabetic mothers at 1 h of age.

Conflicts of Interest

Lecture fees and/or consulting services: Hummel – Astra Zeneca, Boehringer-Ingelheim, Dexcom, Lilly, MSD, Novo Nordisk, Sanofi; Füchtenbusch – Abbott, Astra Zeneca, Berlin Chemie, Boehringer, Glaxo Smith Kline, Lilly, Novo Nordisk, Sanofi; Bührer – Chiesi, Nestlé; Battefeld – Berlin Chemie, Lilly, Novo Nordisk; Groten – Novo Nordisk, JenaPharm; Haak – Abbott, AstraZeneca, MSD, Roche; Kainer – GE Canon; Kautzky-Willer – Novo Nordisk, Lilly, Boehringer Ingelheim, AstraZeneca, Sanofi, Amgen, Novartis; Meissner – Lilly, Novo Nordisk; Nagel-Reupner – Amgen, Boehringer, Novo Nordisk, MSD, Lilly; Schäfer-Graf – Novo Nordik, Sanofi, Berlin-Chemie; Siegmund – Abbott, Astra, Berlin Chemie, Boehringer, Lilly, Medronic, MSD, Novo Nordisk, Roche, Sanofi

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