Diabetes and pregnancy

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Summary

The various types of diabetes can influence pregnancy to a different degree and, most importantly increase the risk for complications. In addition to the existing danger to develop diabetogenic fetopathy, a pre-existing type 1 or type 2 diabetes can lead to diabetogenic embryopathy, predominantly characterized by malformations. The ability of prenatal diagnostics to detect malformations should therefore be thoroughly exhausted. The insulin requirements of pregnant women with type 1 diabetes alter as early as the first and second trimester and should be adequately monitored in cooperation with a diabetologist. In Germany, gestational diabetes, the most common pregnancy-related illness, is only diagnosed in every tenth patient. This is due to the inadequacy of the urine screening test, of which the results are influenced by diverse factors. As screening is recommended in the national maternal health guidelines ("Mutterschaftsrichtlinien"), it should be offered to all pregnant women, if required. Screening has to be paid for by the patients themselves as a so-called "HIS" (= Individual Healthcare Services; in German "Individuelle Gesundheitsleistungen" = IGeL) or may be paid by private health insurances. This procedure certainly does not match the severe consequences of the illness. One-step diagnosis (direct use of the oGTT test) appears to be more effective than using the two-step diagnostic test. In Germany, the intense efforts that have been made to provide good prenatal care for pregnant women have resulted in one of the best developed medical care systems worldwide. This system should be pursued and updated according to the latest findings and measurement methods. In patients with PCO syndrome seeking treatment in order to conceive a child, oral diabetics should only be prescribed following appropriate patient counselling.

Introduction

The results of the HAPO study as well as the recently published guidelines on diabetes during pregnancy have made it necessary to update the prior article on gestational diabetes. For this reason, the following article deals with all types of diabetes and attempts to illustrate those aspects that are of practical relevance.

Definition

In this article we differentiate between the four major types of diabetes mellitus of which each has a different pathogenesis (Tab. 1).

Table 1: Classification of diabetes (according to the American Diabetes Association 2002)

I	Type 1 diabetes: B-cell dysfunction, usually leading to an absolute insulin deficiency
II	Type 2 diabetes: ranging from a predominance in insulin resistance to a predominance of a secretory defect plus genetically caused types
III	Other specific types: based on an underlying disease (secondary diabetes)
IV	Gestational diabetes: diabetes that is first diagnosed during pregnancy (and disappears thereafter)

Type 1 diabetes (earlier known as insulin-dependent diabetes mellitus, IDDM) is characterized by a complete lack of insulin secretion. Due to immunological factors, which will not be dealt with here, the β-cells of the pancreas become entirely dysfunctional, so that they no longer secrete any insulin. This makes the patients with type 1 diabetes insulin-dependent, or else they develop ketoacidosis due to the lacking inhibition of lipolysis (waste product: ketone).

The pathogenesis of type 2 diabetes is entirely different. Patients with type 2 diabetes (previously known as non-insulin-dependent diabetes mellitus, NIDDM or also adult-onset diabetes) suffer from a receptor dysfunction of the insulin target organs. In this case insulin can be either normal or increased (hyperinsulinemia). However, because the target cells do not respond to insulin, the insulin-mediated uptake of glucose does not take place. Apart from a genetic tendency, obesity and a poor diet play a major role in the pathogenesis of type 2 diabetes. Adequate treatment for these patients are oral antidiabetics that either increase the secretion or the sensitivity of the target cells (not to be used during pregnancy). However, clinical studies have come to the conclusion that this group also profits from insulin therapy even if blood sugar levels remain high, which is why the original differentiation between insulin-dependent and non-insulin-dependent has become obsolete.

The third rather rare group consists of patients in whom other diseases have caused extensive secondary damage to the pancreas, for example pancreatitis or drug abuse, leading to a dysfunction of the islet cells.

Type IV, gestational diabetes, is defined as diabetes that is for the first time diagnosed during pregnancy. Naturally, abnormal glucose levels may also be due to type 1 or type 2 diabetes. However, it seems rather unlikely to develop the first symptoms of type 1 diabetes during pregnancy as it is so infrequent. Diagnosing type 2 diabetes is much more likely, as blood sugar levels are seldomly measured in non-pregnant women. As the risk factors for gestational diabetes – obesity, family history of diabetes, and advanced age – are similar to those of type 2 diabetes, it is assumed that pregnant women with gestational diabetes are at a high risk of developing type 2 diabetes, and that the pregnancy is, so to speak, an "anti-insulinary tolerance test". Correspondingly, many patients with gestational diabetes develop type 2 diabetes postpartum. The cumulative incidence is 3 % per year, i. e. after 10 years it reaches 30 % (Catalano et al. 1991; Damm 1998).

Medical Care

Pregnant women already diagnosed with type 1 or type 2 diabetes should be cared for by specialists, therefore only key points that are important to the gynaecologist are mentioned in Table 2. We do not refer to gestational diabetes here, as it is dealt with subsequently.

The monitoring of blood glucose levels sub partu as well as the choice of the type of insulin are not dealt with further. Generally speaking, a woman may continue taking the insulin analogs (Lispro®, Insulin Aspart®) during pregnancy owing to the fact that clinical studies have so far not been able to show any disadvantages. Some studies even observed an improved blood glucose adjustment.

Table 2: Important considerations for pregnant diabetics (type 1 and type 2)

- The risk of abortion or malformation correlates with the HbA1c values at the beginning of the pregnancy. Thus, a preconceptional consultation about the need for blood glucose level adjustment is of great importance.
- The possibilities of prenatal diagnostics (first trimester screening, morphology scans, Doppler) should be completely exhausted as the risk of malformations is significantly increased in this group of patients.
- Characteristically, the insulin requirement decreases between the 12th and 20th week of pregnancy, constituting a risk of hypoglycemia (Cave: inform the patient of the risk!).
- From the 20th week of pregnancy onwards, insulin requirements increase and the dose must therefore be adjusted accordingly; up to 5 times the normal dose may be required.
- Retinoscopy should be carried out at least three times in patients with type 1 diabetics for early recognition and treatment of a possible retinopathy.
- Pregnant women with preexisting diabetes more frequently develop pregnancy-induced hypertension/preeclampsia and must therefore be closely monitored. Their treatment corresponds that of non-diabetic pregnant women.
- Pregnant women with nephropathy as well as macroangiopathy, although rarely encountered among women in fertile age, must be closely monitored.
- Pregnant women with type 1 diabetes often suffer from Hashimoto thyroiditis and should be screened accordingly.
- In general, birth is induced on the due date in pregnant women with type 1 or type 2 diabetes. Only in the case of additional risk factors should delivery take place earlier. We have to take into consideration that the development of the fetal lungs is delayed in this group of patients (Cave: care at a perinatal center!). For this reason, it is no longer common practice to induce birth in the 38th week of pregnancy.
- The care of pregnant diabetics should take place in close cooperation with a diabetologist, whereby contact should also be held with a perinatal center level II-III at an early stage.

Pathophysiology of gestational diabetes

"Pure" gestational diabetes (GDM) does not usually develop until after the 20th week of pregnancy – after which there is also an over-proportional rise in the level of pregnancy hormones. Thus, the rise in blood glucose levels occurring during pregnancy might in part be due to changes in these hormons.

However, apart from hormonal factors, a poor diet plays a great role. Dietary consultation should therefore be the first step of treatment. If GDM is diagnosed before the 20th week of pregnancy, it is usually a case of previously unidentified type 2 diabetes.

All diagnostic and screening measures aim at identifying GDM at an early stage. The optimal screening point is thought to be the 24th-28th week of pregnancy, as carbohydrate intolerance will have developed by this time. Thus, enough time is left for the patient to respond to treatment. The increased risks for mother and child are shown in Table 3 (German Diabetes Association 2001; Kjos 1999).

Table 3: Clinical consequences of diabetes for mother and child

	Mother	Child (see Fig. 1)
ype 1 and ype 2 iabetes nellitus	• Hypoglycemia in the 1st trimester • Abortion	Malformations (diabetogenic embryopathy)
ype 1 and ype 2 iabetes nellitus and estational iabetes	• Infections of the urinary tract/pyelonephritis • Pregnancy-induced hypertension/preeclampsia • Polyhydramnios • Premature rupture of the amniotic sac • Premature birth • Diabetes mellitus in later life • Operative vaginal deliveries • Increased rate of Cesarean section	• Diabetogenic fetopathy: • Hypoglycemia • Hypocalcemia • b-cell hyperplasia of the pancreas • Polycythemia/hyperbilirubinemia • Respiratory dysfunctions • Prematurity • Type 2 and probably also type 1 diabetes • Infans mortuus

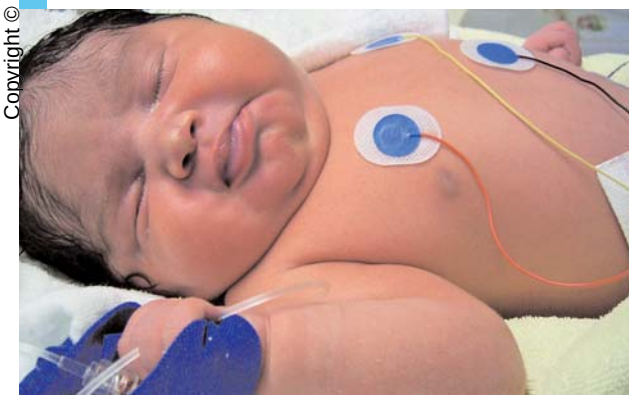

Fig. 1: Child with diabetogenic fetopathy

Despite these facts, general screening for GDM is not part of the Maternal Health Guidelines, although it has been standard practice in the USA for two decades now. Instead, the guidelines recommend a urine test for pregnant women at every medical checkup (Guidelines of the Federal Joint Committee of Physicians and Health Insurance Funds, Version 27th January 1999; A 4). The accuracy of this urine test has yet to be established, especially because its organisational requirements and costs are substantial. The test has got a very low sensitivity (4.3-4.6 %) with regard to the detection of GDM, as was proven in international studies, and in one of the author's own studies (Bühling et al. 2004; Gribble et al. 1995; Hooper 1996; Sermer 1994).

The renal threshold is often lowered during pregnancy, thus blood glucose levels cannot only be determined by quantification of glycosuria. This incoherence is due to an increase in glomerular filtration rate with a relative decrease in reabsorption (Davison et al. 1975). Furthermore, during pregnancy, the pathological blood glucose level already commences at about 140 mg/dl (7.8 mmol/l) and is thereby significantly lower than in non-pregnant patients (German Diabetes Association 2001). Only about 10 % of all pregnant women with GDM present with glycosuria; the positive predictive value, i. e. the number of patients with a positive urine stick test that actually do have GDM is also remarkably low, as we often find glycosuria in healthy pregnant women. Furthermore, the rate of glycosuria depends on the diastolic blood pressure. Thus we can indirectly measure the blood pressure by using the glucose stick just as well or just as badly as measuring blood glucose levels (Bühling et al. 2004).

! Only 10 % of all pregnant women with gestational diabetes suffer from glycosuria. Gestational diabetes cannot be excluded by a negative finding in the urine stick test. !

The perinatal statistics (1997) showed that 0.49 % of all pregnant women in Germany suffer from gestational diabetes, whereas studies on general screening found a frequency of 3-8 %. Accordingly, only every tenth pregnant women with gestational diabetes is currently identified! With almost 720 000 births, this means that there are annually 32 000 unidentified patients suffering from GDM per year. In contrast, in the USA general screening has already taken place for several decades, usually in the form of a 50 g glucose screening test. This test can be carried out – in contrast to the oral glucose tolerance test (oGTT) – "irrespective of the preceding meal and the time of day". An oGTT is only performed when the result is pathological (American Diabetes Association 2002). One of the main reasons that screening has not yet been introduced is the worldwide discussion on threshold values. It has been shown that the rate of obstetric complications increases with rising blood glucose levels (even within the so-called "normal range"). The illness is therefore a continuum, the border between "ill" and "healthy" being blurred. The "Fourth International Workshop Conference" in 1991 ascertained the need for screening for all pregnant women (Metzger 1991).

The German Association of Gynecology and Obstetrics (DGGG) approved of this approach in 1992, in 2001 including a recommendation supporting screening (German Diabetes Association 1992/2001). However, general screening is still not established as part of the Maternal Health Guidelines, so that this important medical check-up is only available as an individual service paid for by the patient (IGeL). Care should be taken that even under these circumstances procedures recommended in the guidelines are made available to patients!

! Every pregnant woman should be informed about the availability and importance of the glucose tolerance test recommended in the guidelines. !

In the meantime, some associations of SHI physicians and also some health insurances offer screening for gestational diabetes within the framework of integrated health care.

Screening

Concerning the available methods for diabetes-screening, the two-step approach was established as the screening test, especially because, according to the recommendations, it can be carried out "irrespective of the preceding meal and time of day" (American Diabetes Association 2002; German Diabetes Association 2001; Metzger 1991). The blood glucose is measured one hour after ingestion of 50 g glucose. If the one-hour value reaches or exceeds the level of 140 mg/dl (7.8 mmol/l), the result of the screening is considered pathological and an oGTT is subsequently performed (so-called two-step approach). The author's own studies showed a sensitivity of 93.5 % in 1416 patients and a specificity of 86.3 %. However, the positive prediction value was only 37.9 % (Bühling et al. 1998). The influence of the preceding meal was not taken into account in the recommendations, which undoubtedly influenced the test results (Achilles et al. 1998; Çetin and Çetin 1997; Coustan et al. 1986; Sermer 1994). In a study carried out by the author, the rate of positive test results fluctuated between 11 % and 43 % (Fig. 2), depending on the length of time that had passed since the preceding meal. Sermer and colleagues inferred that the threshold values should be adapted subject to the time of the preceding meal, which, however, appears to be impracticable (Sermer et al. 1994). Insofar, the 50 g screening test has some disadvantages, which raises the question as to whether it would not be better to perform an oral glucose tolerance test right from the beginning.

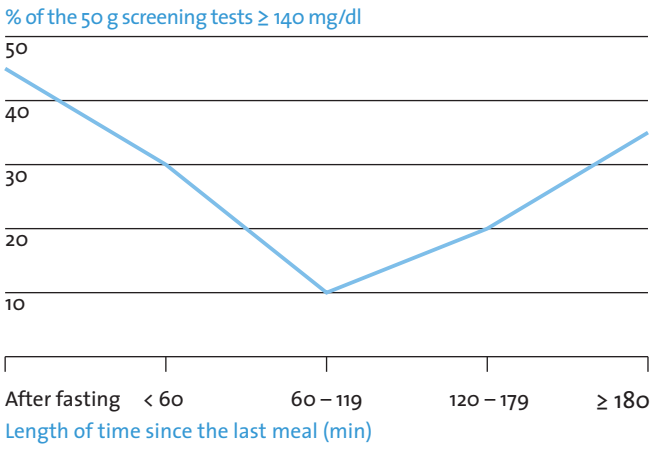

Figure 2: Dependency of the result of the 50g screening tests on the preceding meal

Risk factors

In contrast to the recommendations from the "Fourth International Workshop Conference" which have already been mentioned, the latest recommendations from the "International Workshop Conference" do not suggest any screening for low-risk pregnant women. Low-risk groups include "low-risk ethnic groups", "no first-degree relatives with diabetes", "age < 25 years", "normal body-weight before pregnancy", "no positive anamnesis with regard to diabetes" and "no anamnesis of a bad pregnancy outcome". The author's own studies as well as the clinical impression of other authors were only able to classify about 10 % of the total group as „low-risk patients", i. e. 90 % would require screening in any case. The benefits of this exclusion are therefore doubtful. In one of the author's own studies, GDM was diagnosed in at least 3 % of this "low-risk group" – they had been underdiagnosed.

Diagnosis

The diagnosis "gestational diabetes" is confirmed using an oGTT with 75 g glucose (e.g. Dextro O.G.T®, Roche Diagnostics®). Worldwide, varying threshold values for fasting, the one hour and the two hour test have been established. There is a consensus that pregnant women with only one increased threshold value can be diagnosed as having "Impaired Glucose Tolerance" and must be treated. Pregnant women with two or three increased threshold values are to be classified as gestational diabetics (American Diabetes Association 2002; German Diabetes Association 2001; Metzger 1998). Unfortunately, the unresolved discussions concerning precise threshold values make health policies underestimate the disease. The reason for the ongoing debate is the simple fact that GDM develops continuously.

Additionally, rising blood sugar levels lead to an increase in possible complications. Even in a group of patients with normal 50 g screening test results, we could detect this correlation (Bühling et al. 1998b).

The endpoint of the primary study on threshold values by O'Sullivan and Mahan was not fetal outcome, but solely the incidence of type 2 diabetes after the development of gestational diabetes (O'Sullivan and Mahan 1964). The threshold values of Carpenter und Coustan et al. (1982), which in the meantime have been adapted and adopted by the German Diabetic Association, are also based on these recommendations (Tab. 4). At present, there are no methodically accurate studies that define a threshold value based on fetal outcome. For instance, the studies by Weiss and colleagues use fetal hyperinsulinism as endpoints. Unfortunately, the correlation between fetal hyperinsulism and morbidity in the threshold range is not as narrow as could be desired. A correlation between the (empirically established) level of insulin in the amniotic fluid and fetal outcome is at hand, but a clear cut-off value has not been adequately ascertained. Therefore, the one-hour threshold value of 160 mg/dl called for by Weiss and colleagues must also be viewed with caution (at values between 160 and 169 mg/dl, 8 % of the children suffer from hyperinsulism) (Weiss et al. 1998).

Recently, the eagerly awaited results of the HAPO study were published (HAPO: Hyperglycemia and Adverse Pregnancy Outcome), in which 25 000 pregnant women underwent a single-blind oGTT between the 24th and 28th week of pregnancy. Unblinding only took place when the values of the oGTT exceeded 105 mg/dl fasting and two hours 200 mg/dl postprandial. The frequently described iatrogenic influence (e. g. performance of a Cesarean section in patients with existing diabetes) was thus avoided. The rate of Cesarean section, macrosomia, fetal hyperinsulism, and the rate of hypoglycemia were used as outcome parameters. The results show the expected risks that increase continually with the blood glucose levels so that no cut-off values could be defined as a result of this widespread study, although a good correlation was recently established between anthropometric data of the newborn with the mother's blood glucose levels (HAPO 2008a, HAPO 2008b). In addition, it is questionable whether the results of this study, of which a large proportion were women with Afro-American and Hispanic background, can be transferred to the German population. In this respect, it would be sensible for all colleagues to keep using the international threshold values to enable a good comparison.

Figure 3 shows a flow diagram on possible procedures based on the Guidelines.

Table 4: Performance of the 50 g screening and the oral glucose tolerance test (oGTT)

0 g screening test 50 g glucose oral, "irrespective of the preceding meal and time of day")	After 1 hour: 140 mg/dl** (7.8 mmol/l**)
Oral glucose tolerance test 75 g glucose oral, in the morning after at least eight hours of fasting)*	• After fasting: 90 mg/dl (5.0 mmol/l) • After 1 hour: 180 mg/dl (10.0 mmol/l) • After 2 hours: 155 mg/dl (8.6 mmol/l)

* If only one threshold value is reached or exceeded "Impaired Glucose Tolerance", IGT, is diagnosed; if two or three pathological values are found, the diagnosis is gestational diabetes.

** If the threshold value is reached or exceeded, an oGTT must be performed.

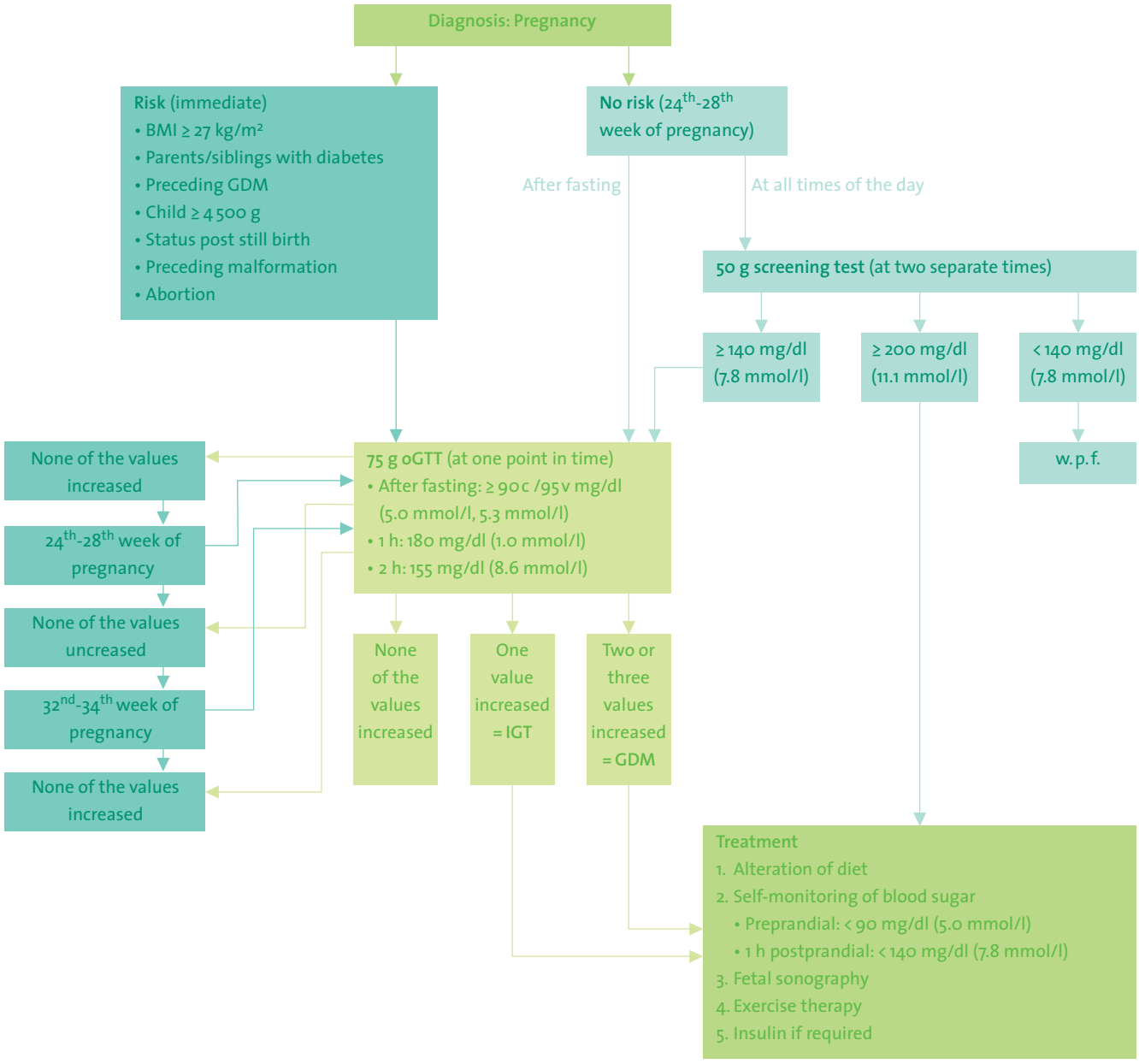

Figure 3: Procedures in gestational diabetes (based on the Guidelines of the German Diabetes Association)
oGTT: oral glucose tolerance test; IGT: Impaired Glucose Tolerance; GDM: gestational diabetes mellitus; BS: blood sugar; w.p.f.: without pathological findings: c: capillary; v: venous

Calculation of the costs of one- versus two-step diagnostics

There is still no consensus regarding the question of one- or two-step diagnostics (oGTT as a screening method or a preceding 50 g test). Independent of the disadvantages of the test, which have already been mentioned, the costs of both procedures should also be considered. In a survey carried out in laboratories in Berlin, the price of the 50 g test was about 6.50 Euros and the 75 g test about 9.33 Euro. Table 5 shows a compilation of the respective costs of one- and two-step diagnostics.

Table 5: Comparison of the costs of one- or two-step diagnostics for 1000 pregnant women (oGTT = oral glucose tolerance test)

0 g screening GTT (75 g)	about 6.50 Euros/test about 9.33 Euros/test
ne-step diagnostic test	
GTT **iagnosis**	9330 Euros **9330 Euros**
wo-step diagnostic test	
creening GTT in 270 pregnant omen **iagnosis**	6500 Euros (about 27 % are pathological) 2455 Euros **8955 Euros**

The possible costs of an additional physician-patient consultation, which may result from a two-step diagnostic test, are not taken into consideration. The costs of the one- and two-step diagnostic tests therefore appear to be comparable to one another. One-step diagnosis has two important advantages: firstly, it is standardized (the test is carried out after fasting), and secondly, the patients are not unnecessarily concerned because of a false-positive screening result. In light of this, we clearly tend towards the one-step diagnostic test.

Treatment of gestational diabetes

The treatment of GDM has got three core principals:

- Alteration of diet
- Physical exercise
- Insulin therapy if required

Diet alteration certainly plays the greatest role in the treatment of GDM. In the past, it has been shown that – apart from a possible restriction in energy – if the proportion of carbohydrates is reduced, the blood glucose values may decrease considerably.

! Calculation of the energy requirements during pregnancy: Currently, the energy requirement is thought to be 30 kcal/kg ideal bodyweight. Adipose pregnant women require 25 kcal/kg ideal bodyweight. The ideal bodyweight is calculated by taking the height in centimeters and deducting 100. Example: a patient with a height of 17 cm has an ideal weight of 70 kg (170 cm–100). This figure multiplied by 30 = 2100 kcal. As a reduction in the proportion of carbohydrates leads to an improvement in glucose values, the proportion of carbohydrates is now set at 40 % (previously 50-60 %). Based on the calculated 2100 kcal, 840 kcal should be provided by carbohydrates (if this is translated into bread units: 1 bread unit = 10-12 g carbohydrates). 10 g carbohydrates have a calorific value of about 50 kcal (1 g carbohydrates = 4.1 kcal), so that this patient should receive 17 bread units per day. !

The composition of the carbohydrates is just as important. Preference should be given to the so-called slowly digestible complex carbohydrates (black instead of white bread, whole grain rice instead of white rice).

! Cave: Cheap black bread very often gets its dark color from sugar; this, however, is quickly metabolized. !

Small meals are also just as important as giving up drinks containing sugar, such as the fruit juice that pregnant women like to drink. After dietary consultation, outpatient check-ups are carried out to monitor the metabolism by way of a blood sugar daily profile.

For the blood glucose daily profile, the patient measures the blood sugar value one hour before and one hour after the beginning of the main meals of the day. The one-hour value correlates to a higher degree with the fetal abdominal girth than the two-hour value, wherefore the first value is preferred. Dietary adjustments are normally sufficient to treat about 80 % of all pregnant women. If threshold values of 90 mg/dl (5 mmol/l) after fasting or 140 mg/dl (7.8 mmol/l) postprandial are repeatedly exceeded, dietary adjustment alone is insufficient. However, this is only the case in every fifth patient; the patient then requires additional doses of insulin. The type of insulin and the insulin schedule depend on the daily blood sugar profile.

The performance of an amniocentesis to determine the amniotic insulin has – due to lack of acceptance – been largely abandoned. It is only performed in cases where the status is unclear (e. g. normal blood sugar values and sonographically significant signs of diabetogenic fetopathy). Sonographic fetal biometry is becoming more and more important. For instance, one study showed that none of the pregnant women with a fetal abdominal girth below the 75th percentile had significantly increased insulin concentrations in the amniotic fluid. It was therefore possible to almost exclude cases of severe diabetogenic damage using sonographic measurement (Schaefer-Graf et al. 2003).

Diabetes mellitus, gestational diabetes and delivery

In principle, it is possible for women with gestational diabetes or a manifest diabetes to give birth vaginally; the diagnosis "diabetes" in itself is not a reason for a Cesarean section. The method of delivery should depend more on general obstetric factors. The estimated fetal weight is of primary importance; the risk of shoulder dystocia is, with an estimated fetal weight of over 4 000 g about 2 % and about 10 % from 4500 g upwards. Currently, the indication for primary section for an estimated weight of > 4500 g is judged varyingly in the literature. Whereas Conway et al. (1999) noted an increased rate of Cesarean section from 21.7 % to 25.1 % with a cut-off at 4 250 g and a rate of shoulder dystocia reduced by a factor of two from 2.4 % to 1.1 %, other authors have taken the far rarer Erb's paresis as an endpoint. According to Ecker et al. (1997), 19 to 162 additional Cesareans would be necessary to avoid shoulder dystocia with plexus paresis. Furthermore, the shoulder dystocia itself is not the feared complication but rather the severe fetal distress and damage to the plexus. Clinical experience shows that severe fetal distress is relatively rare in cases of shoulder dystocia as, after adequate treatment of the shoulder dystocia, delivery is usually possible after a short interval. There remains the damage to the plexus, which, in its persisting form, is very rare (90 % of the damage to plexus is luckily only temporary). According to Rouse et al. (1996), to avoid persisting damage to the plexus an additional 1 800 to 5 400 Cesareans would be necessary.

! By estimating the individual risk, (parity, birth weight of previous vaginally born children, status post shoulder dystocia) the adequate obstetric procedure can be selected. !

The same applies to the question of induced delivery. Unfortunately, no studies have been carried out that fulfil the criteria of evidence-based medicine. This procedure can therefore also only depend on generally accepted obstetric management procedures. Relative (!) induction criteria are:

- Remaining time until the due date: in insulin-dependent gestational diabetes, as well as in type 1 and type 2 diabetes, there is a risk of preterm exhaustion of the placental function.
- Suspected estimated weight of about 4 000 g, if it is perceived that further growth could lead to a Cesarean section for the above-mentioned reasons.
- Inadequate insulin adjustment, in some cases combined with simultaneous sonographic signs of diabetogenic fetopathy (macrosomia + polyhydramnios); the exact risk is difficult to estimate in this case.

With diet-dependent gestational diabetes, monitoring during birth is, at the most, only sporadically necessary. The physical effort inhibits an increase in the mildly raised blood glucose levels. Similarly, in insulin-dependent gestational diabetes insulin is not usually required, as the physical action of the muscles – particularly of the uterus – uses a large amount of glucose, insulin-independent. Only in type 1 diabetes (possibly also in type 2 diabetes, but this type is more similar to gestational diabetes) is close-meshed blood glucose level monitoring necessary. First-line therapy should be the rapid-acting insulins, alternatively an insulin perfusor can be directly applied (intravenous instead of subcutaneous insulin application!). The target values for all patients lie between 70-140 mg/dl (3.9-7.8 mmol/l).

Due to the neonatal risk, a pregnant woman with manifest diabetes or insulin-dependent gestational diabetes should give birth in a perinatal center level II-III. Pregnant women having only diet-dependent gestational diabetes should at least be informed about the advantages of an affiliated neonatology department. Above all, pregnant women with diabetes – irrespective of the type – should be cared for by experienced obstetricians.

Postpartal monitoring of pregestational diabetes and gestational diabetes

Typ-1-Diabetes

A rule of thumb that applies after birth is that the placenta no longer supplies anti-insulin hormones, and insulin requirements decrease rapidly so that about 48 hours later the level of pregravida requirements is reached. This means that during birth and thereafter, rapid-acting insulin should be administered. The insulin requirements on the first postpartal day are between the requirements at the end of pregnancy and the pregravida level.

Gestational diabetes

In the case of "pure" gestational diabetes, insulin doses are generally not required post partal (or also intrapartal). On the third postpartal day a blood sugar daily profile (BSDP) should be performed, or the value after fasting should be determined to exclude a persisiting diabetes (rare). It is, however, important that patients are informed about the risk of developing type 2 diabetes. According to the statistics, in Germany, there is a cumulative incidence of 3 % for the patient to develop diabetes per year (i. e. after ten years, 30 % are affected!). A regular follow-up is therefore extremely important as patients with type 2 diabetes rarely exhibit any symptoms.

Oral antidiabetics during pregnancy

The use of oral antidiabetics (OAD) during pregnancy has become increasingly important in recent years. On the one hand, this is a result of studies evaluating the administration of OAD to GDM patients, for example glibenclamide,

(Langer et al. 2000), and on the other, OADs (of which metformine is most frequently administered) have increased in importance for the treatment of the unfulfilled desire for a child in women with polycystic ovary syndrome. It should first be pointed out that none of the OADs are licensed. In fact, their use is even discouraged during pregnancy, despite the fact that animal experiments have found little evidence of negative effects. Regarding the use of glibenclamide, we in fact find only few advantages, which mainly are restricted to the fact that the medication can be administered in tablet form. Blood glucose level adjustment in this group of patients was similar to that of patients taking insulin; a part of the patients treated with OAD had to convert to insulin, as the target values could not be achieved with oral therapy. In contrast to insulin, OADs pass the placenta and are thus transmitted to the child and may – theoretically – have a negative effect. Even if the transmission rate of glibenclamide is relatively low, it cannot be excluded that this highly potent β-cell stimulant may lead to sustained damage of the fetal pancreas. In so far, its use should be restricted to clinical studies.

This does not go for metformine, as its mode of action is characterized by insulin sensitization. Metformine can decrease the androgen level, as shown in Figure 4, which leads to a higher rate of pregnancy in patients with polycystic ovary syndrome (PCOS) as well as to a lower rate of abortion (Costello and Eden 2003). However, the benefits of the therapy, which cannot be gone into in detail here, are limited to the first half of the pregnancy. We therefore discontinue the use of metformine in the 14th week of pregnancy, as at this stage an exponential increase in pregnancy hormone levels is to be expected, which definitely brings about more benefits than the decrease in androgen levels. Pregnant women with an additional PCOS run an increased risk of (gestational) diabetes. Therefore, an early clarification of this type of diabetes is of particular importance. A study by Glueck et al. (2001) has shown that by continuing metformine treatment, the risk of developing gestational diabetes can be significantly lowered (26 % vs. 3 %). Nevertheless, we have to be aware of the fact that using metformine not only preempts treatment but that 75 % of the patients are treated unnecessarily. This procedure is neither ethical nor comprehensible from an economical point of view. Nevertheless, the knowledge of the high risk of GDM should lead to corresponding close-meshed monitoring.

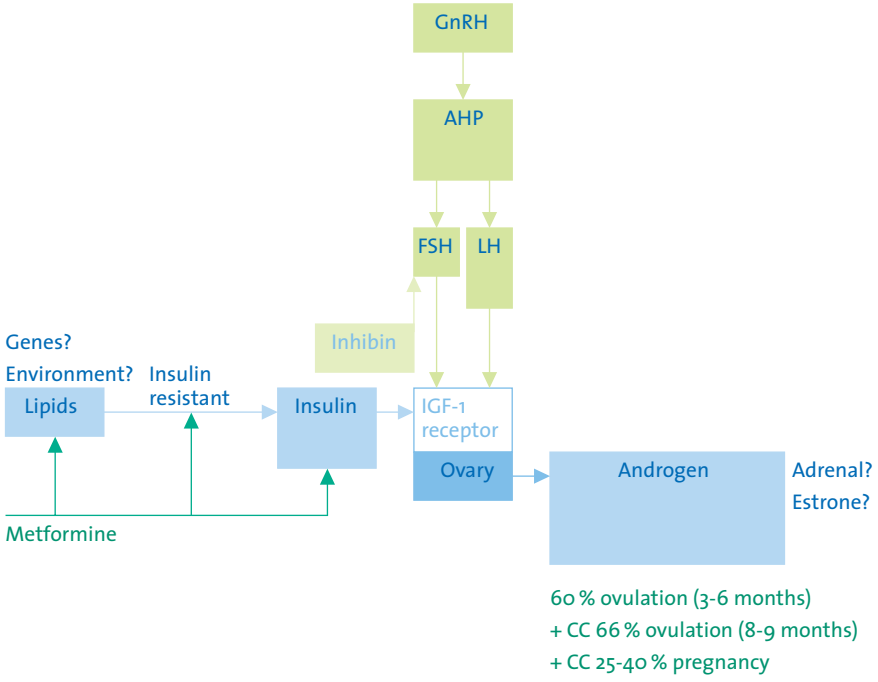

Figure 4: Use of metformine in the treatment of polycystic ovary syndrome (according to Costello and Eden 2003) (CC = clomifene; AHP = adenohypophysis)

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Keywords
Diabetes, pregnancy, gestational diabetes, screening

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Conflict of interest
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CME-Continuing Medical Education

Diabetes and pregnancy

Question 1
Absolute insulin deficiency is a sign of
a. type 2 diabetes,
b. type 1 diabetes,
c. gestational diabetes,
d. answers a and b are correct,
e. answers a, b and c are correct.

Question 2
During pregnancy there is a characteristic alteration in insulin requirements.
This alteration is specified by:
a. an increased requirement in the first half of pregnancy, decreased requirement in the 2nd half of pregnancy
b. invariant requirement in the 1st trimester, increased requirement in the 2nd and 3rd trimester,
c. invariant to a slightly increased requirement in the 1st trimester, decreased requirement in the 2nd trimester, and an increased requirement in the 2nd half of pregnancy,
d. a decreased requirement in the first half of pregnancy, and an increased requirements in the 2nd and 3rd trimester,
e. there is no alteration.

Question 3
According to international studies, the frequency of gestational diabetes is approximately:
a. < 0.5 %
b. 1 %
c. 5-8 %
d. 15 %
e. > 20 %

Question 4
The following procedure is suitable for adequate detection of gestational diabetes:
a. a glucose stick test,
b. patient history (birth weight),
c. oral glucose tolerance test,
d. familial anamnesis (1st or 2nd degree relatives with diabetes),
e. status post birth of a macrosomic child.

Question 5
The oral antidiabetic metformine is increasingly used in the treatment of women that desire a child but suffer from polycystic ovary syndrome. After conception
a. the metformine dose should be increased by 500 mg per day,
b. metformine should be discontinued immediately (high risk of malformation!),
c. metformine should be immediately replaced by insulin therapy,
d. treatment with metformine can be continued until the 12th week of pregnancy,
e. none of the answers are correct.

Question 6
The following oral antidiabetic drug/s is/are approved for use during pregnancy:
1. metformine,
2. glibenclamide,
3. acarbose,
a. answer 1 is correct,
b. answer 2 is correct,
c. answer 3 is correct,
d. answers 1-3 are correct,
e. none of the answers are correct.

Question 7
The energy requirements of pregnant women with a normal body weight are:
a. 10 kcal/kg ideal body weight,
b. 20 kcal/kg ideal body weight,
c. 30 kcal/kg ideal body weight,
d. 40 kcal/kg ideal body weight,
e. 50 kcal/kg ideal body weight.

Question 8
The macronutrients carbohydrates, fats and proteins are the main energy providers in the diet. According to the recommendations of professional associations, the proportion of carbohydrates in the diet of patients with gestational diabetes should be:
a. 20 %
b. 30 %
c. 40 %
d. 50 %
e. 60 %

Question 9
An oral glucose tolerance test with 75 g of glucose is performed to diagnose gestational diabetes. The diagnosis is significant if two or three values are exceeded. The HAPO study has again shown a correlation between blood sugar values and the initial parameters. The current threshold values of the German Association of Gynecology and Obstetrics for capillary whole blood are:
a. 85/160 mg/dl (4.7/8.9 mmol/l)
b. 90/165/145 mg/dl (5.0/9, 2/8.1 mmol/l)
c. –/–/200 mg/dl (–/–/11.1 mmol/l)
d. 90/180/155 mg/dl (5.0/10.0/8.6 mmol/l)
e. –/160/– mg/dl (–/8.9/– mmol/l)

Question 10
Metabolic monitoring in gestational diabetes is carried out in the form of a blood sugar daily profile. The postprandial one-hour value correlates best with fetal outcome. The threshold value for the postprandial one-hour value is:
a. 110 mg/dl (6.1 mmol/l)
b. 120 mg/dl (6.7 mmol/l)
c. 130 mg/dl (7.2 mmol/l)
d. 140 mg/dl (7.8 mmol/l)
e. 150 mg/dl (8.3 mmol/l)