

# UKMI NICE Bites



July 2015: No 77

## A summary of prescribing recommendations from NICE guidance

## **Diabetes in pregnancy**

NICE NG3; 2015

This guideline covers the management of diabetes and its complications in women who are planning pregnancy and those already pregnant.

#### **Definition of terms**

ACEI angiotensin-converting enzyme inhibitor A2RA angiotensin-II receptor antagonist **OGTT** oral glucose tolerance test HbA1c glycated haemoglobin unlicensed

#### Preconception care for women with diabetes

- Ensure that importance of avoiding an unplanned pregnancy is an essential component of diabetes education from adolescence for women with diabetes.
- Advise women with diabetes that they can use oral contraceptives (if there are no contraindications to their use). Choice of contraception should be based on their own preferences and any risk factors as indicated by UK medical eligibility criteria for contraceptive use
- Explain to women with diabetes who are planning to become pregnant that establishing good blood glucose control before conception and continuing this throughout pregnancy will reduce the risk of miscarriage, congenital malformation, stillbirth and neonatal death. Explain that risks can be reduced but not eliminated.
- Give information about how diabetes affects pregnancy and how pregnancy affects diabetes. This should cover
  - > role of diet, body weight and exercise,
  - > risks of hypoglycaemia and impaired awareness of hypoglycaemia during pregnancy,
  - > effect of nausea and vomiting on blood glucose control,
  - > increased risk of having a baby who is large for gestational age, which increases the likelihood of birth trauma, induction of labour and caesarean section,
  - > need for assessment of diabetic retinopathy before and during pregnancy,
  - > need for assessment of diabetic nephropathy before
  - > importance of maternal blood glucose control during labour and birth and early feeding of the baby, in order to reduce the risk of neonatal hypoglycaemia,
  - > possibility of temporary health problems in the baby during the neonatal period,
  - > risk of the baby developing obesity and/or diabetes in later life.
- Advise women with diabetes who are planning to become pregnant:
  - > that the risks associated with pregnancy increase with how long the woman has had diabetes,
  - > to use contraception until good blood glucose control has been established,
  - > that blood glucose targets, glucose monitoring, medicines for treating diabetes (including insulin regimens) and medicines for complications of diabetes will need to be reviewed before and during pregnancy,
  - > that extra time and effort is needed to manage diabetes during pregnancy and that she will have frequent contact with healthcare professionals.

- Offer retinal assessment at first preconception appointment (unless this was assessed in last 6 months) and then annually if diabetic retinopathy is not found.
- Offer renal assessment, including a measure of low-level albuminuria (microalbuminuria), before discontinuing contraception. If serum creatinine is ≥120micromol/litre, urinary albumin:creatinine ratio is >30mg/mmol or eGFR is <45 ml/minute/1.73m<sup>2</sup>, referral to a nephrologist should be considered before discontinuing contraception.

#### Lifestyle advice

Women with diabetes who are planning to become pregnant:

- Offer individualised dietary advice.
- Offer women who have a BMI >27 kg/m<sup>2</sup> advice on how to lose weight, in line with the NICE pathway on obesity.
- Advise women to take folic acid (5 mg/day) until 12 weeks of gestation to reduce risk of having a baby with a neural tube defect.

#### **Monitoring**

Women with diabetes who are planning to become pregnant:

- Offer monthly measurement of HbA1c level.
- Offer a meter for self-monitoring of blood glucose.
- If a woman needs intensification of blood glucoselowering therapy, advise her to increase the frequency of self-monitoring of blood glucose to include fasting levels and a mixture of pre-meal and post-meal levels.
- Offer women with type 1 diabetes blood ketone testing strips and a meter, and advise them to test for ketonaemia if they become hyperglycaemic or unwell.

#### Target blood glucose and HbA1c levels

Women with diabetes who are planning to become pregnant:

- Agree individualised targets for self-monitoring of blood glucose taking into account the risk of hypoglycaemia.
- Advise women to aim for the same capillary plasma glucose target ranges as recommended for all people with type 1 diabetes.
- Advise women to aim to keep their HbA1c level <48mmol/mol (6.5%), if this is achievable without causing problematic hypoglycaemia.
- Reassure women that any reduction in HbA1c level towards the target of 48mmol/mol (6.5%) is likely to reduce risk of congenital malformations in the baby.
- Strongly advise women with diabetes whose HbA1c level is >86mmol/mol (10%) not to get pregnant.

#### **Gestational diabetes Assessment**

- To enable women to make an informed decision about risk assessment and testing for gestational diabetes,
  - > in some women, gestational diabetes will respond to changes in diet and exercise,
  - > the majority of women will need oral blood glucoselowering agents or insulin therapy if changes in diet and exercise do not control gestational diabetes effectively,
  - > if gestational diabetes is not detected and controlled, there is a small increased risk of serious adverse birth complications,





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- a diagnosis of gestational diabetes will lead to increased monitoring, and may lead to increased interventions, during both pregnancy and labour.
- Assess risk of gestational diabetes. At the booking appointment, offer women with any of the following risk factors testing for gestational diabetes:
  - > BMI >30 kg/m<sup>2</sup>,
  - > previous macrosomic baby weighing ≥4.5kg,
  - > previous gestational diabetes,
  - Family history of diabetes (first-degree relative with diabetes) or minority ethnic family origin with a high prevalence of diabetes.
- Do NOT use fasting plasma glucose, random blood glucose, HbA1c, glucose challenge test or urinalysis for glucose to assess risk of developing gestational diabetes.
- ◆ Be aware that glycosuria of ≥ 2+ on one occasion or ≥1+ on two or more occasions detected by reagent strip testing during routine antenatal care may indicate undiagnosed gestational diabetes. If this is observed, consider further testing to exclude gestational diabetes.
- Use the 2-hour 75g OGTT to test for gestational diabetes in women with risk factors.
- Offer women who have had gestational diabetes in a previous pregnancy:
  - > early self-monitoring of blood glucose, or
  - a 75g 2-hour OGTT as soon as possible (whether in the first or second trimester), and a further 75g 2-hour OGTT at 24 to 28 weeks if the results of the first OGTT are normal.
- Offer women with any other risk factors for gestational diabetes a 75g 2-hour OGTT at 24 to 28 weeks.

#### **Diagnosis**

- Diagnose gestational diabetes if the woman has either a:
   Fasting plasma glucose level of ≥5.6mmol/litre or
   2-hour plasma glucose level of ≥7.8mmol/litre.
- Offer women with a diagnosis of gestational diabetes a review with the joint diabetes and antenatal clinic within one week.
- Inform the primary healthcare team when a woman is diagnosed with gestational diabetes.

#### Information and advice

- Explain to women:
  - about the short and long term implications of the diagnosis for her and her baby,
  - that good blood glucose control throughout pregnancy will reduce the risk of fetal macrosomia, trauma during birth, induction of labour and/or caesarean section, neonatal hypoglycaemia and perinatal death,
  - > that treatment includes changes in diet and exercise, and could involve medicines.
- Teach the woman about self-monitoring of blood glucose.
- Offer advice about changes in diet and exercise.
- Advise eating a healthy diet during pregnancy, and emphasise that foods with a low glycaemic index should replace those with a high glycaemic index. Refer all women to a dietician.
- Advise regular exercise to improve blood glucose control.

See NICE pathway: Diabetes in pregnancy

## Pharmacological treatment

#### **Pre-existing diabetes**

- Women may use metforminU as an adjunct or alternative to insulin in the preconception period and during pregnancy, when likely benefits from improved blood glucose control outweigh potential for harm. All other oral blood glucose-lowering agents should be discontinued before pregnancy and insulin substituted.
- Data from clinical trials and other sources do not suggest that rapid-acting insulin analogues (aspart and lispro) adversely affect pregnancy or the health of the fetus or newborn baby.
- Use isophane insulin (also known as NPH insulin) as first choice for long-acting insulin during pregnancy.
- Consider continuing treatment with long-acting insulin analogues U (insulin detemir or insulin glargine) in women who have established good blood glucose control before pregnancy.
- ACEIs, A2RAs and statins should be discontinued before conception or as soon as pregnancy is confirmed.
- Alternative antihypertensive agents suitable for use during pregnancy should be substituted.

#### **Gestational diabetes**

- Tailor blood glucose-lowering therapy to the blood glucose profile and personal preferences of the woman.
- First-line: offer a trial of changes in diet and exercise to women with a fasting plasma glucose level <7mmol/litre at diagnosis.
  - If blood glucose targets are not met within 1 to 2 weeks:
- Second-line: offer metforminU. If metformin is contraindicated or unacceptable - offer insulin. If blood glucose targets are not met:
- Third-line: add insulin to changes in diet/ exercise and metformin.
- ◆ Consider glibenclamideU for women:
  - in whom blood glucose targets are not achieved with metformin but who decline insulin therapy, or
  - > who cannot tolerate metforminU.
- For women with a fasting plasma glucose level of:
  - > ≥7.0mmol/litre at diagnosis, offer immediate treatment with insulin, with or without metformin, as well as changes in diet and exercise,
  - between 6.0 and 6.9mmol/litre, consider immediate treatment with insulin, with or without metformin, as well as changes in diet and exercise, if there are complications such as macrosomia or hydramnios.

#### Insulin treated diabetes in pregnancy

- Consider use of rapid-acting insulin analogues (aspart and lispro) as these have advantages over soluble human insulin during pregnancy.
- Advise women of the risks of hypoglycaemia and impaired awareness of hypoglycaemia in pregnancy, particularly in the first trimester.
- Advise pregnant women to always have available a fastacting form of glucose e.g. dextrose tablets or glucosecontaining drinks.
- Provide glucagon to pregnant women with type 1 diabetes for use if needed. Instruct the woman and her partner or other family members in its use.
- Offer subcutaneous insulin infusion (insulin pump therapy) if adequate blood glucose control is not obtained by multiple daily injections of insulin without significant disabling hypoglycaemia.

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#### Monitoring during pregnancy Target blood glucose levels

- Agree individualised targets for self-monitoring of blood glucose, taking into account the risk of hypoglycaemia.
- Advise pregnant women with any form of diabetes to maintain their capillary plasma glucose **below** the following target levels, if these are achievable without causing problematic hypoglycaemia:
  - > fasting: 5.3mmol/litre, AND
  - > 1 hour after meals: 7.8mmol/litre, OR
  - > 2 hours after meals: 6.4mmol/litre.
- Advise pregnant women who are on insulin or glibenclamide to maintain their capillary plasma glucose level >4mmol/litre.

### Blood glucose

#### Type 1 diabetes

 Advise women to test their fasting, pre-meal, 1-hour postmeal and bedtime blood glucose levels daily during pregnancy.

#### Type 2 or gestational diabetes

- Advise women to test their fasting and 1-hour post-meal blood glucose levels daily during pregnancy if they are:
  - > on diet and exercise therapy, OR
  - taking oral therapy (with or without diet and exercise therapy) or single-dose intermediate-acting or longacting insulin.
- Advise women on a multiple daily insulin injection regimen to test their fasting, pre-meal, 1-hour post-meal and bedtime blood glucose levels daily during pregnancy.

#### Continuous glucose monitoring

- Do NOT offer continuous glucose monitoring routinely to pregnant women with diabetes.
- Consider continuous glucose monitoring for pregnant women on insulin therapy:
  - who have problematic severe hypoglycaemia (with or without impaired awareness of hypoglycaemia), OR
  - who have unstable blood glucose levels (to minimise variability), OR
  - to gain information about variability in blood glucose levels.
- Ensure support is available for pregnant women who are using continuous glucose monitoring from a member of the joint diabetes and antenatal care team with expertise in its use.

#### **HbA1c levels**

#### **Pre-existing diabetes**

- Measure HbA1c levels at the booking appointment to determine the level of risk for the pregnancy.
- Consider measuring HbA1c levels in the second and third trimesters of pregnancy to assess the level of risk for the pregnancy.
- Be aware that level of risk for the pregnancy increases with an HbA1c level >48mmol/mol (6.5%).

#### **Gestational diabetes**

 Measure HbA1c levels at the time of diagnosis to identify those who may have pre-existing type 2 diabetes.

#### Any form of diabetes

 Do NOT use HbA1c levels routinely to assess a woman's blood glucose control in the second and third trimesters of pregnancy.

#### Ketone testing and diabetic ketoacidosis

- Advise women with any form of diabetes to seek urgent medical advice if they become hyperglycaemic or unwell.
- Test urgently for ketonaemia if a pregnant woman with any form of diabetes presents with hyperglycaemia or is unwell, to exclude diabetic ketoacidosis.
- Immediately admit women who are suspected of having diabetic ketoacidosis for level 2 critical care, where they can receive both medical and obstetric care.

#### Type 1 diabetes

 Offer women blood ketone testing strips and a meter.
 Advise them to test for ketonaemia and seek urgent medical advice if they become hyperglycaemic or unwell.

#### Retinal and renal assessment - see NICE pathway

#### Preventing pre-eclampsia

 See <u>NICE pathway: Hypertension in pregnancy</u> for guidance on using antiplatelet agents to reduce risk of pre-eclampsia.

#### **Antenatal care appointments**

- ◆ Timetable of antenatal appointments see NICE pathway
- At 20 weeks, offer an ultrasound scan for detecting fetal structural abnormalities, including examination of fetal heart (4 chambers, outflow tracts and 3 vessels).

#### Intrapartum care

- Diabetes should not be considered a contraindication to attempting vaginal birth after a previous caesarean section.
- Explain to pregnant women with diabetes who have an ultrasound-diagnosed macrosomic fetus about the risks and benefits of vaginal birth, induction of labour and caesarean section.

#### Type 1 or type 2 diabetes

- Advise women with no other complications to have an elective birth (by induction of labour, or by elective caesarean section if indicated) between 37<sup>+0\*</sup> weeks and 38<sup>+6\*</sup> weeks of pregnancy.
- Consider elective birth before 37<sup>+0\*</sup> weeks if there are metabolic or any other maternal or fetal complications.

### Gestational diabetes

- ◆ Advise women to give birth no later than 40<sup>+6</sup>\* weeks, and offer elective birth (by induction of labour, or by caesarean section if indicated) to women who have not given birth by this time.
- Consider elective birth before 40<sup>+6\*</sup> weeks if there are maternal or fetal complications.

#### Blood glucose control during labour and birth

- Monitor capillary plasma glucose every hour during labour and birth, and ensure it is maintained between 4 and 7mmol/litre.
- If general anaesthesia is used for the birth, monitor blood glucose every 30 minutes from induction of general anaesthesia until after the baby is born and the woman is fully conscious.
- Intravenous dextrose and insulin infusion should be considered for women with type 1 diabetes from the onset of established labour.
- Use intravenous dextrose and insulin infusion during labour and birth for women with diabetes whose capillary plasma glucose is not maintained between 4 and 7mmol/litre.

<sup>\*</sup>Defined as the number of weeks plus days of the pregnancy

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#### **Neonatal care**

See NICE pathway for further information.

- Advise women with diabetes to give birth in hospitals where advanced neonatal resuscitation skills are available 24 hours a day.
- Babies of women with diabetes should:
  - stay with their mothers unless there is a clinical complication or abnormal clinical signs that warrant admission for intensive or special care.
  - have blood glucose testing at 2 to 4 hours after birth. Carry out blood tests for polycythaemia, hyperbilirubinaemia, hypocalcaemia and hypomagnesaemia for babies with clinical signs.
- Do NOT transfer babies of women with diabetes to community care until they are at least 24 hours old, and not before you are satisfied that the baby is maintaining blood glucose levels and is feeding well.

#### Postnatal care Pre-existing diabetes

- Reduce insulin immediately after birth and monitor blood glucose levels carefully to establish appropriate dose.
- Explain to women with pre-existing insulin-treated diabetes they are at increased risk of hypoglycaemia in the postnatal period, especially when breastfeeding, and advise them to have a meal or snack available before or during feeds.
- Women with pre-existing type 2 diabetes who are breastfeeding can resume or continue to take metforminU and glibenclamideU immediately after birth, but should avoid other oral blood glucose-lowering agents.
- Women who are breastfeeding should continue to avoid any medicines for treatment of diabetes complications that were discontinued for safety reasons in the preconception period.
- Refer women with pre-existing diabetes back to their routine diabetes care arrangements. Remind them of the importance of contraception and the need for preconception care when planning future pregnancies.

#### **Gestational diabetes**

- Discontinue blood glucose-lowering therapy immediately after birth.
- Test blood glucose to exclude persisting hyperglycaemia before being transferred to community care.
- Remind women who were diagnosed with gestational diabetes of symptoms of hyperglycaemia.
- Explain risks of gestational diabetes in future pregnancies, and offer testing for diabetes when planning future pregnancies.
- For women whose blood glucose levels returned to normal after birth:
  - > offer lifestyle advice (including weight control, diet and exercise),
  - > offer a fasting plasma glucose test 6 to 13 weeks after birth to exclude diabetes (for practical reasons this might take place at 6-week postnatal check),
  - if a fasting plasma glucose test has not been performed by 13 weeks, offer a fasting plasma glucose test, or if this is not possible an HbA1c test after 13 weeks.
- Do NOT routinely offer a 75g 2-hour OGTT.

## Advise women having postnatal fasting plasma glucose test with a fasting plasma glucose level:

- <6.0mmol/litre that they:</p>
  - > have a low probability of having diabetes at present,
  - » should continue to follow lifestyle advice (including weight control, diet and exercise) given after birth,
  - will need an annual test to check that their blood glucose levels are normal,
  - have a moderate risk of developing type 2 diabetes. Offer advice and guidance in line with the NICE pathway on preventing type 2 diabetes\*\*
- between 6.0 and 6.9mmol/litre that they are at high risk of developing type 2 diabetes. Offer advice, guidance and interventions in line with the <u>NICE pathway on preventing</u> type 2 diabetes\*\*
- ≥7.0mmol/litre that they are likely to have type 2 diabetes.
   Offer a diagnostic test to confirm diabetes.

## Advise women having postnatal HbA1c test with an HbA1c level:

- ♦ <39 mmol/mol (5.7%) that they:
  </p>
  - > have a low probability of having diabetes at present,
  - » should continue to follow lifestyle advice (including weight control, diet and exercise) given after birth,
  - » will need an annual test to check that blood glucose levels are normal,
  - have a moderate risk of developing type 2 diabetes. Offer them advice and guidance in line with the <u>NICE</u> <u>pathway on preventing type 2 diabetes</u>\*\*.
- between 39 and 47mmol/mol (5.7% and 6.4%) that they
  are at high risk of developing type 2 diabetes, and offer
  advice, guidance and interventions in line with the with the
  NICE pathway on preventing type 2 diabetes.\*\*
- ≥48mmol/mol (6.5%) that they have type 2 diabetes and refer for further care.
- Offer an annual HbA1c test to women who were diagnosed with gestational diabetes who have a negative postnatal test for diabetes.
- Offer women who were diagnosed with gestational diabetes early self-monitoring of blood glucose or an OGTT in future pregnancies. Offer a subsequent OGTT if the first OGTT results in early pregnancy are normal.

### See NICE pathway: Diabetes in pregnancy

\*\*Note that the threshold for defining a moderate risk of developing type 2 diabetes postnatally for women who have had gestational diabetes is different from that given in NICE pathway on preventing type 2 diabetes, because of the different populations.

**Recommendations** – wording used such as 'offer' and 'consider' denote the strength of the recommendation.

**Drug recommendations** – the guideline assumes that prescribers will use a drug's <u>Summary of Product Characteristics</u> (<u>SPC</u>) to inform treatment decisions