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Pregnancy in type 1 diabetes mellitus

DWM Pearson
Consultant Diabetologist, Aberdeen Royal Infirmary, Foresterhill, Aberdeen, Scotland

ABSTRACT In women with type 1 diabetes mellitus, meticulous glycaemic control, before and during pregnancy, usually results in a healthy baby. However, national and regional audits show poorer outcomes than the background population. Despite great efforts by mothers and their Diabetes Care Teams, the babies are often large for gestational age, delivered early by Caesarean section (64%), and spend some time in intensive care. In Scotland, perinatal mortality in diabetic pregnancy has reduced in recent years, but offspring continue to have more congenital abnormalities than the non-diabetic population. The risk of stillbirth and infant mortality are also in excess of the non-diabetic population. In clinical practice, a comprehensive pre-pregnancy and pregnancy care package delivered by a multidisciplinary team to address all risk factors will reduce congenital anomalies and other adverse outcomes. Maintaining very tight control throughout pregnancy can prove difficult. The management of acute and chronic complications of diabetes is challenging and requires individualised solutions underpinned by knowledge of maternal physiology and the impact of maternal metabolism on the developing fetus and newborn.

KEYWORDS Pregnancy, Type 1 Diabetes Mellitus

LIST OF ABBREVIATIONS Scottish Intercollegiate Guidelines Network (SIGN), Angiotensin-converting enzyme (ACE), angiotensin II antagonists (AIIA), diabetic ketoacidosis (DKA)

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Correspondence to ***Dr DWM Pearson, Consultant Diabetologist, Diabetes Centre, Woolmanhill Hospital, Woolmanhill, Aberdeen, AB25 1LD***

tel. ***+44 (0)1224 552 258***

fax ***+44 (0) 1224 551 186***

email
dwm.pearson@arh.grampian.scot.nhs.uk

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OVERVIEW

Introduction

Type 1 diabetes mellitus is one of the most common medical conditions affecting young women during their reproductive years. Girls diagnosed with type 1 diabetes when under five years of age may have been exposed to the effects of chronic hyperglycaemia for over 20 years by the time they plan to, or become, pregnant and, on average, women will have had type 1 diabetes for around 13 years at the time of pregnancy and will be around 30 years of age.

Pre-pregnancy care

The importance of pregnancy planning should be discussed, in a sensitive manner, with all girls who have type 1 diabetes, from menarche onwards. Support, education, and encouragement for adolescents and young women with diabetes can help to achieve optimal glycaemic control. Infants whose mothers with diabetes receive multidisciplinary, pre-pregnancy care have significantly fewer major congenital malformations. Attendance for structured pre-pregnancy care is also associated with a reduction in the rate of spontaneous abortion and other complications of pregnancy. The essential components of a pre-pregnancy care programme are shown in Table 1.

Good blood glucose control is important before and during pregnancy since it will reduce congenital anomalies, stillbirth rate, neonatal hypoglycaemia, and neonatal respiratory distress syndrome. Women should thus strive to maintain blood glucose levels as near the non-diabetic range as possible without excessive risk of hypoglycaemia. This usually means targeting blood glucose levels between 4 and 7 mmol/l. The Diabetes Team, but in particular Diabetes Specialist Nurses and Specialist Midwives, have an important role in educating women on the need for home blood glucose monitoring (usually four to six times a day) and introducing intensive, e.g. basal bolus, insulin regimens if they are not already on intensive therapy.

While an insulin regimen is very important, many factors will influence insulin action and effectiveness. Injection site and injection technique can influence absorption, thus it is prudent to consider and review all the practical aspects of insulin administration.

Dietary advice is also essential before, during, and after pregnancy. Such advice will encourage foodstuffs with high levels of complex carbohydrates, soluble fibre, and vitamins. Neural tube defects in high-risk pregnancies are associated with lower levels of folate and prescription of 4 mg of folate supplement pre- and peri-conceptionally provides some protection against neural tube defects in women at high risk. The SIGN guideline recommends that all women with type 1 diabetes mellitus should take 5 mg of folic acid pre-conceptionally and continue it during pregnancy until around 12 weeks of gestation.

TABLE I A pre-pregnancy care programme for type 1 diabetes mellitus.

Achieve optimal glycaemic control

- Haemoglobin A1c level as near to the non-diabetic range as possible while avoiding disabling hypoglycaemia
- Monitor blood glucose four to six times daily
- Review the insulin regimen. Most women need intensive treatment with a multiple injection, basal bolus regimen
- Set blood glucose targets, e.g. fasting and pre-meal 4·0–5·5 mmol/l; two-hour post prandial <7·0 mmol/l
- Discuss lifestyle issues which may affect glycaemic control, e.g. difficult work patterns
- Assess general health fitness for pregnancy and screen for factors which could disturb glycaemic control, e.g. infection

Medical history

- Review all medications and consider potential teratogens
- Arrange dietetic review and commence folic acid 5 mg daily (high dose recommended in view of the risk of neural tube defects)
- Ensure other medical conditions, e.g. thyroid disorders, are optimally managed
- Screen for associated autoimmune disorders, e.g. coeliac disease
- Check rubella status
- Review menstrual and gynaecological factors that could impair fertility
- Reinforce anti-smoking advice

Screen for evidence of microvascular complications and assess blood pressure

- Check retinal findings and treat proliferative retinopathy if identified
- Characterise urine protein excretion as normal, microalbuminuria, or proteinuria
- Check baseline renal function
- Assess blood pressure at each visit and optimise blood pressure control

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Medical issues during pregnancy

Diabetic retinopathy

Diabetic retinopathy is common in pregnancy. In the Scottish National Audit of those examined in the first trimester, 21% had mild non-proliferative retinopathy, 3% pre-proliferative retinopathy, and 6% proliferative disease. Such retinal disease can deteriorate during pregnancy. Poor glycaemic control in the first trimester and pregnancy-induced chronic hypertension are independently associated with the progression of retinopathy. Effective blood pressure control is important in modifying the effect of pregnancy on retinopathy. Fundal examination prior to conception and during each trimester is recommended, with more frequent assessment in those with poor glycaemic control or severe retinopathy. Early ophthalmology referral is advised due to the potential for rapid development of neovascularisation. If macular oedema is noted, particularly if aggressive, early delivery may be necessary.

In the longer term, parous women with type 1 diabetes have significantly lower levels of all retinopathy compared with nulliparous women. The associated significant difference in HbA1c suggests that improved glycaemic control associated with pregnancy may be sustained over time.

Diabetic nephropathy

Diabetic nephropathy is less common than retinopathy in pregnancy. There is an association between pre-existing nephropathy (microalbuminuria or albuminuria) and a poorer pregnancy outcome. Proteinuria increases during pregnancy and the incidence of worsening chronic hypertension or pregnancy-induced hypertension/pre-eclampsia is high. Worsening nephropathy and superimposed pre-eclampsia are common causes of pre-term delivery in women with diabetic nephropathy.

The management of pregnant women with diabetic nephropathy should follow SIGN recommendations with a target blood pressure of <140/80 mmHg. Angiotensin-converting enzyme inhibitors and AIIA should be avoided in pregnancy. Fetal renal perfusion in the second trimester depends on an intact rennin–angiotensin–aldosterone system and, thus, renal mal-development can follow maternal use of these drugs. Women who are on ACE inhibitors pre-pregnancy should switch to an alternative agent such as methyldopa. If methyldopa is not tolerated, nifedipine can be used. Careful monitoring of blood pressure is essential to help identify optimal timing of delivery. Pre-term delivery and delivery by Caesarean section are much more frequent in women with hypertension and diabetic nephropathy. After delivery efforts are made to continue optimal blood glucose and blood pressure control. An ACE inhibitor, with appropriate contraception, can be reintroduced.

Acute metabolic problems in pregnancy

Hyperglycaemia and hypoglycaemia

Pregnancy leads to insulin resistance and women need to increase their doses of insulin gradually and steadily, particularly after 28 weeks. On average, women at term are on double their early pregnancy insulin requirements.

Very tight blood glucose control is associated with the risk of hypoglycaemia. Hypoglycaemia is classified as mild, moderate, or severe. Around 40% of pregnant women with type 1 diabetes may have one or more episodes of severe hypoglycaemia, i.e. help is needed from another person. This is most likely to occur in the first trimester or after delivery.

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The warning symptoms of hypoglycaemia may change during pregnancy and some women lose awareness. The autonomic symptoms of hypoglycaemia usually precede the neuroglycopenic symptoms but during pregnancy the reverse may happen. Partners need instruction on use of Hypostop™ and glucagon. Hypoglycaemia occurs especially in those with long-duration diabetes, very tight glycaemic control, and women with recurrent episodes of severe hypoglycaemia. Symptoms of hypoglycaemia return to normal after delivery. After delivery, insulin requirements fall to pre-pregnancy levels and insulin doses need to be adjusted to avoid hypoglycaemia. Breast-feeding increases insulin sensitivity. Insulin doses and carbohydrate intake should thus be modified to accommodate breast-feeding.

Diabetic ketoacidosis

Uncontrolled catabolism due to relative insulin deficiency leads to the development of ketoacidosis. Outwith pregnancy, a modest elevation of insulin level is sufficient to inhibit ketogenesis; however, the insulin resistance of pregnancy predisposes to the rapid development of ketosis. During pregnancy most episodes of DKA are precipitated by intercurrent infection. Administration of high dose steroids for pre-term labour can also precipitate DKA. Ketoacidosis should be avoided by prompt recognition and action. The fetus can tolerate maternal hypoglycaemia but is very sensitive to maternal ketoacidosis which results in a high incidence of fetal loss at all gestations. Pregnant women should have equipment for the measurement of urinary or blood ketones. Elevation of blood glucose to >10 mmol/l should prompt a test for ketones. The presence of non-fasting ketonuria is an indication for increased insulin dosage and urgent further clinical assessment by an experienced team.

Clinical care during pregnancy

In Scotland, in most centres, care is delivered by a multidisciplinary combined Obstetric/Diabetic Team with very regular out-patient reviews to assess metabolic control and obstetric progress. Home blood glucose monitoring results are assessed and the insulin regimen and dietary intake modified to optimise glycaemic control and HbA1c. Most women present for booking at around eight weeks' gestation when an early scan will provide an accurate estimate of gestational age. This is important to determine optimal timing of delivery. Routine screening is performed for Down's syndrome and neural tube defects. A detailed ultrasonic scan at around 20 weeks is performed to detect severe congenital anomalies. Frequent scanning is performed later in pregnancy to monitor fetal growth. In the third trimester regular cardiotocography, Doppler ultrasound, and fetal movement charts are used to monitor fetal progress.

Labour, delivery, and neonatal care

In two recent national Scottish audits there were no pregnancies delivered after 40 weeks. The median gestation at delivery was 37 weeks (range 26–40 weeks). Most pregnancies delivering before 36 weeks receive prenatal steroids.

Around two-thirds of women with type 1 diabetes mellitus have a Caesarean section. During labour, blood glucose control is maintained by an insulin and dextrose infusion. This is continued until the woman is eating normally after delivery. Infants of mothers who have type 1 diabetes should be delivered in a centre where there is immediate availability of specialist paediatric neonatal support. Not all babies need admission to the neonatal unit but all babies need careful monitoring to identify and treat neonatal hypoglycaemia and respiratory problems. Pre-term babies need particular supervision. Breast-feeding is initiated in over half of women with type 1 diabetes and, as mentioned, is associated with a significant reduction in insulin requirements and a need for increased carbohydrate intake to avoid hypoglycaemia. In two recent national audits, the vast majority of babies born to mothers with type 1 diabetes in Scotland were above the 50th centile and many weighed above the 95% centile. While there is a relationship with HbA1c levels, particularly in the second trimester, much of the variance in birthweight is not explained by HbA1c levels and home blood glucose monitoring results. Even with current intensive insulin regimens and very frequent home blood glucose monitoring, the infants of mothers with type 1 diabetes still tend to be heavy for dates.

In conclusion, the outcomes of pregnancy in women with type 1 diabetes continue to improve although adverse outcomes are higher than in the background populations and the mothers and their babies need a lot of education, monitoring, and active management.

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HIGHLIGHTS

- Plan and prepare for pregnancy by optimising blood glucose control before and during pregnancy.
- Manage during pregnancy with an integrated, multidisciplinary combined Obstetric/Diabetic/Neonatal Team.
- Warn women about the increased risk of hypoglycaemia and diabetic ketoacidosis in pregnancy.
- Monitor retinopathy, renal status, and blood pressure carefully during pregnancy.
- Deliver babies in a hospital with access to specialist obstetric facilities and neonatal care.

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FURTHER READING

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EDUCATION AND UPDATE FROM THE COLLEGIATE MEMBERS' COMMITTEE

The Collegiate Members' Committee are active in organising a wide range of educational and social events. These are NOT exclusively for Collegiates, and we welcome the participation of Fellows, Members, Associates, their families and other members of the medical and allied professions.

Collegiate Members' Symposium 2005, First Announcement

UPDATES IN INTERNAL MEDICINE

Friday 28th October 2005

The Symposium will be an ideal medical update for anyone working in Internal Medicine or General Practice. Planned sessions include: *Recognising and Managing the Sick Patient outside ITU, Respiratory Emergencies, Acute Coronary Syndromes in the Elderly, Early Management of Brain Infections, GI Emergencies in the Admissions Ward, Surviving Sepsis: Reducing Mortality from Acute Infection, an interactive session on Imaging in Acute Medicine, and the 32nd Croom Lecture (Title to be confirmed).*

Call for Abstracts:
Submissions are invited from Collegiate Members and Associates of the RCPE to present seven minute clinical case presentations in a session entitled 'Clinical Lessons'. Prizes will be awarded for the best Collegiate Member presentation and for the best Associate presentation.

For details of how to apply for either of these sessions, please contact *c.gray@rcpe.ac.uk*

The evening programme consists of a dinner and ceilidh.

The Symposium is free to Collegiate Members and Associates of the RCPE. The dinner is free to all Collegiates who have joined the College since 31 July 2000 and who have not attended a Collegiate Members' dinner previously.

Evening Medical Update Sessions are held at the College (7.30 to 9.30 pm) with various centres around the UK participating by video-link. The events are free, but people attending in Edinburgh should register in advance (see below).

Topics from September to December 2005 include:

Haematology – 6 September
Medicine for the Elderly – 18 October
Neurology – 13 December
Membership Exam – 27 September
Gastroenterology – 15 November

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For more details on all the above events, contact: c.gray@rcpe.ac.uk,
or, see: www.rcpe.ac.uk/events/events.html

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