Improving outcomes for pregnant women with diabetes

Tight glycaemic control during pregnancy and birth often proves difficult. Yet maternal hyperglycaemia can have devastating consequences for mother and child. So in May the Joint British Diabetes Societies published guidelines to support pregnant women with diabetes who are admitted to obstetric wards. Meanwhile, the recent CONCEPTT study suggests that continuous glucose monitoring should become part of standard care for pregnant women with type 1 diabetes.

Mark Greener examines why the JBDS guidelines and CONCEPTT strengthen health care professionals’ ability to reduce the morbidity and mortality associated with diabetes in pregnancy.

Diabetes during pregnancy can have devastating consequences for mother and child. Poorly-controlled type 1 diabetes (T1D), for instance, increases the risk of pre-eclampsia, caesarean section, preterm delivery, mortality, congenital abnormalities, being born large for gestational age (macrosomia) and admission to neonatal intensive care. Indeed, about half of children born to mothers with T1D experience complications arising from the maternal hyperglycaemia.

Yet tight glycaemic control before and during pregnancy often proves elusive. For instance, changes in insulin sensitivity combined with considerable variations in insulin absorption during late pregnancy add to the difficulties of adjusting the insulin dose. Indeed, only 16.2% and 38.3% of pregnant women with T1D and T2D respectively in the UK achieve target HbA1c levels (<48mmol/mol; 6.5%). This analysis of 3044 pregnancies managed in 155 NHS maternity clinics also found that, at 24 weeks’ gestation, just 40.0% and 76.0% of pregnant women with T1D and T2D respectively achieved this target, despite attending antenatal clinics every two weeks and frequent contacts with health care professionals (HCPs) between visits.

Furthermore, in 2015, the stillbirth rate was 10.7 per 1000 among the offspring of women with T1D and 10.5 per 1000 in those born to people with T2D, a marked increase compared to the rate of 4.7 per 1000 in the general maternity population. The stillbirth rate was, however, almost 2.5-fold lower than in 2002/2003. The neonatal death rate was 8.1 per 1000 for T1D and 11.4 per 1000 in women with T2D. In this case, however, the rates had not changed significantly since 2002/2003. The prevalence of all major and minor congenital anomalies was 46.2 per 1000 for T1D and 34.6 per 1000 for T2D. According to Public Health England, the rate of congenital anomalies was 20.5 per 1000. Tighter glycaemic control could prevent many maternal and neonatal complications. So, in May the Joint British Diabetes Societies (JBDS) published guidelines ‘to support management of glycaemic control when pregnant women with diabetes are admitted to obstetric wards’.

New guidelines

Rather than diabetes specialists, the JBDS aimed the guidelines at obstetric HCPs, including midwives, health care assistants, diabetes teams, junior doctors, anaesthetists, obstetricians and paediatricians. ‘Most medicine is now super-specialised,’ says Helen Murphy, Professor of Medicine (Diabetes and Antenatal Care) at Norwich Medical School and Professor of Women’s Health at King’s College London who was involved in the guideline’s development. The obstetric teams are trained to deliver babies. It’s not really reasonable to expect them to be experts in diabetes management as well.’

‘Neonatal hypoglycaemia continues to affect nearly 30% of babies born to mothers with diabetes,’ adds Umesh Dashora, Consultant in Endocrinology and Diabetes at East Sussex Healthcare NHS Trust and the guideline’s lead author. ‘The evidence suggests that tightly controlling blood glucose in mothers during labour and birth to between 4 and 7mmol/L, in line with NICE guidance, can reduce the risk of hypoglycaemia. Achieving this, however, remains a challenge.’

The guidelines, for example, highlight the ‘considerable variation in the criteria used for diagnosing and managing diabetes in pregnancy and considerable variation in the protocols across NHS trusts where they exist’. Diagnosis and management of diabetes in pregnancy has been variable internationally and nationally, Dr Dashora says. ‘One reason for this inconsistency is a lack of high-quality data and evidence. Hopefully by following a standardised approach, as outlined in the guidelines, we will not only improve care but also collect vital data to support evidence-based practice in future.’

Towards a consensus...

For instance, the guidelines note that there is no consensus about whether intravenous or subcutaneous insulin is most appropriate before and during delivery, and no clearly defined threshold for neonatal hypoglycaemia. Some studies suggest ‘a slightly relaxed’ blood glucose target of 4.0–8.0mmol/L, which would often avoid the need for variable rate intravenous insulin infusion (VRIII) and possibly reduce the risk of maternal hypoglycaemia. On the other hand, the relaxed targets may increase the risk of neonatal hypoglycaemia. There is also a lack of consensus about the optimal management of capillary blood glucose levels when steroids are administered to reduce the complications of preterm labour.

Clearly, several areas are worthy of further investigation. ‘Often we cannot wait for the results of randomised controlled trials before implementing improvements,’ Professor Murphy adds. ‘The number of pregnant women with T1D is relatively small, which makes performing a trial challenging and time consuming. There is, however, considerable empirical evidence, expertise and experience in managing diabetes in pregnancy. There
were disagreements, such as around the “relaxed” targets, as we developed the guidelines. But in the absence of really clear evidence upon which to base management, the guidelines represent the wider view of specialists managing diabetes in pregnancy and aim to help services meet the NICE targets in more women.

The guidelines recognise that different types of diabetes (T1D, T2D or gestational) may require individualised approaches depending on each woman’s risk factors, treatment history, the risks of hypoglycaemia and anaesthesia, and presence of complications, including macrosomia and polyhydramnios (excessive amniotic fluid). But the guidelines summarise some basic principles, such as advocating hourly blood glucose monitoring during established labour and when pregnant women receive steroids. The guidelines suggest that VR III is the most effective way to control steroid-induced hyperglycaemia, but note that women may continue insulin pump therapy and revert to VR III if necessary.

The guidelines also stress the importance of, for example, maintaining capillary glucose levels within the NICE range (4–7 mmol/L) during labour. The level of glucose control achieved is, however, more important than the method of insulin delivery (VR III or insulin pump therapy). Women with T1D who are unable to maintain capillary glucose levels within the NICE range (4–7 mmol/L) and some women with T2D or gestational diabetes will require VR III during labour. The infusion rate may need to be halved or changed to the lowest scale after placental delivery. The diabetes team should then review insulin requirements: the dose may be 25% less than that at the end of the first trimester. The guidelines also suggest providing written postnatal plans for women using insulin pumps.

The need for more intensive management doesn’t end when the woman leaves the delivery room. The JBDS guidelines note that breastfeeding mothers are at increased risk of hypoglycaemia and should have additional carbohydrate with meals or as a snack. Breastfeeding women with T2D can take metformin and glibenclamide, but should avoid other oral antidiabetic treatments and should not take drugs that were stopped after conception.

In some cases, however, the obstetric team needs to take a back seat. ‘Pregnant women with diabetes may encounter many HCPs who have little knowledge of diabetes,’ Professor Murphy adds. ‘The women, in contrast, are often experts in self-managing diabetes. They can feel highly vulnerable leaving their glucose control “in the hands” of less experienced staff. If a woman is best placed to control the diabetes, the team needs to facilitate self-management.’

The JBDS guidelines suggest standardised protocols and charts, which can help achieve NICE targets during delivery and steroid administration for prematurity. ‘We hope that auditing the outcomes will gather much-needed evidence in this area and improved care will follow,’ Dr Dashora notes. ‘Audit could, for example, identify the ideal capillary glucose level during delivery, birth and steroid administration that avoids neonatal hypoglycaemia and any other complications, and whether any associated increase in maternal hypoglycaemia is clinically significant.’

CGM: part of standard care

In the meantime, continuous glucose monitoring (CGM) should become part of the standard care package for pregnant women with T1D, Professor Murphy believes. ‘Unfortunately, there is no compelling evidence supporting CGM use during labour and delivery,’ she says. ‘Obstetric teams should, however, be aware that increasing numbers of women will be using CGM to support optimal self-management.’

Professor Murphy was the senior author of the recently published open-label CONCEPTT trial, which randomised 215 pregnant women and 110 planning pregnancy to CGM or standard measurements. CGM did not seem to routinely benefit all women planning to become pregnant. However, in pregnant women mean HbA1c was 0.2% lower in the CGM arm. Furthermore, pregnant women using CGM spent an additional 1.7 hours or 68% of the time within the glucose target range (3.5–7.8 mmol/L) compared to 61% of the time in controls. Pregnant women using CGM also spent approximately 1 hour less time hyperglycaemic (27% and 32% respectively). Both these differences were statistically significant. No significant difference emerged in severe hypoglycaemia episodes (18 and 21 respectively) and time spent hypoglycaemic (3% and 4% respectively), although rates were low in both the CGM and control groups.

CGM was also associated with improved neonatal outcomes. For instance, the odds ratio of having an infant born large for gestational age declined by 49% in the CGM group compared to controls. The odds ratio of neonatal intensive care admissions lasting more than 24 hours declined by 52% and of neonatal hypoglycaemia by 55% in the CGM group.

‘In my view, the evidence is strong enough to offer CGM routinely to pregnant women using intensive insulin therapy,’ Professor Murphy says. ‘Moreover, the results were consistent across the 31 centres in six countries in CONCEPTT and consistent among insulin pump and insulin injection users. So the results seem to be reliable and robust. The numbers needed to treat to avoid a neonatal complication are between 6 and 8, which is much lower than for many other established interventions. There’s no doubt that CGM use during pregnancy is a clinically effective intervention.’

Hospital stay was shorter by one day in the CGM group. Professor Murphy speculates that the shorter hospital stay and the fewer neonatal intensive care admissions might offset the costs of CGM. ‘We need a health economic analysis,’ she says. ‘But I expect that CGM will prove cost effective and it is certainly better for the patient.’

The guidelines and CONCEPTT strengthen HCPs’ ability to prevent much of the morbidity and mortality associated with diabetes in pregnancy. As Professor Murphy concludes: ‘Services need to develop the best way to implement CGM and the new guidelines locally to optimise glucose control and improve outcomes for mothers and their babies.’

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References

References are available online at www.practicaldiabetes.com.
References


