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Insulin during pregnancy, labour and delivery

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Optimal glycaemic control is of the utmost importance to achieve the best possible outcome of a pregnancy complicated by diabetes. This holds for pregnancies in women with preconceptional type 1 or type 2 diabetes as well as for pregnancies complicated by gestational diabetes. Glycaemic control is conventionally expressed in the HbA1c value but the HbA1c value does not completely capture the complexity of glycaemic control. The daily glucose profile measured by the patients themselves through measurements performed in capillary blood obtained by finger stick provides valuable information needed to adjust insulin therapy. Hypoglycaemia is the major threat to the pregnant woman or the woman with tight glycaemic control in the run-up to pregnancy. Repetitive hypoglycaemia can lead to hypoglycaemia unawareness, which is reversible with prevention of hypoglycaemia. A delicate balance should be struck between preventing hyperglycaemia and hypoglycaemia. Insulin requirements are not uniform across the day: it is low during the night with a more or less pronounced rise at dawn, followed by a gradual decrease during the remainder of the day. A basal amount of insulin is needed to regulate the endogenous glucose production, short-acting insulin shots are needed to handle exogenous glucose loads. Insulin therapy means two choices: the type of insulin used and the method of insulin administration. Regarding the type of insulin, the choice is between human and analogue insulins. The analogue short-acting insulin aspart has been shown to be safe during pregnancy in a randomised trial and has received registration for this indication; the short-acting analogue insulin lispro has been shown to be safe in observational studies. No such information is available on the long-acting insulin

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analogues detemir and glargine and both are prescribed off-label with human long-acting insulin as obvious alternatives. Randomised trials have not been able to show superiority of continuous subcutaneous insulin administration (CSII (insulin pump)) over intensive insulin injection therapy (multiple-dose insulin (MDI)) on any maternal or foeto-neonatal end point. However, group sizes were far too small to allow assessment of superiority and issues such as manageability of the disease and quality of life were never assessed. These two issues are of major importance to patients. The first trimester is often the period of most hypoglycaemic events, and insulin therapy should be especially closely monitored and adjusted in this period. After midterm, insulin requirements increase. Continuous glucose monitoring can offer better insights into the glycaemic profile than self-monitoring of blood glucose levels by the patients but the place of these new monitoring techniques has yet to be established more clearly. Insulin therapy during labour means short-acting insulin adjusted to achieve glucose levels between 4 and 8 mmol l^{-1} to prevent neonatal hypoglycaemia as much as possible. After delivery, glycaemic control must be relaxed to prevent hypoglycaemia, especially in women who breastfeed.

Insulin therapy is the mainstay to achieve optimal glycaemic control during pregnancy complicated by any form of diabetes. In general, the diabetic pregnancy is associated with an excess of adverse foetal/neonatal and maternal pregnancy outcomes.[1–11] Foetal/neonatal risks include congenital malformations, foetal growth acceleration and macrosomia, premature birth, birth trauma and neonatal hypoglycaemia and hyperbilirubinaemia; maternal complications are pre-eclampsia and haemolysis, elevated liver enzymes, low platelets (HELLP) syndrome and primary or secondary caesarean section. These complications are directly or indirectly linked to the degree of glycaemic control.

Insulin therapy is a complex therapy and success of treatment depends on many factors and choices. Choices include the type of insulin used (human insulin or analogue insulin), the method of subcutaneous insulin administration (multiple-dose insulin injection therapy (MDI)) or externally worn insulin pump with subcutaneous insulin delivery (continuous subcutaneous insulin infusion (CSII)), the possibilities of self-monitoring of blood glucose levels by patients (self-measurement of blood glucose (SMBG) levels), the possibility of continuous glucose monitoring (continuous glucose monitoring (CGM)), the risk of (severe) hypoglycaemia and the targets used for blood glucose levels. All these issues will be dealt with in this article.

The diabetic pregnancy is a very complex adventure for the woman involved, her family and the health-care team, and still constitutes a high-risk pregnancy fraught with difficulties. A reliable estimation of the risk of adverse outcomes can only be established in large series. Apart from optimal insulin therapy, other issues are of great importance in this area to achieve the best result. Preconceptional planning and preparation are essential. The issue of fertility, pregnancy and adequate birth control should be discussed at appropriate moments with all women of fertile age. At that moment, choices about optimal insulin therapy should be discussed, considered and made. Potentially teratogenic medications must be discussed and at an appropriate time, when there is a wish to have a pregnancy, conducting a full clinical survey and laboratory assessment is mandatory.

General considerations on glycaemic control

Expressing glycaemic control using HbA1c values

Adequate glycaemic control is a major goal in treating diabetes in pregnancy. The goal defined in general terms is to achieve an HbA1c-value within or as close to the normal range as possible. HbA1c has gained the stature of ‘gold standard’ and provides an easy digital parameter but it has some