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MINIREVIEW

Intrapartum application of the continuous glucose monitoring system in pregnancies complicated with diabetes: A review and feasibility study

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Abstract

Intrapartum maternal normoglycemia seems to play an important role in the prevention of adverse perinatal, maternal and neonatal outcomes. Several glucose monitoring protocols have been developed, aiming to achieve a tight glucose monitoring and control. Depending on the type of diabetes and the optimal or suboptimal glycemic control, the treatment options include fasting status of the parturient, frequent monitoring of capillary blood glucose, intravenous dextrose infusion and subcutaneous or intravenous use of insulin. Continuous glucose monitoring system (CGMS) is a relatively new technology that measures interstitial glucose at very short time intervals over a specific period of time. The resulting profile provides a more comprehensive measure of glycemic excursions than intermittent home blood glucose monitoring. Results of studies applying the CGMS technology in patients with or without diabetes mellitus (DM) have revealed new insights in glucose metabolism. Moreover, CGMS have a potential role in the improvement of glycemic control during pregnancy and labor, which may lead to a decrease in perinatal morbidity and mortality. In conclusion, the use of CGMS, with its important technical advantages compared to the conventional way of monitoring, may lead into a more etiological intrapartum management of both the mother and her fetus/infant in pregnancies complicated with DM.

Key words: Diabetes mellitus; Pregnancy; Intrapartum management; Glucose monitoring protocols; Continuous glucose monitoring system

Core tip: In pregnancies complicated with diabetes, intrapartum maternal normoglycemia seems to play an important role in the prevention of adverse perinatal outcomes. Several glucose monitoring protocols have been developed, aiming to achieve a tight glucose monitoring and control intrapartum. The continuous glucose monitoring system is a relatively new technology; its intrapartum application in pregnancies complicated with diabetes is feasible, allows for a closer observation of glucose concentrations and is expected to lead to a more etiological management of both the mother and her fetus/infant.

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INTRODUCTION

The incidence of diabetes mellitus (DM) continues to rise worldwide[1,2]. Obviously, this increase affects the incidence of hyperglycemia in pregnancy[3]. The co-existence of DM and pregnancy, commonly encountered in clinical practice, is important both from a pathophysiology and clinical point of view as it is associated with short and long-term morbidity and mortality for the foetus/infant and the mother. Generally, it is accepted that tight glycemic control during pregnancy and labor leads to a decrease in perinatal morbidity and mortality. Pregnancies complicated with DM are treated intrapartum under this principle.

The continuous glucose monitoring system (CGMS) is a relatively new technology that measures interstitial glucose every 1 to 10 min for a maximum of 3 to 6 d, depending on the monitor used. The resulting profile provides a more comprehensive measure of glycemic excursions than intermittent home blood glucose monitoring. Clinical indications for CGMS use include conditions where tight control is crucial[4].

The aim of this review is to present the intrapartum glucose monitoring protocols in pregnancies complicated with DM. The potential role of CGMS as a tool in the achievement of the optimal glycemic control intrapartum is discussed in detail.

SIGNIFICANCE OF INTRAPARTUM NORMOGLYCEMIA

Although the need for normoglycemia during pregnancies complicated with DM has been well established[5-8], the importance and need for intrapartum normoglycemia arise from epidemiological studies only[9-13]. Poor glycemic control intrapartum is associated with adverse maternal (hypoglycemia, ketoacidosis) and neonatal (hypoglycemia, ketoacidosis and respiratory distress syndrome) outcomes[14]. Neonatal hyperglycemia, specifically, has an impact not only on immediate morbidity but also seems to affect long-term neurological development[14].

It is generally accepted that the main target of intrapartum management in pregnancies complicated with DM is to achieve optimal glycemic control. On the other hand, the definition of "optimal" remains a matter of debate. In the literature, there is a great variance in the recommended targets for blood glucose control during labor, ranging from 4.0-6.5 mmol/L[15] to 4.0-8.0 mmol/L[16] and 3.88-6.5 mmol/L[17].

INTRAPARTUM GLUCOSE MONITORING PROTOCOLS

Different protocols for glycemic control during labor have been developed worldwide. The controversies in the literature concerning the management of pregnancies complicated with DM in the delivery room led to the adoption of different local policies[18-23]. Depending on the type of DM and the optimal or suboptimal glycemic control, the treatment options include fasting status of the parturient, frequent monitoring of capillary blood glucose, intravenous dextrose infusion and subcutaneous or intravenous use of insulin.

Most of the protocols are based on the intravenous dextrose and insulin infusion when the concentration of blood glucose is not maintained in the desired range. The insulin infusion rate usually depends on capillary blood glucose, which is monitored hourly during labor[17,23-25]. Specific algorithms that include simultaneous adjustment of both dextrose and insulin infusion rates during labor have been published. These are considered as the standard of care since their efficacy and safety in reducing the risk for maternal hypoglycemia or ketoacidosis have been tested in many studies[23,26-28].

Insights into the pathophysiology and the intrapartum management of pregnancies complicated with insulin-requiring DM suggest that the amount of insulin required during the onset of labor is often zero; thus, it seems that the probability of ketoacidosis due to the prolonged fasting status constitutes a real problem[20-29].

CLINICAL INDICATION OF CGMS USE

The main clinical indications of the CGMS include: (1) adjustment of anti-diabetic treatment; (2) quantitative assessment of the effect of anti-diabetic therapy; (3) assessment of the effect of lifestyle changes in glycemic control; (4) situations where strict glycemic control is particularly important; (5) diagnosis and prevention of hypoglycemia, particularly during sleep; and (6) diagnosis and prevention of post-prandial hyperglycemia[4,30,31].

The most common use of CGMS is during the adjustment of anti-diabetic therapy towards a better glycemic control[30]. These adjustments include modification of insulin dosage before meals, change of the type of insulin administered, changes in the composition of the diet in carbohydrates, decrease in the dose of insulin during periods of intense physical exercise and changes in diet or DM treatment during the night in an attempt to avoid the "dawn phenomenon"[4,31]. CGMS have been also used in clinical trials concerning anti-diabetic agents in an attempt to obtain accurate data about their effect on patients' glycemic profile[32]. CGMS have been used to monitor glucose levels not only in patients with DM, but also in other populations with high risk of hyperglycemia or hypoglycemia. Much attention has been paid to patients with cystic fibrosis[33,34] who face an increased risk of developing DM, in patients hospitalized in intensive care units[35] who are at a high risk of hypoglycemia[36,37] or hyperglycemia[35,38] and in patients with glycogen storage diseases[39] who also face an increased risk of hypoglycemia.

The aim of a very recent publication of a task force

of experts appointed by the Endocrine Society was to formulate practice guidelines for determining settings where patients are most likely to benefit from the use of CGMS[40]. Indications and implications of the use of CGMS in the perinatal and intrapartum setting were not evaluated and so still need to be assessed.

USE OF CGMS IN PREGNANCY

Although publications on the use of CGMS in pregnancies with or without DM are scarce, their significance is of great importance due to the proposed changes in the therapeutic approach.

The main research aims concerning the use of CGMS during pregnancy include comparison of CGMS to intermittent blood glucose monitoring (finger prick self-monitoring)[41-44], determination of the ideal time to measure post-prandial glucose concentrations[44-50] and day to day variability of the glycemic profile[41,51-54]. Additionally, some studies have evaluated the reliability, specificity and accuracy of the CGMS's readings. In particular, the ability of CGMS to detect asymptomatic episodes of hypoglycemia and hyperglycemia has been studied in pregnant women with DM type 1[41,42].

INTRAPARTUM APPLICATION OF CGMS

In 2008, two pilot studies concerning intrapartum application of CGMS were published. In a prospective study by Stenninger *et al*[55], a CGMS was used to monitor the glucose profile of fifteen pregnant women with insulin-treated DM in the last 120 min before delivery. The capillary plasma glucose concentrations were checked hourly and rapid-acting insulin analogues were injected subcutaneously if these levels exceeded 7 mmol/L, in an attempt to reduce the frequency of early neonatal hypoglycemia. In their conclusions, researchers state that parturients with insulin-treated DM coped well with CGMS. They also emphasized the correlation between strict normoglycemia and occurrence of postnatal hypoglycemia. Their suggestion was that CGMS is a feasible and valuable method for close glucose monitoring intrapartum. The interpretation emerges from the superiority of CGMS over intermittent blood glucose monitoring when maximal information about glucose fluctuations is vital.

In the second study, Iafusco *et al*[56] used a real time CGMS to monitor the glucose profile of eighteen pregnant women with DM type 1 in two phases: antenatal, during treatment with bethamethasone for fetal lung maturation and intrapartum. The main target in both phases was to achieve normoglycemia by using intravenous administration of insulin and glucose fluctuation monitoring. In their conclusions, the researchers state that no infant experienced hypoglycemia or respiratory distress syndrome at the moment and within the first hours after birth. They also emphasized the importance of strict glycemic control in these two phases in pregnant women with DM type 1, considering the CGMS as an important tool to achieve it.

More recently, our group conducted a feasibility study[57] with the primary aim to assess the feasibility of the CGMS in the deliveries of pregnancies complicated with DM; a secondary aim was to examine CGMS acceptance by the women. The study involved twelve pregnant women with GDM. The minimally invasive microdialysis-based CGMS (Gluco-Day, Menarini Diagnostics) was used to record glucose profile during labor. The device was installed 6 h before delivery for a total of 48 h. As far as the primary aim is concerned, no pain was reported during sensor installation and removal. Subcutaneous application into the abdominal wall did not affect the obstetric interventions. In the case of vaginal delivery, even an operative one, CGMS did not affect the continuous electronic fetal monitoring, the application of epidural analgesia, or the use of ultrasonography, when needed. In the case of caesarean section, the selection of the site for the placement of the sensor (far enough from the incision) and its careful immobilization guaranteed the successful recording. In two cases, the monitoring failed (breaking of the microdialysis fiber, device disconnection). As far as the secondary aim is concerned, the mode of delivery was associated with the acceptance of the device postpartum: all women that gave birth vaginally (n = 6) reported discomfort in contrast to the women that underwent caesarean section (n = 6). This can be attributed to different levels of postpartum mobility between the two groups. All women coped well with the CGMS and reported feeling secure by checking glucose concentrations in real-time.

CONCLUSION

In pregnancies complicated with DM, both perinatal and intrapartum normoglycemia is an important milestone in the ultimate goal of reducing perinatal morbidity and mortality. Once diagnosed with DM, pregnancies receive special obstetric management by intense monitoring and adjustment of therapeutic interventions. Even then, the absolute absence of any complication is not guaranteed. Intrapartum glucose monitoring protocols were developed in the name of strict glucose control, although there is still much to be elucidated in the pathophysiology of DM and its behavior intrapartum. CGMS is a tempting and promising technology, with its reliability, specificity and accuracy being evaluated and tested in recent clinical trials. The intrapartum application of CGMS in pregnancies complicated with DM allows for a closer observation of glucose concentrations and is expected to lead to a more etiological management of both the mother and her foetus/infant. As a future perspective, a large, prospective study is needed to determine the clinical implications of intrapartum application of CGMS.

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