THE USE OF INTRAVENOUS LOW-DOSE INSULIN INFUSION IN THE INTRAPARTUM MANAGEMENT OF DIABETES MELLITUS

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INTRODUCTION

In the last two decades, the rigid control of maternal blood glucose throughout pregnancy (1), early management of antenatal complications and close intrapartum monitoring (2) have contributed to an improved perinatal outcome in diabetic pregnancies. However, the newborn baby is still at risk during the neonatal period (3). Infants of diabetic mothers (IDMs) showed an increased insulin response to a glucose load at birth compared with those of normal mothers (4) as a result of pancreatic beta-cell hyperplasia (5, 6). Even mild gestational diabetes has effects upon the fetal endocrine pancreas (7). Symptomatic hypoglycemia is rare but chemical hypoglycemia is seen in 16% of infants of gestational-diabetic mothers (8). Pedersen (9) observed that infants of mothers with well-controlled diabetes were smaller but had higher blood sugar levels. Light (10) reported that the higher the cord blood glucose at the time of delivery, the more rapid the decrease of neonatal blood glucose and hypoglycemia in the first few hours of life.

Current interest in the blood sugar levels of the newborn stems from the realisation that hypoglycemia can have deleterious effects on the function of the relatively mature glucose-dependent brain.

The importance of antenatal control of maternal blood glucose in the prevention of pancreatic beta-cell hyperplasia and neonatal hyperinsulinism is well known (11). But fastidious control of blood glucose in the intrapartum period may be equally essential in preventing islet-cell stimulation. There is considerable variation of the intrapartum management in most centres involved in the treatment of diabetic pregnancies.

The technique of combined glucose and low-dose insulin infusion devised for the treatment of diabetic ketoacidosis (12) provided an optimal method of intrapartum blood glucose control. Initial studies (13, 14) of this technique have yielded satisfactory maintenance of maternal euglycemia in labour.

The following study was carried out in the University Department of Obstetrics and Gynaecology to assess the efficacy of this technique in the maintenance of maternal blood glucose within physiological ranges. The effects of low-dose insulin infusion on maternal serum potassium and neonatal glucose levels were also examined. The feasibility of this technique in a busy labour ward will also be discussed.

Eight patients with varying severity of diabetes were studied (Table 1). All were seen regularly at the Diabetic Pregnancy Clinic and had required insulin therapy.

Of the eight patients, two were established diabetics and six were gestational diabetics (with normal glucose tolerance at six weeks post-partum). One patient had a history of two macerated stillbirths in India. Four patients had superimposed hypertensive disease and one had mild hydramnios.

On the day before delivery, insulin was given normally and the patients were fasted after 2200 hours. On the morning of induction an intravenous cannula was inserted and blood was taken for matching and for the estimation of serum potassium and blood glucose concentrations. A five per cent dextrose infusion was set up in the opposite arm and dextrose was administered at a rate of

six grams per hour (i.e. 500 millilitres in four hours) throughout labour. No oral intake was allowed till two hours after delivery.

TABLE 1

PATIENT PARTICULARS AND ANTENATAL INSULIN REQUIREMENTS

Case No	Age	Gravida	Para	Diabetes	Antenatal Insulin Requirements
1	28	1	0	Gestational	IZS 16U om
2	31	1	0	Gestational	IZS 30U om
3	27	2	1	Established	IZS 36U om
4	29	4	3	Gestational	SI 12U tds
5	28	4	2	Gestational	IZS 16U om
6	29	3	2	Gestational	IZS 24U om
7	26	1	0	Gestational	IZS 12U om
8	33	1	0	Established	IZS 20U bd and SI 28U bd

Syntocinon Infusion (Table 2) Intrapartum Management

Labour was induced by low amniotomy and intravenous syntocinon (Orasthin) via a B. Melsungen infusion pump which was connected to the Dextrose cannula. Five units of syntocinon was diluted in fifty millilitres of normal saline to give a concentration of 100 milli-Units per millilitre. The infusion was started at 4.5mU per hour and increased hourly till adequate contractions were registered on the external tocographic monitor. In none of the patients was there a need to exceed 18.3 mU/Hr. A new infusion solution was prepared every six hours.

TABLE 2

SYNTOCINON INFUSION BY B. MELSUNGEN PUMP

(Concentration of 100 milliUnits per millilitre)

Mark No	Volume Delivered (ml/Hr)	Syntocinon Dose (mU/Hr)	Equivalent
2	1.2	1.83	1 Unit at 18 dpm
3	3.0	4.5	2 Units at 20 dpm
4	6.0	9.0	2 Units at 45 dpm
5	12.0	18.3	4 Units at 40 dpm

Insulin Infusion (Table 3)

A separate B. Melsungen Infusion pump was used for the insulin infusion. However, the insulin infusion was also connected to the same intravenous cannula that delivered dextrose and syntocinon.

Twelve units of soluble insulin (Actrapid) was diluted in twenty millilitres of normal saline in the sterile twenty millilitre Luer-Lok glass syringe. The infusion was started for all patients irrespective of antenatal insulin requirements at 1.0 Unit per hour and adjusted subsequently according to the blood sugar level estimated two-hourly. The aim was to maintain the blood sugar level between 4.0 and 6.7 millimoles per litre throughout labour.

A fresh insulin solution was prepared every six hours. The insulin infusion was discontinued two hours after delivery.

TABLE 3

INSULIN INFUSION BY MELSUNGEN PUMP

(Concentration of 0.6 Units per millilitre)

Mark No on Pump	Volume Delivered (ml/Hr)	Insulin Dose (Units/Hr)
2	0.6	0.4
3	1.7	1.0
4	3.3	2.0
5	6.6	4.0

Intrapartum Monitoring

(a) Blood glucose estimations were done just before the commencement of insulin infusion and subsequently two hourly until two hours after delivery. All blood glucose estimations were performed by the same person using the Dextrostix-Eyetone-System placed at the bedside. When the levels of blood glucose deviated by more than 1.0 millimole per litre from the preceding value, a duplicate estimation was done and this was followed by hourly estimations.

(b) Serum potassium levels were estimated before and after the insulin infusion was commenced. It was done two-hourly for six hours and then four hourly till delivery.

(c) Any symptoms of hypoglycemia were recorded. All blood samples for glucose and potassium estimations were obtained from an indwelling intravenous cannula kept patent with a dilute solution of sterile heparin.

(d) Urine output was charted. Tests for urine glucose and ketones were done four-hourly.

(e) Progress of labour was assessed by abdominal and vaginal examinations four hourly and findings were recorded on partograms.

(f) Continuous intrapartum monitoring was available by means of external toco-transducers and fetal scalp electrodes.

The neonatal pediatrician was present at each delivery to assess the condition of the newborn and to institute any treatment, if necessary.

Postpartum

(a) Mothers were allowed oral feeds two hours postdelivery after the last blood glucose estimation. Insulin infusion was also discontinued.

(b) The one-minute Apgar scores of the newborn babies were recorded.

(c) Blood glucose levels of the newborn babies were estimated thirty minutes after birth, just before the first feeds were given.

RESULTS (Table 4)

(A) Outcome of Labour

There was no evidence of intrapartum fetal distress and all delivered vaginally. Four patients had prophylactic forceps deliveries. There was no maternal or perinatal mortality.

(B) Blood Glucose Control and Insulin Infusion Rate

The mean infusion rate (± SD) of soluble insulin (Actrapid) ranged from 1.0 to 1.6 ± 0.6 Units per hour. These infusion rates were adequate even in cases which had earlier experienced difficult antenatal blood glucose control. A total of sixty-two blood glucose estimations were made. The mean intrapartum blood glucose level (± SD) ranged from 4.0 ± 0.2 to 5.7 ± 0.9 mmol/L. Euglycemia was maintained in those cases where diabetes had been well controlled whereas rapid correction of blood glucose level was seen in cases exhibiting fluctuations before induction of labour.

None of the patients reported any symptoms of hypoglycemia. There was no ketonuria and patients were clinically well hydrated. Urine output was satisfactory.

(C) The mean serum potassium concentrations (± SD) ranged from 3.65 ± 0.1 to 4.26 ± 0.5 milli-Equivalents per litre.

(D) Birthweights of the newborn babies ranged from 2,500 to 3,420 grammes with a mean (± SD) of 2,966 ± 286 grammes. The mean one-minute apgar score was 7.4. None of the newborn babies showed any clinical or biochemical evidence of hypoglycemia. The mean blood glucose level at thirty minutes of life was 3.5 ± 0.5 mmol/L.

TABLE 4

RESULTS OF LOW-DOSE INSULIN INFUSION

Case No	Mean Intrapartum maternal blood glucose (mmol/L)	30-minute Blood Glucose of Neonate (mmol/L)	Mean Serum Potassium (meq/L)	One-minute Apgar
1	4.3	2.8	3.7	7
2	4.0	3.9	3.8	8
3	4.8	3.3	4.3	6
4	5.7	4.4	3.9	7
5	5.7	2.8	4.0	9
6	5.3	3.6	4.2	8
7	4.4	3.5	4.3	7
8	5.7	3.3	4.0	8

DISCUSSION

Page [12] described the technique of low-dose insulin infusion in the management of diabetic ketoacidosis. This was an attractive concept and the advantages of this technique were borne out by later studies on diabetic ketoacidosis.

In this study, little difficulty was encountered in maintaining blood glucose values within the optical range from 4.0 to 6.7 mmol/L employing the low-dose infusion technique.

None of the mothers had biochemical or clinical evidence of hypoglycemia even two hours postpartum. Ketonuria was not encountered in the course of the labours studied.

These results are in agreement with those obtained by West and Lowy (13) and Yeast (14). It is interesting to note that blood glucose fluctuations experienced antenatally by two patients on high subcutaneous insulin doses were not seen in the intrapartum period when low-dose insulin was administered.

This study also showed that the low-dose infusion could adequately control blood glucose levels in most patients with less than the usual antepartum insulin dose. Similar impressions were also recorded in studies by Parsons (15) and Yeast (14). The latter reported rates of insulin infusion as varying from 0.25 to 2.00 units per hour irrespective of the pre-infusion insulin requirements.

None of the newborn babies showed any biochemical or clinical evidence of hypoglycemia. Though most reports on the use of intrapartum insulin infusion did not describe the blood glucose levels of the newborns, similar favourable neonatal outcome were reported based on clinical assessment.

Fluctuations of potassium levels were minimal and denoted a negligible degree of intracellular potassium shift with intravenous insulin infusion. Should a general anesthetic be necessary, no pre-operative correction of serum potassium deficit was necessary. The advantages of this technique of continuous low dose insulin infusion during labour are many. Intravenous infusion exerts the insulin effect almost immediately and causes a more gradual fall of blood glucose levels. The infusion ensures a uniform effective insulin level in the circulation despite the rapid plasma clearance. The level of insulin can also be altered or ended instantaneously as desired. As maternal insulin requirements fall after delivery, the infusion rate can then be lowered accordingly without causing any postpartum hypoglycemia.

Low-dose infusion of insulin also carries minimal risk of intracellular potassium shift (16) and the dangers of hypo-kalemia are negligible. This attribute is of special importance when a general anesthetic is necessary in the peripartum period.

The constant dextrose infusion further provides hydration and calories, both very important in the prevention of starvation ketosis in labouring diabetic mothers.

A disadvantage of the low dose insulin infusions technique is that the system may be unable to deliver the desired insulin dose as a result of possible adsorption of insulin to the surface of tubings and syringe (17). Sonksen (18) had described the significant reduction of effective insulin concentration if protein-carriers were not added to the insulin solution.

However, albumin or other protein-carriers are not needed if excessively dilute insulin solutions are avoided, and the insulin is used in concentrated solution as in a Luer-Lok syringe with a Melsungen infusion pump (19, 20). In order to minimisw this adsorp-

tion loss, the insulin solution as used in this study, was discarded after every six hours and a fresh solution was prepared.

Another disadvantage is that in patients with insulin antibodies, this antibody of unknown capacity and affinity may compete with insulin receptors for available hormone. Therefore if the loading dose is insufficient as is likely with low-dose infusion, then the initial few hours of treatment may be spent saturating antibodies rather than receptors (21). This may be corrected with an initial loading dose by intramuscular injection.

Throughout the study, blood glucose estimations were done at the bedside with the Dextrostix-Eyetone System (DES).

The DES gives the result of estimation almost within two minutes and correlation between the DES and glucose-oxidase method is highly significant (22). Moreover, DES allows frequent estimations to be made with little inconvenience and patient acceptance of this technique was high. This simple and versatile technique of glucose estimation was an important accompaniment of the infusion technique.

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