RESEARCH

Intraoperative glucose management in children < 1 year or < 10 kg: an observational study

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Background: Infants may be at risk of hypoglycaemia in the perioperative period. Current evidence has led to the global use of maintenance fluid with low-concentration dextrose in these patients. This study aimed to analyse the current practice of anaesthetists in the authors' institution with regard to blood glucose management, and to assess its adequacy.
Methods: Ninety-nine patients under one year of age, or less than 10 kilograms, who required anaesthesia were enrolled. The intraoperative management of intravenous dextrose administration and blood glucose monitoring was at the discretion of the attending anaesthetists. Data collected included patient demographics, period of starvation, dose of dextrose administered and blood glucose measurements taken.
Results: Nine infants had at least one glucose value lower than 3.7 mmol/l at any time during the procedure, while all received intravenous dextrose intraoperatively. The hypoglycaemic episode occurred on initial measurement (start of surgery) in five infants and later on in the procedure in four infants. This subgroup had an average age of 1.5 months, and average weight of 2.9 kg. Seven of these infants had significant co-morbidities and/or prematurity and low birthweight.
Conclusions: The findings indicate that anaesthetists adhere to current recommendations regarding glucose management, and confirmed the safety of intraoperative administration of 0–2.5% dextrose in isotonic solution to healthy infants. The authors' observations also emphasised that smaller infants and those with significant co-morbidities are at particular risk of developing hypoglycaemia, despite preoperative and intraoperative dextrose administration. It remains important to check glucose levels in patients at risk of hypoglycaemia.

Keywords: dextrose, infants, intraoperative, hypoglycaemia, hyperglycaemia

Introduction

During fasting, hypoglycaemia develops earlier in younger children, as was borne out in an analysis of children between 0 and 18 years of age.[1] Children have low glycogen stores in the liver, which results in a rapid decrease in endogenous glucose production (EGP). This explains why in particular children younger than three years experience hypoglycaemia more readily than adults do during periods of fasting.[2]

The brain derives 90% of its energy from glucose during times of fasting and the ratio of a baby's brain-to-body weight is six times higher than that of an adult: the brain of a 3 kg newborn weighs 400 g, while an adult's brain weighs 1400 g.[2] This may partially explain why infants have an EGP of 5–8 mg/kg/min, as opposed to adults' 2–3 mg/kg/min.[3,4]

Limited adaptation of glucose metabolism is particularly evident in preterm infants. They have very low liver glycogen stores, as well as immature gluconeogenic enzymes and hormonal responses.[5] A prospective study showed that up to 20% of preterm infants who were ready for discharge were still at risk of hypoglycaemia when a feed was delayed.[5]

Children and neonates are at particular risk of hypoglycaemia when suffering from sepsis (shown with malaria, diarrhoea, pneumonia, meningococcal disease), and neonates may additionally suffer hypoglycaemia in association with asphyxia and hypothermia.[2,3,5,6] In contrast, surgery and critical illness may cause hyperglycaemia.[3]

Hypoglycaemia can affect neurodevelopmental outcome.[3,4] Hyperglycaemia may also be harmful to the nervous system, especially when associated with ischaemia or hypoxia, and may additionally lead to an osmotic diuresis with subsequent dehydration.[7]

Careful glucose management is therefore required in neonates and small infants, especially in infants with co-morbidities. Under anaesthesia the metabolic rate, and therefore demand, decreases while the stress response leads to an increase in endogenous glucose production. It was shown that giving 0.9% or 1% dextrose in Ringer's lactate as maintenance in anaesthetised children maintained glucose levels, and even improved glucose levels in some hypoglycaemic patients, without causing hyperglycaemia.[8] The Association of Paediatric Anaesthetists of Great Britain and Ireland's guidelines on perioperative fluid management do not recommend that dextrose-containing maintenance fluid be given to healthy infants, and that infants at risk of hypoglycaemia be monitored intraoperatively while dextrose can be added to maintenance fluid.[9] Others, including the European Association of Paediatric Anaesthetists, recommend the use of an isotonic maintenance solution containing 1–2.5% dextrose for infants.[10,11]

Our institution has no set protocol to guide the administration of intravenous glucose to patients in theatre, but it is recommended that at least one glucose measurement be taken intraoperatively in small infants, and glucose is monitored in critically ill children or children undergoing prolonged surgical procedures. We were confident that our clinicians adhered to acceptable practice, but

we expected to find a number of hypoglycaemic patients. Our study aimed to collect data on the current practice of clinicians regarding intraoperative glucose supplementation, and to investigate whether it results in acceptable glucose levels.

Methods

This observational study was done following institutional review board approval. All infants under one year of age, or weighing less than ten kilograms, who required any procedure under anaesthesia in theatre were eligible. Informed consent was obtained from a parent or legal guardian and the following data were collected: patient age, weight, presence of prematurity and post-conceptional age where applicable, procedure planned, co-morbidities, duration of starvation (for solids, breast milk and clear fluids respectively), duration of surgery, administration of intravenous maintenance fluid preoperatively, volume of intravenous fluids and dose of intravenous dextrose given intraoperatively (both boluses and infusions), and glucose values measured. Capillary blood glucose measurements were done via either HemoCue Glucose 201® (HemoCue AB, Ängelholm Sweden) or Accu-Chek Active® (Roche Diabetes Care, Burgess Hill, UK) systems.

Anaesthetists were instructed to follow their normal practice regarding dextrose administration and blood glucose monitoring. The concentration and volume of intravenous dextrose administered, the timing of blood glucose measurements and the response to these measurements was at the full discretion of the anaesthetist in charge of that patient. Anaesthetists were required to record all measurements and interventions on the data collection sheet. The only instruction to anaesthetists was to do a minimum of one glucose measurement at the conclusion of the procedure.

Results

One hundred infants were enrolled, but one was excluded because insufficient data had been recorded. The characteristics of the study group are summarised in Table 1.

Table 1: Characteristics of study group (*n* = 99)

Characteristic	*n*
Age (months)	5.1 (0–19.5)
Weight (kg)	5.4 (0.75–12.6)
Ex-premature (number)	24
Post-conceptual age if ex-premature (weeks)	42 (30–64)
Emergency surgery (number)	33
Patients with co-morbidities (number)	45

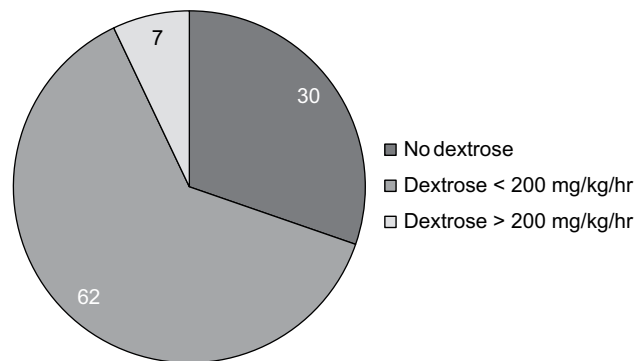Note: Values are expressed as: mean (range) or absolute numbers.

Figure 1: Intraoperative dextrose administration by anaesthetists.

The average (range) duration of starvation was 16.2 (3.5–48), 6.2 (1–13.5) and 4.3 (2–9.5) hours for solids/formula, breast milk and clear fluids respectively. Twelve infants were starved for longer than 9 h without receiving intravenous fluids preoperatively, and the longest time of starvation without preoperative administration of intravenous fluid was 15 h. Starvation information was not recorded in two cases.

Figure 1 depicts intraoperative dextrose administration. Thirty infants received no dextrose, 62 received less than 200 mg/kg/hour dextrose (averaged over the duration of the surgery) and seven received more than 200 mg/kg/hour. In Table 2 data from these seven patients are summarised. Of the seven, five were administered a bolus of intravenous dextrose. In four cases this was in response to a blood glucose measurement < 3.7 mmol/l during the procedure as shown in the table. Two cases (35, 41) received boluses without infusions for very short procedures (15–30 min). All cases except patient no. 77 were emergency cases. One infant (77) was maintained on the 10% dextrose infusion he had been on preoperatively. The average (range) blood glucose value at the end of surgery in these seven infants was 6.9 (3.0–9.1) mmol/l. The 92 infants who received 0–200 mg/kg/hr dextrose had an average (range) glucose measurement of 7.5 mmol/l (3.5–16.2) at the end of surgery.

The composition of the maintenance fluid selected by our anaesthetists consisted of 0–2.5% dextrose in isotonic solution in 96 of the patients. Of the three that received higher concentrations, two had been on preoperative intravenous maintenance, and were continued on it. The third patient was an ex-premature infant who had been starved for 11 h before surgery. The percentage dextrose mixed into isotonic crystalloid, given as intravenous maintenance fluid to the 99 patients, can be seen in Figure 2. This excludes intravenous dextrose boluses.
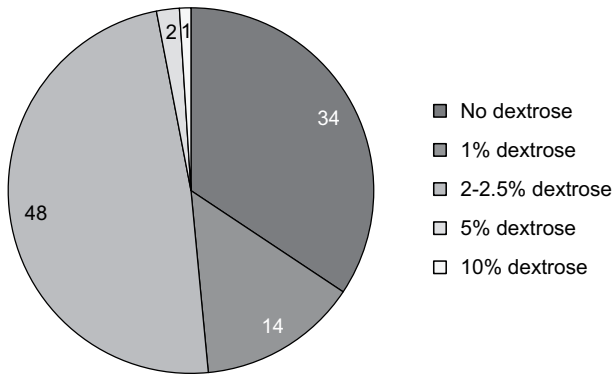
Table 2: Patients receiving > 200 mg/kg/hr of dextrose intraoperatively

Patient no.	Fasting time (hrs)	Preoperative IV maintenance	Average dose of dextrose (mg/kg/hr)	Dextrose concentration used		Lowest glucose measurement	Timing of measurement < 3.7	Last glucose measurement
				Infusion	Bolus			
13	3	No	527.0	2%	10%	3.0	End of surgery	3.0
26	5	Yes	523.3	1%	10%	2.2	Start of surgery	7.4
35	9	No	774.2	Nil	2%	2.4	Start of surgery	4.3
41	6	Yes	259.7	Nil	2%	6.8		6.8
49	9	Yes	295.5	2%	5%, 2%, 2.5%	3.6	During surgery	4.1
56	24	Yes	276.3	10%	Nil	4.4		4.4
77	11	No	285.7	5%	Nil	7.4		9.1

Figure 2: Number of patients who received various concentrations of dextrose (from 0% to 10%) as maintenance solutions in theatre.

Legend:
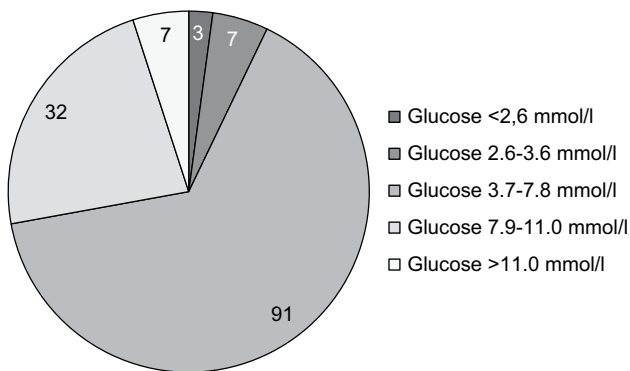- No dextrose
- 1% dextrose
- 2-2.5% dextrose
- 5% dextrose
- 10% dextrose

Figure 3: Distribution of all intraoperative blood glucose (in mmol/l) measurements obtained.

Legend:
- Glucose <2,6 mmol/l
- Glucose 2.6-3.6 mmol/l
- Glucose 3.7-7.8 mmol/l
- Glucose 7.9-11.0 mmol/l
- Glucose >11.0 mmol/l

In total 140 blood glucose measurements were done in the 99 enrolled infants. The distribution of these measurements is depicted in Figure 3. These include measurements done at the start of the procedure, during the procedure and the obligatory measurement at the end of the procedure. Nine infants had at least one glucose measurement reading lower than 3.7 mmol/l at any time during the procedure, despite all of them receiving intravenous dextrose for the duration of the anaesthetic. The characteristics of these patients are presented in Table 3. This subgroup had an average age of 1.3 months and average weight of 2.9 kg. Four of them had been born prematurely, and two were born at term but had low birthweights. Seven babies had significant co-morbidities (with or without prematurity and low birthweight). In five of these nine infants, the lowest blood glucose value was recorded at the start of the procedure, and three of these measurements were below 2.6 mmol/l. In two of the nine patients, the lowest blood glucose value was recorded during the procedure, and in the other two patients only one measurement was done (at the end of the procedure).

Six of these infants with hypoglycaemia received intravenous dextrose maintenance infusions preoperatively. Of the three infants with a starting blood glucose value of less than 2.6 mmol/l, two did not receive any preoperative intravenous dextrose despite both infants being fasted for nine hours preoperatively.

Discussion
Normal glucose values
Hyperglycaemia can be defined in terms of diabetes, which is diagnosed in children if the fasting glucose is 7.0 mmol/l or higher, or the post-oral glucose challenge value is 11.1 mmol/l or higher.[12] Determining the lower limit of normal for glucose values in infants is more difficult.

Children under 24 months have lower non-fasting glucose values than older children.[1] Glucose values as low as 2.2 mmol/l have been used as cut-off for 'hypoglycaemia'.[1,2] Another suggestion is a cut-off of 2.5 mmol/l for neonates,[2,4] 3.0 mmol/l for older children, and 3.9 mmol/l for adults.[2] Determination of a cut-off value could be based on an epidemiologic approach (based on values attained from a cohort), a clinical approach (hypoglycaemia diagnosed by the presence of symptoms), a neurophysiological approach (looking at effects on, for example, somatosensory evoked potentials), a metabolic/endocrine based approach, or a neurodevelopmental outcome based approach.[4,13]

Table 3: Patients with a glucose measurement less than 3.7 mmol/l

Patient no.	Age (m)	Weight (kg)	Ex-prem	Co-morbidities	Fasting time (hrs)	Preop. IV dextrose	Average dextrose (mg/kg/hr)	Lowest blood glucose	Timing of lowest blood glucose	Last blood glucose
3	2.00	3.2	Yes	Cyanotic heart disease, severe sepsis	3.5	Yes	46.9	3.3	Start of surgery	3.6
8	3.50	2.8	No	Arthrogryposis multiplex congenita	9	No	190.5	2.4	Start of surgery	4.5
13	0.07	2.3	No	Low birthweight, foetal alcohol exposure	3.25	No	527.0	3.0	End of surgery	3.0
26	2.50	2.79	No	Low birthweight, laryngeal cleft, aspiration pneumonia, poor growth	5	Yes	523.3	2.2	Start of surgery	7.4
35	0.80	3.1	No	Nil	9	No	774.2	2.4	Start of surgery	4.3
36	0.13	2.3	Yes	Nil	NR	Yes	173.9	3.2	During surgery	4.1
49	0.93	4.4	No	Renal failure, hypoplastic lungs secondary to oligohydramnios, PDA	9	Yes	295.5	3.6	During surgery	4.1
84	2.00	3.4	Yes	Liver failure	12	Yes	121.1	3.5	End of surgery	3.5
100	0.03	1.8	Yes	Acute abdomen	24	Yes	188.9	3.3	Start of surgery	5.7

Note: NR = not recorded.

Interpretation of any glucose value should take into account the accuracy of the measurement. Measurements taken with point-of-care devices can differ from the true values by as much as 1.1 mmol/l, especially at low glucose values. Other factors that can influence accuracy include a high haematocrit, hyperbilirubinemia and acidosis.[14] Therefore a cut-off value for hypoglycaemia set at 3.6 mmol/l may be safest.

Using this cut-off value, we report hypoglycaemia in nine of our patients. Of these patients, six had a lowest recorded measurement between 3.0 and 3.6 mmol/l, two had a measurement of 2.4 mmol/l, and one had a measurement of 2.2 mmol/l.

Dextrose concentration in maintenance

It is estimated that term neonates need a dextrose infusion of 3–4 mg/kg/min (180–240 mg/kg/hr) to prevent hypoglycaemia.[15] This is in keeping with the utilisation of 5% dextrose-containing maintenance fluid. In 1931 Karelitz and Schick described using a 5% dextrose solution to treat dehydrated children while preventing hypoglycaemia. Holliday and Segar's recommendation for maintenance fluid also contained 5% dextrose. Infants do suffer a stress response to surgery, though, and a study by Welborn *et al.* in 1986, as well as other studies, showed that adding 5% dextrose to maintenance solutions can cause significant hyperglycaemia intraoperatively.[16] Infusions of solutions containing 0–2.5% dextrose therefore grew in acceptance, and are now part of guidelines issued by various anaesthetic societies (as mentioned earlier).

This stress response is also relevant postoperatively. In an intensive care study Verbruggen *et al.* assigned eight infants to either 150 or 300 mg/kg/hr dextrose maintenance infusions after surgery for craniosynostosis. Patients receiving 300 mg/kg/hr were hyperglycaemic, while the group receiving 150 mg/kg/hr were normoglycaemic without suffering more protein catabolism.[17]

Running a 2.5% dextrose solution (as per current recommendation) at 4 ml/kg/hr will deliver 100 mg/kg/hr glucose.

Hypoglycaemic patients

Our observations emphasise that certain individuals are at higher risk of hypoglycaemia than others. In keeping with the literature, we noted hypoglycaemia in ex-premature infants, patients with low birthweight, and patients with significant co-morbidities. Administration of preoperative intravenous maintenance fluid containing dextrose was not protective against hypoglycaemia in six of the nine patients who developed hypoglycaemia, despite the administration of intraoperative intravenous dextrose, and should therefore not be relied upon to prevent hypoglycaemia.

Conclusion

The importance of individual blood glucose monitoring in children, as well as the risks to patients with ex-prematurity or low birthweight, and significant co-morbidities are emphasised.

Most anaesthetists in this study administered low-concentration dextrose, as recommended by literature. We confirmed that administration of 0–2.5% dextrose in isotonic solution as intravenous maintenance fluid intraoperatively results in acceptable glucose levels in most healthy infants, and that it may even be associated with hyperglycaemia.

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