PAEDIATRIC GLUCOSE HOMEOSTASIS DURING ANAESTHESIA

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SUMMARY

The perioperative blood glucose regulatory response was compared in 20 healthy children (aged 1–5 yr) presenting for minor surgery and allocated randomly to either a fasted or a glucose group. All children received a milk feed at midnight. The fasted group received no oral intake thereafter, whereas the glucose group received 5% dextrose water 10 ml kg⁻¹ orally about 4 h before operation. The mean plasma glucose concentrations in the two groups were similar before operation and were within normal limits. The pattern of change in the concentrations of plasma glucose, insulin, cortisol, growth hormone and glucagon were also similar between the two groups. Ten percent of patients in the fasted group and 33% in the glucose group had gastric aspirates in excess of 0.4 ml kg⁻¹. The pH of all gastric samples was less than 2.5. The results suggest that healthy preschool children were able to maintain glucose homeostasis after 8 h of fasting. Feeding within 4–6 h before surgery may increase the risk of pulmonary aspiration.

KEY WORDS


Preoperative hypoglycaemia in children was reported by Watson [1], who found an incidence of 10%, and Thomas [2] who found an incidence of 28%. This may have led to the widely accepted practice of giving sweetened clear oral fluids 4–6 h before operation to small children. However, more recent work [3–6] has demonstrated that children may tolerate a considerable period of starvation (range 2.5–21 h) without evidence of hypoglycaemia. Moreover, hyperglycaemia has been shown to occur commonly in paediatric surgical patients [4, 7–10] and it has been suggested that this is associated with the endocrine and metabolic stress response [7–10].

The present study was undertaken to examine the effect of preoperative oral glucose administration on perioperative plasma glucose concentrations in children aged 1–5 yr, and the relationship of these glucose concentrations to the pattern of the endocrine response.

PATIENTS AND METHODS

We studied 20 healthy children aged 1–5 yr who presented for routine minor surgery (herniotomy, repair of hydrocele and circumcision) before 09:00. The procedure was approved by the Faculty of Medicine Ethics Committee. Informed consent was obtained from the parents of all the children studied. The patients were allocated randomly to one of two groups, a fasted group and a glucose group. All children received a milk feed at midnight, but those in the glucose group were given in addition a drink of 5% dextrose solution 10 ml kg⁻¹ approximately 4 h before surgery.

All the patients were premedicated orally with trimeprazine 1.5 mg kg⁻¹ (up to a maximum of 30 mg) 3 h before surgery and morphine 0.2 mg kg⁻¹ (up to a maximum of 10 mg) with atropine 0.02 mg kg⁻¹ (up to a maximum of 0.6 mg) by i.m. injection 1 h before surgery.

Anaesthesia was induced with nitrous oxide and halothane in oxygen. A 22-gauge cannula was inserted into a peripheral vein on the dorsum of each hand for collection of blood samples. Tracheal intubation was facilitated with tubocurarine.

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0.6 mg kg⁻¹. The lungs were ventilated with 70% nitrous oxide in oxygen using an Ayre's T-piece breathing attachment and a ventilator (Nuffield 200, Penlon Ltd). The fresh gas flow was adjusted to maintain an end-tidal carbon dioxide partial pressure of approximately 4 kPa (Normocap CD 102, Datex Instrumentarium). At the end of surgery, the residual neuromuscular block was antagonized with neostigmine 80 µg kg⁻¹ and atropine 20 µg kg⁻¹. I.v. fluids were not administered during the study. The same anaesthetist and surgeon performed all the procedures, which were comparable for mean duration of surgery (fasted group 19.9 (SD 5.3) min, glucose group 16.7 (SD 6.5) min).

Serial venous blood samples were collected before the operation (after induction of anaesthesia but before tracheal intubation), at the end of the operation, and 30, 60 and 120 min after the operation. The samples were analysed for plasma glucose, cortisol, growth hormone, glucagon and insulin concentrations. Plasma glucose concentrations were assayed enzymatically by the glucose oxidase method using a Beckman Astra-8 analyser, the inter-assay coefficients of variation at 5.4 mmol litre⁻¹ and 17.3 mmol litre⁻¹ being 2.8% and 2.5%, respectively. Hypoglycaemia was defined as a plasma glucose concentration of less than 2.2 mmol litre⁻¹ and hyperglycaemia as more than 11 mmol litre⁻¹ [11]. Samples for measurement of cortisol, growth hormone, glucagon and insulin concentrations were collected in a sample tube containing EDTA and aprotinin (Trasylol, Bayer) as a preservative (1000 units/ml of blood). The samples were placed on ice and centrifuged as soon as possible. The plasma was stored at −70 °C until the hormone concentrations were measured. All hormones were assayed in duplicate using commercial radioimmunoassay kits (cortisol and growth hormone: Diagnostic Products Corporation kits; glucagon: Biodata kits; insulin: Pharmacia kits). The inter-assay coefficients of variation for cortisol were 20% at 43 nmol litre⁻¹, 7.6% at 506 nmol litre⁻¹ and 11.8% at 970 nmol litre⁻¹; those for growth hormone were 12.6% at 4.5 miu litre⁻¹, 16.3% at 10.9 miu litre⁻¹ and 21.4% at 25.8 miu litre⁻¹. The sensitivity of the assay for glucagon was 14.5 ng litre⁻¹ and the inter-assay coefficient of variation was 2.5% at 87.9 ng litre⁻¹; the standard curve was in the range 15–800 ng litre⁻¹. The hormone concentrations were corrected for the volume of aprotinin added.

A nasogastric tube was passed into the stomach after induction of anaesthesia and the stomach contents were aspirated, as completely as possible, by moving the tube and gently compressing the abdomen. The volume aspirated was recorded and the pH of the gastric contents was measured with an indicator strip pH 0–6 (Acilit, Merck).

Statistical analysis

Student's t test was used to compare the groups. Statistical differences in the concentrations of various analytes were determined by analysis of variance for repeated measures. The Mann–Whitney U test was used to test the difference in the volume of gastric aspirate between the two groups. Correlations were determined using the Kendall Rank correlation test. P values less than 0.05 were considered significant.

RESULTS

There were no differences between the glucose and fasted groups with respect to the ages and weights of the children: 35.3 (SD 11.2) and 37.7 (14.9) months and 13.7 (2.6) and 14.4 (2.4) kg, respectively.

None of the patients in each group was found to be hypoglycaemic before operation. The mean

![FIG. 1. Changes in plasma concentrations of glucose (mean, SEM) in the glucose (■) and fasted (□) groups before and after surgery. A = After anaesthesia before tracheal intubation; ES = end of surgery; P30 = 30 min after surgery; P60 = 60 min after surgery; P120 = 120 min after surgery.](image-url)
preoperative blood concentration of glucose in the fasted group was 4.64 (SEM 0.21) mmol litre\(^{-1}\) and in the glucose group 4.58 (0.36) mmol litre\(^{-1}\) (ns) (fig. 1). The mean plasma glucose concentrations increased significantly \((P < 0.01)\) following operation and peak values were found 30 min after the end of the operation. Plasma glucose values subsequently decreased gradually towards preoperative values.

The mean plasma concentrations of glucose were generally greater in the fasted group, but the differences between the two groups were not significant.

The time course of mean plasma concentrations of cortisol, growth hormone, glucagon and insulin in the two groups are shown in figures 2, 3, 4 and 5, respectively. There were no significant differences between the two groups in the plasma concentrations of any hormone measured before the operation.

All hormone concentrations increased significantly following the operation \((P < 0.01)\). Cortisol concentrations increased four-fold by 2 h after operation. Growth hormone, glucagon and insulin values increased to a lesser extent. However, the differences between the two groups were not statistically significant. Only the pattern of change in plasma concentrations of insulin followed that of plasma concentrations of glucose, with a similar trend, reducing towards the preoperative concentrations.

The mean volumes of residual gastric aspirates were 0.53 (range 0–2.9) ml kg\(^{-1}\) and 0.16 (range 0–0.47) ml kg\(^{-1}\), respectively, for the glucose and fasted group (ns). Gastric aspirate was unobtainable from one patient in the glucose group and three patients in the fasted group. In all cases, the
pH of the aspirate was less than 2.5. One patient in the fasted group and three patients in the glucose group had gastric aspirates in excess of 0.4 ml kg$^{-1}$. One patient in the glucose group had a residual gastric aspirate of 35 ml (2.9 ml kg$^{-1}$) with a pH of 1.8.

There was a significant correlation between the volume of residual gastric aspirate and age ($P = 0.03$) and body weight ($P = 0.02$) in the fasted group, but no such correlation in the glucose group ($P = 0.91$ and 0.28, respectively).

There was no vomiting or regurgitation in either group during induction of anaesthesia, operation or recovery.

**DISCUSSION**

The study has confirmed the ability of healthy children aged 1–5 yr undergoing minor surgical procedures to maintain glucose homeostasis after a reasonable period of fasting (about 8 h) [3–6].

Diurnal variations in the concentrations of circulating hormones were obviated by studying only patients who were scheduled for operation between 08:00 and 09:00. Basal blood samples were collected immediately after an inhalation induction, but before tracheal intubation, as sampling might itself have induced stress and so altered the plasma concentrations of hormone.

None of the preoperative plasma glucose concentrations was indicative of hypoglycaemia in either group, and this suggests that the children were capable of regulating their plasma glucose within normal limits after a reasonable period of fasting. This is in agreement with the findings of other recent studies [3–6]. However, the results in our study may have been affected by trimeprazine syrup given as premedication. This contains sucrose 68% w/v, which is hydrolysed by sucrase in the intestine and absorbed as glucose and fructose. The latter is converted readily to glucose in the liver. The dose used (1.5 mg kg$^{-1}$) for both groups provided a potential source of glucose in the range 85–170 mg/kg body weight, which is approximately 17–34% of the oral glucose administered (500 mg kg$^{-1}$) in the glucose group. Our premedication regimen was similar to that of Watson [1]; trimeprazine was given 3 h before anaesthesia. However, 10% of his paediatric patients were hypoglycaemic (< 2.2 mmol litre$^{-1}$) before operation. Thomas [2] gave trimeprazine 4 h before operation and found a 28% incidence of hypoglycaemia. In our study, there was no preoperative hypoglycaemia and the contribution of the glucose from the trimeprazine to the blood concentration is likely to have been minimal by the time the blood samples were taken. It is difficult to explain the difference between our results and those of Watson and Thomas, as the only variation in method was that we used an inhalation induction with halothane, whereas they used thiopentone.

The plasma concentrations of glucose in the present study may be greater than the true preinduction concentrations. Van der Walt and Carter [5], have shown that the mean plasma concentration of glucose in arterialized capillary blood increased by 0.5 mmol litre$^{-1}$ from before to 5 min after induction of anaesthesia. If the plasma concentrations of glucose in this study are adjusted to take account of this change, the values are still not within the hypoglycaemic range.

Hyperglycaemia is the most consistent metabolic effect following surgery [12–14]. The mechanism may be related to concurrent changes in secretion of insulin and counter-regulatory hormones [15]. In adult studies [16–18], an increase in plasma concentration of glucose has been shown during surgery, with suppression of insulin secretion. Suppression was not found in our study, but plasma concentrations of insulin increased after surgery in parallel with plasma glucose. This
finding is similar to that after i.v. infusion of glucose in paediatric patients following surgery [19]. The reason for this difference between adults and children in their response of insulin secretion to surgical stress is not clear.

There was no consistent relationship between the plasma concentration of any of the other counter-regulatory hormones and the changes in plasma glucose. This observation supports the findings of de Fronzo, Sherwin and Felig [15] and Göschke and colleagues [17] that glucose homeostasis is a consequence of the combined effects of insulin, glucagon, growth hormone, cortisol and catecholamine activity. The present study suggests that minor surgical procedures under general anaesthesia do not suppress insulin secretion and activity in paediatric patients and insulin appears to play a predominant rôle in the glucose regulatory process.

The mean plasma concentrations of glucose in the glucose group were, paradoxically, less than those in the fasted group. This may be caused by insulin release following oral glucose and is supported by the insulin concentrations.

A gastric pH < 2.5 and a residual volume > 0.4 ml kg \(^{-1}\) are generally considered to be necessary for pulmonary damage from acid aspiration. Using these criteria, the risk of acid aspiration syndrome in paediatric patients has been reported variously as 3.5% to 76% [5, 20–22]. The risk in our study was 33% in the glucose group and 10% in the fasted group. These observations suggest that the patients in the glucose group were at a greater risk of acid aspiration than those in the fasted group. There was a correlation between the volume of gastric aspirate and the age and weight of the children in the fasted group, but not in the glucose group. This may suggest that glucose has an effect on gastric emptying. In Van der Walt and Carter’s study of gastric volume and pH in infants [5], the incidence of patients with both necessary factors was 3.5% when 5% glucose 10 ml kg \(^{-1}\) was given orally 4 h before surgery. All the children were younger than 1 yr, whilst our patients were older, which may account for the difference between the studies. The difference may be related also to the opioid and atropine premedication used in our study. However, Salem and colleagues [23] showed that premedication with morphine and pentobarbitone with or without atropine or hyoscine did not alter gastric volume in children.

In conclusion, this study has confirmed that healthy children aged 1–5 yr undergoing minor surgical procedures were able to maintain their glucose homeostasis after 8 h of fasting. Preoperative feeding within 4–6 h may increase the risk of pulmonary aspiration, especially if an opioid has been used in the premedication. However, there is great variation in individual response and children waiting for surgery should be observed for hypoglycaemia. The findings may not be applicable in infants younger than 1 yr.

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REFERENCES


