Intraoperative fluid management in children — a comparison of three fluid regimens

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Abstract

Background: Fluid therapy is essential for safe perioperative management. Numerous reports of serious complications as a result of inappropriate fluid management, including brain damage and death of children, have been published. The aim of this study was to assess the effects of intraoperative fluids on serum glucose and electrolyte concentrations as well as serum osmolality.

Methods: 91 children, ASA I and II, undergoing elective ENT surgery were enrolled to this prospective, randomized, open-label study. They were randomly assigned to receive: group G5W: 5% glucose in water solution, group GNaCl: 3.33% glucose in 0.3% NaCl, and group RA: Ringer’s acetate. Serum glucose, sodium, potassium, phosphate concentrations and serum osmolality were analysed before the induction of anaesthesia, immediately following the completion of surgery and 60 minutes after that.

Results: Postoperative hyperglycaemia was observed in 94% of children in group G5W and in 37% of group GNaCl. In all the groups glucose concentration increased significantly after surgery. Postoperative hyponatraemia occurred in 36% of patients in the group G5W, and in 3.7% in the group GNaCl. Neither hyperglycaemia nor hyponatraemia occurred in group RA. Postoperative osmolality decreased significantly in groups G5W and GNaCl and remained unchanged in group RA.

Conclusions: As Ringer’s acetate did not cause significant changes in glucose and electrolyte concentrations, it seems to be the safest for intraoperative use in children undergoing elective surgery. As hypotonic fluids may cause hyperglycaemia and hyponatraemia, they should be avoided intraoperatively.

Key words: perioperative fluid therapy, fluid management, hypotonic fluid, children, glucose, hyponatraemia, hyperglycaemia, hypoglycaemia, glucose solutions, complications, safety

Ensuring the safety of children undergoing anaesthesia and the avoidance of complications are the essential goals of anaesthetic management. One of the underestimated aspects affecting patients’ safety is perioperative fluid therapy. In recent decades, numerous reports have been published demonstrating the risk of acute hyponatraemia in children who have been administered effectively hypotonic fluids i.e. with a sodium content lower than that in plasma [1–3]. Acute hyponatraemia can cause brain oedema and lead to its permanent damage or even death. Despite the British consensus guidelines on perioperative fluid management in children published in 2007 [4] and the European guidelines of 2011 [5, 6], new reports are still emerging. This shows a lack of awareness that administration of hypotonic fluids perioperatively is unacceptable in children [7]. Although there are many case reports and observational studies (usually retrospective), only a few randomised studies confirming a direct relationship between the use of hypotonic fluids and the development of hyponatraemia. Therefore, I have decided to publish the results of the study carried out before 2005, i.e. before the publications of any guidelines on perioperative fluid management. Hypotonic fluids were extensively used in Poland (the author’s unpublished questionnaire study), as well as worldwide [8, 9] during this time.

The aim of the study was to assess the effects of intraoperative intravenous fluids used during ENT surgical proce-
dures in children on the selected parameters of homeostasis: glycaemia and water-electrolyte balance. Additionally, the risk of hypoglycaemia after long-term preoperative fasting (8–16 h) was evaluated.

METHODS

The design of the study was approved by the Ethics Committee, Medical University of Warsaw. Having obtained parental informed consent, the prospective, open-label, randomized study was carried out on children scheduled for elective ENT surgery. The following inclusion criteria were used: children > 1 year of age, ASA I or II, scheduled for elective ENT surgery. The exclusion criteria were diseases and/or drugs that can affect carbohydrate and water-electrolyte metabolism and lack of the parents’ consent. Children were randomly assigned (computer randomisation) to one of the three groups to receive: group GSW — 5% glucose in water solution, group GNaCL — 5% glucose in water solution with 0.9% NaCl, the volume ratio: 2:1, and group RA — Ringer’s acetate (Baxter Terpol). The volume of fluids infused was identical in all groups, i.e. the first hour of anaesthesia — 25 mL kg\(^{-1}\) in children < 4 years of age and 15 mL kg\(^{-1}\) in older children. In longer procedures, 6 mL kg\(^{-1}\) h\(^{-1}\) of the selected fluid was infused during the subsequent hours. The duration of preoperative fasting was 8–16 hours; there were no intergroup differences. Children did not receive i.v. fluids before surgery and were not premedicated; a parent was allowed to be present at anaesthesia induction. Concentrations of glucose, sodium, potassium and phosphates were determined in all patients. Serum osmolality was analysed using the cryoscopic method. The first blood sample was collected before the induction of anaesthesia and the randomly selected fluid was administered. The second sample was collected before recovery from anaesthesia. Depending on the individual indications, concentrations of glucose and electrolytes were re-determined after 1–2 hours. Fasting glucose levels > 120 mg dL\(^{-1}\) and concentrations > 200 mg dL\(^{-1}\) after fluid infusion were considered significant hyperglycaemia. Normal hospital concentrations > 200 mg dL\(^{-1}\) were considered normal.

Serum glucose concentrations before anaesthesia and fluid infusion were re-determined after 1–2 hours. Fasting glucose levels > 120 mg dL\(^{-1}\) and concentrations > 200 mg dL\(^{-1}\) after fluid infusion were considered significant hyperglycaemia. Normal hospital laboratory values were considered the reference values for sodium, potassium, phosphorus and osmolality, i.e. Na 135–145 mmol L\(^{-1}\), K 3.5–5.5 mmol L\(^{-1}\); the reference values for phosphate concentrations differ according to age and gender. In the case of serum osmolality, the values of 275–295 mOsm kg\(^{-1}\) were considered normal.

Children were anaesthetised in a standardised manner. Anaesthesia was induced intravenously with 3 mg kg\(^{-1}\) of propofol and 30 µg kg\(^{-1}\) of alfentanil for adenotonsillotomy or 5 µg kg\(^{-1}\) of fentanyl for nasal septum surgery. Muscle relaxation was provided with 0.1 mg kg\(^{-1}\) vecuronium, and an endotracheal intubation was performed. Anaesthesia was maintained with a mixture of \(\text{N}_2\text{O}\) and \(\text{O}_2\), at the ratio of 65%:35%. In cases where elevated arterial pressure and/or a heart rate above 15% of the baseline value were observed, an additional opioid dose was administered, 10 µg kg\(^{-1}\) of alfentanil or 1 µg kg\(^{-1}\) of fentanyl and 1 mg kg\(^{-1}\) of propofol, respectively.

Statistical analysis was carried out using STATISTICA 5.0 (StatSoft, Tulsa, USA). The conformity of distributions of quantitative variables with a normal distribution was checked applying the Kolmogorow-Smirnow and Shapiro-Wilk W tests, and with a log-normal distribution using the Kolmogorow-Smirnow test and χ\(^2\). Variables of the normal distribution were described with a mean and standard deviation (SD), those of a log-normal distribution with a geometric mean and range, while variables of a different distribution were described with the median and range. The normal distribution variables were compared using an analysis of variance after checking the homogeneity of variance (Levene’s test). The remaining (of non-normal distribution) variables and those of normal distribution but non-homogenous variances were compared using the Kruskall-Wallis ANOVA. The variables in the study groups before and after surgery were compared using the sign test. Intervariable correlations were tested using the Spearman rank test. \(P < 0.05\) was considered as statistically significant.

RESULTS

Ninety-one children aged 2–12 years, 60 boys and 31 girls, were initially enrolled to the study. The study groups were not significantly different in terms of age, body weight or gender distribution (Table 1). One child was excluded from group GNaCl due to bleeding, requiring the change in fluid regimen; the data of 90 patients were ultimately analysed.

The glucose concentrations before anaesthesia and fluid infusion did not show statistically significant intergroup differences (\(P = 0.355\)). Although a statistically significant increase in glucose concentration was observed postoperatively in all of the groups (Table 2), glucose concentrations between groups were significantly different (\(P < 0.0001\)) (Fig. 1). The highest concentration was found in group GSW whereas the lowest was in group RA. Significant hyperglyc-
caemia occurred only in groups G5W and GNaCl. In group G5W receiving the solution of 5% glucose, concentrations of glucose > 200 mg dL\(^{-1}\) were observed in 31 of 33 (93.93%) cases. In group GNaCl there were 10 (36%) cases of significant hyperglycaemia > 200 mg dL\(^{-1}\). The distribution of glycaemia in groups after surgery is illustrated in Fig. 2.

Detailed data regarding glucose concentrations before and after surgery are shown in Table 2.

The glucose concentrations after surgery were significantly different between groups G5W and RA, GNaCl and RA, as well as GSW and GNaCl (\(P < 0.0001\)) (Fig. 2). The concentration of glucose one hour after the completion of surgery tended to normalise in the majority of patients.

Before anaesthesia, there were no intergroup differences in sodium concentrations (\(P = 0.277\)). Mild hypernatraemia was found in 11 (12.2%) children. Immediately after surgery, serum sodium concentrations decreased significantly in all of the groups (Table 3). The highest differences were noted in group G5W (\(P < 0.0001\) as compared to the preoperative value) and in group GNaCl (\(P < 0.0001\) as compared to the preoperative value). A statistically significant decrease in sodium concentration was also found in group RA (\(P = 0.021\)). The highest incidence of hyponatraemia, i.e. in 12 of 33 children (36.3%), was observed in group GSW while there were no cases of hyponatraemia in group RA. The distribution of postoperative sodium concentrations in the study groups is presented in Fig. 3.

Significant intergroup differences in serum sodium concentrations after surgery were noted (Fig. 4). Although the comparison of postoperative sodium concentrations between the groups GSW versus RA and GNaCl versus RA,
revealed statistically significant differences (in both cases P < 0.0001), no significant differences were observed between groups G5W and GNaCl.

There were no clinically significant changes in potassium and phosphate concentrations in children before and after surgery. The results of phosphate concentrations are listed in Table 4.

There were no intergroup differences in preoperative serum osmolality (P = 0.737). After surgery, osmolality decreased significantly in groups GSW (P = 0.043) and GNaCl (P < 0.001). In group RA, osmolality did not change significantly compared to baselines values (P = 0.263) and was normal in all children. However, osmolality below normal values was observed in group GSW and GNaCl. No significant intergroup differences in postoperative serum osmolality were demonstrated after surgery (P = 0.323). The results are presented in Table 5.

**DISCUSSION**

The study was carried out in order to determine whether the type of fluid infused during minor surgery under general anaesthesia could affect water-electrolyte balance and glycaemia, hence the safety of anaesthetized children. Although intraoperative fluid therapy in healthy children during non-extensive surgical procedures of short duration can seem a minor problem, the present study’s findings and literature data [1, 10−12] contradict this statement. It is noteworthy that such surgical procedures are sometimes performed in hospitals for adults or on an outpatient basis. Under such conditions, the diagnosis and treatment of glucose and electrolyte imbalance can be delayed and lead to irreversible consequences.

In the study, some patients developed hypotoniaemia due to the administration of effectively hypotonic fluids, i.e. with a sodium concentration substantially lower than that in plasma (groups GSW and GNaCl). Indeed, the above-mentioned relationship has been earlier observed by other authors. In a retrospective study carried out by Arieff et al. [1] and involving 24,412 children undergoing surgery, significant hypotoniaemia (Na < 128 mmol L\textsuperscript{−1}) was observed in 0.34% of patients, 9% of them (7) died. In the same study, the authors described 16 children aged 1.5 to 15 years, with perioperative symptomatic hypotoniaemia caused by the administration of hypotonic fluids, which resulted in permanent CNS damage or death. Ten of these 16 children underwent post-mortem examinations. Brain oedema with subtentorial herniation was found in 9 of the 10 patients. Of the 16 children in question, 5 had undergone a tonsillectomy, 4 had had fracture reductions; while the remainder include appendectomy, orchidopexy, posterior tamponade due to nosebleed and implantation of the ventricular-peritoneal valve, thus typical non-extensive procedures. Recent studies have confirmed that this problem is still occurring [7, 13]. The important contributing factor favouring the development of electrolyte imbalance is a hormonal stress response, first and foremost, an increase in antidiuretic hormone release. In consequence, the access of water cannot be excreted. In such circumstances the infusion of hypotonic fluids leads to the development of acute hypotoniaemia and decreased plasma osmolality which causes the shifting of water into the cell and results in brain oedema [11, 14].

The most common disorder observed in the present study was hyperglycaemia. Relatively high thresholds for significant hyperglycaemia were assumed; at more restrictive values, hyperglycaemia would be recognised in a higher percentage of patients. It has not been fully elucidated whether
short-term hyperglycaemia in a healthy child can lead to adverse outcomes. For methodological and ethical reasons, studies that could confirm or exclude the above relationship are difficult to perform. Recent studies, however, concerning children undergoing cardiac surgery, do not seem to confirm the relationship between hyperglycaemia and the occurrence of complications adverse outcome [15−17].

In contrast, the relationship between hyperglycaemia and poor neurologic outcomes has been observed in children after brain trauma injury [18]. Unfortunately, the setting up a prospective study protocol that could prove such a relationship would encounter many difficulties. The negative impact on neurologic outcomes of even short episodes of hyperglycaemia in association with hypoxia has been demonstrated in animal studies [19, 20]. In cases of hypoxia, glucose undergoes an anaerobic metabolism that results in an increase in lactate concentrations, a decrease in intracellular pH and mitochondrial dysfunction. This may cause cell damage or even cell death. More details on the perioperative use of glucose solutions are included in the author’s review [21].

In the study population of 91 despite an extremely long preoperative fast, only one case of asymptomatic hypoglycaemia was observed before the induction of anaesthesia (46 mg dL⁻¹), inconsistent with the current recommendations. The above findings are in accordance with the studies carried out in the last two decades by other authors, who estimated the risk of hypoglycaemia at 0−1% [22]. At present, this problem can be considered marginal due to shortened preoperative fasting- unlimited clear fluids are allowed up to 2 hours before anaesthesia [5].

The study confirms data coming from case reports and observational studies that the intraoperative use of hypotonic fluids can induce hyperglycaemia and hyponatraemia, thus presenting a risk to patients’ safety and should be avoided. Isotonic fluids with low glucose concentration (1−2% maximum) should become commercially available also in Poland, even though the present study findings, multicentre worldwide clinical practice, as well as (least importantly) the author’s personal experience, demonstrate safety of the intraoperative use of glucose-free fluids in children. No literature reports describing complications resulting from hypoglycaemia induced by intraoperative glucose-free fluids in children without risk factors for hypoglycaemia have been found.

CONCLUSIONS

1. The composition of intraoperative fluid is important for maintaining normal concentrations of glucose, sodium and serum osmolality.

2. All the patients who had Ringer’s acetate as an intraoperative infusion maintained glucose and electrolyte concentrations, as well as osmolality within safe limits. This type of fluid can be recommended as an intraoperative fluid of choice for surgical procedures in children.

3. As infusions of effectively hypotonic solutions can cause significant hyperglycaemia and sometimes hyponatraemia, they should not be used intraoperatively in children.

4. Hyponatraemia was the most commonly found water-electrolyte imbalance. It was observed only in children who had had infusions of hypotonic solutions containing glucose, predominantly, a 5% glucose solution in water.

5. The risk of hypoglycaemia during preoperative fasting and surgery in healthy children without risk factors for hypoglycaemia seems to be very low.

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