

# Comparison of capillary blood glucose level at 1 h after induction of general anesthesia in children receiving intraoperatively either Ringer's lactate with glucose 1% or Ringer's lactate alone



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Submission: 23-01-2022

Revision: 29-05-2022

Publication: 01-07-2022

## ABSTRACT

**Background:** Perioperative fluid therapy in children is quite challenging job for anesthesiologists. Variable glycemic control has been reported in the literature regarding the use of balanced electrolyte solution with or without 1–2% glucose supplementation.

**Aims and Objectives:** Hence, this study was planned to determine the capillary blood glucose level (CBG) in the intraoperative period at 1 h after induction of general anesthesia in children (1–6 years of age) receiving either Ringer's lactate (RL) with glucose 1% or RL alone. **Materials and Methods:** A total of 60 patients of either gender, aged 1–6 years, of American Society of Anesthesiologists Physical Status Classes 1 and 2 were included for this interventional study. All children received protocolized general anesthesia with strict adherence to standard fasting guidelines. The children received either RL alone (Group A, n=30) or RL plus 1% glucose solution (Group B, n=30) as intraoperative fluid. The pre-operative CBG was recorded. Intraoperative fluid was given at 10 mL/kg/hr. The CBG was checked again at 30 min and 1 h after induction of anesthesia. The glycemic status at 1 h in the intraoperative period was compared (primary outcome) between the two groups.

**Results:** The hemodynamics and intraoperative consumption of fluid were comparable between the groups. The mean CBG values at 30 min and at 1<sup>st</sup> h were considerably higher in groups receiving RL with 1% glucose compared with those receiving RL alone. However, these differences were not clinically significant. No adverse event was observed. **Conclusion:** RL alone or RL plus glucose 1% can be used as intraoperative fluid in children (1–6 years of age). None developed clinically significant hypoglycemia or hyperglycemia. However, the optimal amount of glucose which can be safely used in the perioperative period needs to be determined with a larger trial.

**Key words:** Hyperglycemia; Hypoglycemia; Intravenous fluid; Pediatric; Perioperative

### Access this article online

**Website:**

<http://nepjol.info/index.php/AJMS>

**DOI:** 10.3126/ajms.v13i7.42569

**E-ISSN:** 2091-0576

**P-ISSN:** 2467-9100

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## INTRODUCTION

Perioperative fluid management in pediatric patients is a challenging job for the anesthesiologists due to the unique physiology and the need for delicate balancing of IV fluid administration in respect of tonicity, glucose content, and

the total volume in this population. They are prone not only to hypovolemia or hypervolemia but also to either hypoglycemia or hyperglycemia.<sup>1,2</sup> Inappropriate fluid therapy in respect with sodium and glucose concentration can lead to serious morbidity and mortality during the perioperative period even in previously healthy pediatric

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patients.<sup>3-6</sup> For intraoperative IV fluid administration in neonates and infants, isotonic fluid with low concentration (1–2%) glucose is recommended by different statutory bodies worldwide.<sup>6,7</sup> The current literature favors the use of balanced solutions with 1–2.5% glucose to start with and then adjust the infusion according to clinical parameters.<sup>8,9</sup> However, non-adherence to international guidelines, either due to unawareness or ignorance on the part of medical professionals, can play a major role in this aspect. In spite of repeated reporting about post-operative hyponatremia with the use of hypotonic solution and warning issued in this respect since last four decades, a current survey (in 2018) reveals that 0.18% NaCl plus 4–5% glucose is still being used intraoperatively in infants and children.<sup>1</sup>

Similar to adults, isotonic fluid has become the intraoperative fluid of choice for infants and children. Variable glycemic status in the intraoperative period has been reported with the use of Ringer's lactate (RL) enriched with 1%, 2% or 4% dextrose in neonates.<sup>10</sup> This study, however, indicates that normal glycemic control in the intraoperative period is possible even in neonates with the intraoperative use of isotonic solution with low glucose as well as with the use of isotonic solution (RL) alone.<sup>10</sup> Another study indicates that RL alone in the intraoperative period is sufficient to maintain euglycemia in infant and children.<sup>11</sup> It has been observed that routine glucose supplementation is not essential in maintaining intraoperative euglycemia in infant<sup>11</sup> and children.<sup>12</sup> Although guidelines recommend for brief fasting, it is not feasible always due to the busy OT schedule. Naturally, there is a concern for hypoglycemia in the intraoperative period due to the effect of extended pre-operative fasting and variable waiting period. Thus, a conflict or dilemma often plays in the mind of practicing anesthesiologists about whether to rely solely on RL or to enrich RL with low concentration of glucose (1–2%) to maintain euglycemia in the intraoperative period in small children.

In the recent past, the intraoperative use of an isotonic balanced electrolyte solution with 1% glucose (BS-G1) at a mean infusion rate of 10 ml/kg/h had been found to be safe in surgical neonates<sup>13</sup> and in children.<sup>14</sup> The use of such solution in the intraoperative period was found to be beneficial not only in preventing hyponatremia and hypoglycemia but also not producing hyperglycemia. However, there is paucity of studies evaluating RL with low concentration of glucose and RL alone in small children population between 1 year and 6 years of age. Hence, a conflict still exists regarding the fact whether RL alone is sufficient to maintain intraoperative euglycemia or to enrich it with low glucose (1–2%) supplementation. The evidence is still growing in this aspect.

## Aims and objectives

To address the afore-mentioned gap in the literature, the present study was carried out to determine the capillary blood glucose level (CBG) in the intraoperative period at 1 h after induction of general anesthesia in children (1–6 years of age) receiving either RL with glucose 1% or RL alone. The CBG measured at such time point was compared to find out any considerable difference between the two groups. This was the primary outcome of the present study. The incidents of intraoperative adverse events, if any, were also observed. It was hypothesized (alternative hypothesis) that there would be a considerable difference in the CBG in the intraoperative period at 1 h after induction of general anesthesia between the children receiving RL and RL plus 1% glucose.

## MATERIALS AND METHODS

After obtaining permission from the Institute's Ethics Committee (No./NMC/802, Dated February 14, 2020), this interventional study was performed on pediatric patients (1–6 years of age) undergoing elective non-cardiac and non-thoracic surgeries of more than 1 h of duration in the pediatric surgery operating room. Children undergoing surgeries such as posterior sagittal anorectoplasty, anterior sagittal anorectoplasty, urethroplasty, and colostomy closure were included for this study. Informed and written consent was obtained from the parents of the selected patients in their own language. They were given the option to opt out from the study at any time. Children requiring regional anesthesia in addition to general anesthesia or having diabetes mellitus or anticipated to require intraoperative blood-product transfusion or inotrope infusion were excluded from the study.

### Sample size calculation

On review of the previous literature, it was observed that there is about 27 mg/dl of difference in the mean value of glucose level in the intraoperative period at 1 h between the groups receiving RL enriched with 1% glucose solution and RL alone.<sup>11</sup> Furthermore, in another study, the median (inter quartile range) value of the glucose level was found to be approximately 110 (21) and 98 (21) between the RL plus 1% glucose group and RL alone group, respectively.<sup>12</sup> On the basis of above evidence, it was assumed for the present study that at least a 15 mg/dl increase in the level of glucose would be achieved intraoperatively at 1 h using RL enriched with 1% glucose solution in comparison with RL alone. This was considered as the "effect size" or the Minimal Clinically Important Difference<sup>15</sup> or the smallest difference which would be tested in this study. Setting the confidence interval at 95% ( $\alpha=0.05$ ) and power ( $1-\beta$ ) of

the study at 80%, a sample size for each group was obtained to be 27. Expecting a dropout rate of 10%, a final sample size of 30 for each group was arrived. Hence, a total of 60 patients were recruited.

For this study, a total of 60 patients of either gender, aged 1–6 years, of American Society of Anesthesiologists Physical Status Classes 1 and 2, were selected based on the inclusion and exclusion criteria. The children were evaluated preoperatively and those who have adhered to standard fasting guidelines (i.e., 6 h for light meal and non-human milk, 6 h for infant formula milk, 4 h for breast milk, and 2 h for clear non-glucose containing liquids) were enrolled.<sup>16</sup> In the operating room, an intravenous (i.v.) line was established with a 22-G or 24-G cannula. The children were anesthetized and intubated according to institutional protocol for general anesthesia. For intubation, cuffed endotracheal tube (Microcuff, HALYARD, M/s Halyard Health India private limited, Maharashtra, India) of appropriate size was used.

The group allocation was performed before induction of anesthesia and intubation. This procedure for group allocation was performed for every child by opening one sealed opaque envelope that is kept as sequentially numbered. There were 60 sealed envelopes each containing one piece of paper marked either “A” or “B” (30 papers marked as “A” and another 30 papers marked as “B”). All the sealed envelopes were placed in a container after shuffling. To perform group allocation for each patient, one envelope was picked up and opened. The alphabet displayed (“A” or “B”) corresponds to the group allocation of the child. This envelope was then discarded. Thus, the allocated groups were as follows: Group A (n=30), patients receiving RL as intraoperative fluid, and Group B (n=30), patients receiving RL plus 1% glucose solution as intraoperative fluid. The glycemic status at 1 h in the intraoperative period was compared between the two groups.

A pre-operative CBG was recorded. The children received the allotted fluid intraoperatively at 10 mL/kg/h. For preparing RL with 1% dextrose, at first 20 mL of RL was withdrawn with aseptic precaution and then 20 mL of 25% dextrose was added.<sup>17</sup> In case of hypotension (fall in mean arterial pressure [MAP] by more than 20% of baseline)<sup>10</sup>, rescue fluid was administered as boluses of 1 mL/kg of RL only, as per the hemodynamic response. Hypoglycemia is defined as blood sugar <70 mg/dL and hyperglycemia as blood sugar >150 mg/dL.<sup>18,19</sup> In case of hypoglycemia, it was supposed to be treated with bolus of 25% dextrose at a dose of 1 mL/kg, double diluted with saline.<sup>11</sup> Blood sugar level was checked twice, one at 30 min and another at 1 h after induction of anesthesia. Intraoperative electrocardiogram, peripheral arterial oxygen saturation

(SpO<sub>2</sub>), MAP, heart rate (HR), and end-tidal CO<sub>2</sub> (EtCO<sub>2</sub>) were monitored and noted at 30 min interval. The CBG at 1 h after induction of general anesthesia was compared between the two groups. In the post-operative period, patients were maintained on standard post-operative maintenance fluid in accordance with pediatric surgical ICU protocol.

### Statistical methods

The data were decoded and tabulated using Microsoft Excel. It was then processed and analyzed with suitable statistical software with the help of a biostatistician. For statistical analysis, data were entered into a Microsoft Excel 2016 spreadsheet and then analyzed by SPSS version 22. (SPSS Inc., Chicago, IL, USA). Continuous data are expressed as mean±standard deviation (SD) and was analyzed with Student’s t-test. The categorical data are expressed as number of patients (Proportion) and have been analyzed using Pearson’s Chi-square test with Fischer’s exact test, as appropriate. P≤0.05 was considered for statistically significant.

## RESULTS

The study was conducted over around 1 year, from March 2020 to August 2021. Data from all 60 patients were available for analysis. The patients of both groups were comparable in respect with the demographic characteristics (Table 1).

The mean values of CBG at baseline were comparable between the two groups. However, the mean values of CBG values at 30 min and at 1 h time points were considerably higher in groups receiving RL with 1% glucose compared with those receiving RL alone. In the present study, the mean CBG at 1 h of intraoperative period in the Group B receiving RL with 1% glucose was considerably higher than those Group A receiving RL alone (approximated mean values being 139 and 118, respectively). The difference of mean CBG in both the groups was noted to be 14 mg/dl and 21 mg/dl at 30 min and 1 h intraoperative period, respectively (Table 2 and Figure 1). However, these differences were not clinically significant as none in the Group A developed hypoglycemia

**Table 1: Demographic data**

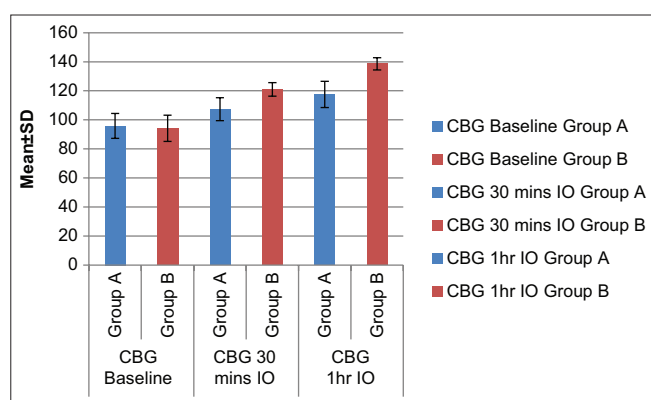
Parameters	Group A	Group B	P-value
Age (months)	34.90±18.37	44.77±16.83	0.034
Sex (M: F)	19:11	22:8	0.405
Weight (Kg)	13.3±3.4	12.1±4.7	0.251
ASA-PS (I/II)	30:0	30:0	-

Data are presented as mean±SD for continuous variables (age and weight) and analyzed with students’ “t” test. Categorical data (sex, ASA) is presented as number of patients (proportion) and analysis of these categorical data is done using Chi-square test, ASA-PS: American Society of Anesthesiologists-Physical Status

**Table 2: The mean CBG at baseline, at 30 min and at 1 h time points**

Parameters	Group A	Group B	P-value
CBG baseline			
Mean±SD	95.9±8.5	94.2±9	0.456
Min-Max (median)	80–110 (96.5)	82–110 (94)	
CBG at 30 min			
Mean±SD	107.3±7.9	121±4.7	<0.0001
Min-Max (median)	92–122 (110)	114–131 (120.5)	
CBG at 1 h			
Mean±SD	117.5±8.9	138.6±4.2	<0.0001
Min-Max (median)	102–132 (118)	130–146 (138)	

Continuous data are presented as mean±SD and analyzed with Students' "t" test



**Figure 1:** The mean capillary blood glucose level at baseline, at 30 min and at 1 h time points

and none in the Group B developed hyperglycemia as per study protocol.

On analysis, the differences of HR between the groups were found significant at baseline, at 30 min and at 1 h (Table 3). The mean MAP was considerably low in Group B at baseline. However, MAP was found comparable at 30 min and 1 h time points (Table 3). Although the HR and MAP were significant at certain points on statistical analysis, the values observed were not significant clinically. The total amount of intraoperative infused fluids was comparable between the two groups. The EtCO<sub>2</sub> was comparable between the groups at all-time points (Table 3). No adverse event was noted in any of the groups.

## DISCUSSION

In the present study, the difference between the mean of CBG in both the groups is found to be statistically significant at 1 h time point. In addition, the difference of mean CBG is also found to be statistically significant at 30 min time point as well. The difference of mean value was noted 14 mg and 21 mg at 30 min and 1 h, respectively.

**Table 3: Hemodynamic parameters and infused fluid**

Parameters	Group A (n=30)	Group B (n=30)	P-value
Heart rate (HR)			
HR_baseline	116.8±4.6	114.4±3.2	0.024
HR_at 30 min	105.5±5.2	102.4±3.8	0.012
HR_at 1 h	96.1±6.5	91.4±4.4	0.002
Mean arterial pressure (MAP)			
MAP_Baseline	70.4±4.6	66.9±3.4	0.001
MAP_at 30 min	69.9±2.6	69.4±2.3	0.469
MAP_at 1 h	69.1±2	69.5±2.1	0.379
EtCO <sub>2</sub>			
EtCO <sub>2</sub> at baseline	39.5±2.8	38.8±2.7	0.330
EtCO <sub>2</sub> at 30 min	39.5±2.8	39.7±3.2	0.767
EtCO <sub>2</sub> at 1 h	38.5±2.7	39.5±2.9	0.173
Total fluid consumed			
Infused IV fluids (ml)	173.1±50.0	186.2±29.1	0.220

Continuous data are presented as mean±SD and analyzed with Students' "t" test

These differences (14 mg and 21 mg) were not considered clinically significant because the mean values in the group receiving supplemental glucose had not reached to the dangerously high level of blood glucose (hyperglycemia). Again, the mean CBG values in the group not receiving supplemental glucose (Group A) also had not suffered from dangerously low level of blood glucose (hypoglycemia). Rise in blood glucose in the group receiving only RL was explained by metabolic and endocrine response to surgical stress resulting in an increase in counterregulatory hormones. However, the effect of increase in surgical stress and the depletion of stored glucose may become evident in prolonged duration of surgery. Moreover, those surgeries where prolonged NPM status is needed in the postoperative period, the observation of CBG level in postoperative period may reveal any different value in those receiving supplemental glucose in comparison with those not receiving supplemental glucose.

There had been a lingering fear among anesthesiologists that hypoglycemia might go unrecognized in infants and young children under anesthesia. This concern has stemmed the practice of infusion of 5% glucose-containing solutions in the intraoperative period in pediatric patients.<sup>20,21</sup> Young et al.,<sup>22</sup> reported the incidence of hypoglycemia in 33 (6%) patients with pre-operative fasting of 9.9±4.8 h. In a recent study<sup>23</sup> involving 258 pediatric patients (aged <14 years), scheduled for elective procedures with overnight fasting, 62 (26.2%) patients suffered hypoglycemia (blood glucose level <54mg/dl) after induction of anesthesia. The authors in that study<sup>23</sup> concluded that prolonged pre-operative fasting cannot affect in terms of hypoglycemia during the operation, although it has impact on systolic blood pressure. Hypoglycemia, hypotension, and discomfort in children can be avoided by following standard fasting

guidelines and allowing glucose-containing clear fluids till 2 h preoperatively. With poor human resource and with a long list of surgery, it is rather impractical to follow the fasting guidelines accurately and stringently. In reality, the true incidence of fasting hypoglycemia might be more common than this study reports. It should be noted that fasting hypoglycemia was not determined in this study.

The concept of adding glucose to the maintenance fluids stems from providing approximately 20% of the normal caloric needs to avoid starvation ketoacidosis and protein degradation.<sup>24</sup> Moreover, it limits the post-operative energy deficit and can avoid perioperative hypoglycemia. Various concentrations of glucose as supplementation to IV fluids had been studied in the previous decades. RL with 1% glucose had been shown to avoid perioperative hypoglycemic events while imparting only moderate degree of post-operative hyperglycemia.<sup>25,26</sup>

Larsson et al.,<sup>20</sup> compared the effect of using Ringer's acetate with 10% glucose and Ringer acetate alone in 30 neonates undergoing major surgery. In that study, they used the fluid infusion rate of 15–20 mL/kg during 1 h followed by 10 mL/kg/h in both groups so as to provide glucose at the rate of 0.25–0.30 g/kg/h. They observed rise in blood sugar in both the groups during surgery, more so in the glucose supplemented group. Hypoglycemia was noticed in a few neonates only in those receiving Ringer acetate alone. Sandstorm et al.,<sup>21</sup> studied the effect of using Ringer's acetate with 10% glucose and Ringer's acetate alone in 14 neonates. They observed a rise in blood sugar in both the groups. It may be due to the fact that the starved neonates without intraoperative supply of glucose maintain blood glucose concentration with mobilized fat.<sup>19,21</sup>

Studies have shown that use of RL alone during the perioperative period did not result in hypoglycemia.<sup>27,28</sup> At the same time, it was also shown that addition of 2% dextrose to RL, although resulted in an increase in intraoperative blood glucose level, did not increase it beyond the normoglycemic limits. Sümpelmann et al.,<sup>13</sup> observed that balanced electrolyte solution with 1% glucose (BS-G1) as intraoperative fluid can maintain normoglycemia in neonate. However, in another study<sup>14</sup> carried out in infants and older children, it was observed that the same fluid (BS-G1) led to hyperglycemia in the intraoperative period, but returned to normal levels in the post-operative period. In this study, it was found that blood glucose level was increased with the use of 1% glucose, but none developed hyperglycemia. Blood glucose level has also increased in those receiving no glucose supplementation. The rise of intraoperative glucose was lesser in those receiving no supplementation of glucose than in those receiving supplementation with 1% glucose.

The safety of intraoperative administration of 0–2.5% glucose in isotonic solution has been confirmed for use in healthy infants.<sup>29</sup> In that study,<sup>29</sup> the authors emphasized that smaller infants (<1 years or <10 kg) and those with significant comorbidities are at particular risk of developing hypoglycemia, despite pre-operative and intraoperative glucose administration. It is essential to check glucose levels at frequent intervals in patients at risk of hypoglycemia.<sup>30,31</sup>

The infusion of isotonic solutions with 1–2.5% dextrose perioperatively in children is now well established. In 2010, the European Society for Pediatric Anesthesiology<sup>7</sup> recommended that an intraoperative fluid should have an osmolarity close to the physiological range to avoid hyponatremia and an addition of 1–2.5% instead of 5% dextrose be administered to avoid hypoglycemia, lipolysis, or hyperglycemia and that it should include metabolic anions (acetate, lactate, or malate) as bicarbonate precursors to prevent hyperchloremic acidosis.

#### Limitations of the study

It was planned to include the surgeries of more than 1 h of duration. Moreover, in reality, the duration of surgery was such that only two observations were possible – at 30 min and at 1 h time points. The inclusion of more extensive surgeries lasting for more than 2 or more h, and thereby further checking the CBG level at time points of 2 h and 3 h, might reveal clinically significant differences. Age-related sub-group analysis of data was not possible due to smaller sample size. Intraoperative arterial blood gas (ABG) monitoring was not feasible due to logistic issues. ABG could be beneficial in better analyzing the result regarding the utilization of glucose from glucogenic substances during surgical and anesthetic stress in those not receiving glucose supplementation.

## CONCLUSION

It can be concluded that RL alone or RL plus glucose 1% can be used as intraoperative fluid in children (1–6 years of age). None developed clinically significant hypoglycemia or hyperglycemia. It is safe to add small amount of glucose (1%) in the intraoperative fluid to prevent any hypoglycemic event in the intraoperative period when patients are under general anesthesia. However, the exact amount of dextrose needed in the perioperative period depends on individual surgical needs. With the use of dextrose containing solutions, definite benefit in terms of improvement surgical outcomes is still to be proven and warrant larger trials.

## ACKNOWLEDGMENT

We wish to thank Dr. Moushumi Khanra, Tutor, Department of Anesthesiology, Nil Ratan Sircar

Medical College, Kolkata, for her selfless help during this study.

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**Authors Contribution:**

**SS-** Participated in study design, conduct of study, data collection, and writing of first draft; **SM-** Helped in study design, interpretation of result, review of literature, and revision of first draft; **JC-** Helped in study design, guidance and conduct, review of literature, and revision of first draft; and **MM-** Concept and design of study, guidance and conduct, data analysis, logical conclusion, and revision of first draft.

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**Source of Support:** Nil, **Conflict of Interest:** None declared.