Original Article

Factors affecting blood glucose and serum sodium level with intraoperative infusion of 1% dextrose in ringer's lactate in neonates undergoing surgery

ABSTRACT

Context: Under anesthesia, blood glucose level in term neonates varies widely due to stress induced glucose mobilisation due to various factors. Postoperative hyponatremia occurs with intraoperative infusion of large volume of hypotonic fluid. There is a growing consensus on the intraoperative use of 1–4% glucose containing isotonic fluid in them.

Aims: To know the relation of duration of surgery, infusion rate, fluid bolus, blood transfusion with blood glucose level and effect on serum sodium level with intraoperative 1% dextrose ringer's lactate (1% DRL) in neonates undergoing surgery.

Settings and Design: Prospective single-center study in tertiary institute.

Subjects and Methods: A total of 100 neonates undergoing various surgeries under general anesthesia with or without caudal anaesthesia were included. 1% DRL was used as maintenance and replacement fluid intraoperatively. Blood glucose level at hourly interval throughout surgery and serum sodium concentration before and after infusion was documented.

Statistical Analysis Used: Student's *t* test (two tailed, independent) has been used for statistical analysis.

Results: After the infusion of 1% DRL during surgery, mean blood sugar levels were increased above the base line in all neonates at successive hourly interval. Serum sodium levels remained within physiological range in all neonates.

Conclusion: Intraoperative hyperglycemia is more obvious with higher intravenous fluid infusion rate, prolonged duration of surgery, and requirement of fluid bolus as well as blood transfusion intraoperatively. Use of 1% DRL in neonates undergoing surgery is effective in preventing dysnatremia.

Key words: Blood glucose level; duration of procedure; fluid bolus blood transfusion; infusion rate; intraoperative 1% dextrose ringer's lactate; neonates; serum sodium concentration

Introduction

Neonate requires 4–8 mg/kg/min of glucose for brain development.[1,2] Various intraoperative factors like infusion rate, procedure duration, fluid bolus, and blood transfusion has influence on blood glucose level. Postoperative hyponatremia occurs with large volume of hypotonic fluids infused intraoperatively and lead to adverse neurological manifestations.[3] Use of balanced isotonic electrolyte solutions with 1–2.5% glucose is recommended to avoid electrolyte imbalance and deranged glucose concentration intraoperatively.[4]

Access this article online	
Website: www.saudija.org	Quick Response Code
DOI: 10.4103/sja.SJA_784_18	

How to cite this article: Tandale SR, Kelkar KV, Khedkar SM, Desale JR. Factors affecting blood glucose and serum sodium level with intraoperative infusion of 1% dextrose in ringer's lactate in neonates undergoing surgery. Saudi J Anaesth 2019;13:197-202.

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Present study is conducted to know the relation of duration of surgery, infusion rate, fluid bolus, blood transfusion with blood glucose level, and effect on serum sodium level with intraoperative 1% dextrose ringer's lactate (1% DRL) in neonates undergoing surgery.

Subjects and Methods

This observational study was conducted after approval from Hospital Ethics Committee, Departmental permission and informed parental consent from August 2016 to January 2018. The study was registered in the clinical trial registry of India (CTRI/2017/10/010216; www.ctri.in). total of 100 consecutive term neonates undergoing surgeries like tracheoesophageal fistula repair, congenital diaphragmatic hernia repair, laparotomy for intestinal atresia, malrotation and anorectal malformation, ventriculoperitoneal shunt insertion, and meningomyelocoele repair, etc. were included. Neonates with low birth weight (<2 kg), large for gestational age (birth weight greater than 90th percentile for that gestational age), small for gestational age (birth weight lesser than 10th percentile for that gestational age), sepsis, first 2 days of life, blood sugar level of <3.6 mmol/L and >11.1 mmol/L prior to induction of anesthesia and neonates requiring inotropes infusion in preoperative and intraoperative period were excluded from the study.

Antenatal history, neonatal history, and examination were recorded in preoperative visit. Investigations like complete blood count, serum electrolytes, and chest x-ray were noted. All neonates were optimized in preoperative period with respect to hydration, blood glucose, haemoglobin, and electrolyte. They received standard maintenance fluid (Isolyte P-) preoperatively as per neonatal intensive care unit protocol. On the day of surgery, soon after the arrival of neonate inside the operation theatre standard maintenance fluid was disconnected followed by collection of blood sample for measurement of serum electrolytes and blood glucose with the help of bedside glucose analyser.[5] Neonates with blood glucose level more than 3.6 mmol/L were included in the study and 1% DRL was given at the rate of 4 mL/kg/h for maintenance. (Composition of RL - Na^+ 131 mmoles/L, K^+ 5 mmoles/L, Ca^{++} 2 mmoles/L, Cl^-111 mmoles/L, bicarbonate as lactate 29 mmoles/L, calculated osmolarity 278 mosmol/L).1% DRL was prepared by removing 20 cc of ringer lactate solution from a 500 mL bottle of the same (point of entry of intravenous infusion set) and then adding 20 mL of 25% of dextrose in it using sterile syringe and needle and fluid was observed for any precipitate after adding dextrose.

Neonates were monitored by using standard American Society of Anaesthesiologist (ASA) monitors. They were premedicated with intravenous glycopyrrolate 5 mcg/kg, ondansetron 0.1 mg/kg, hydrocortisone 2 mg/kg, and dexamethasone 0.1 mg/kg as per institute protocol. General anesthesia was given with oxygen and gradually increasing concentration of sevoflurane using face mask via Jackson Rees circuit. After loss of consciousness and muscle tone, trachea was intubated with appropriate sized uncuffed endotracheal tube under direct laryngoscopy. Caudal analgesia was given for neonates undergoing laparotomy with bupivacaine 1.5 mg/kg and total volume 1 ml/kg after dilution with normal saline. Intercostal block was given for neonates undergoing thoracotomy with bupivacaine 1.5 mg/kg and total volume 2–3 mL. Paracetamol suppository was inserted per rectal in dose of 7.5 mg/kg and intravenous in dose of 7.5 mg/kg if rectal route was not permissible. Analgesia was given with intravenous fentanyl 1 mcg/kg and incision site infiltration in indicated cases. Anesthesia was maintained with oxygen, nitrous oxide, and isoflurane (nitrous oxide was avoided in neonates with tracheoesophageal fistula and congenital diaphragmatic hernia). Intermittent boluses of atracurium were given for muscle relaxation. 1% DRL was given at the rate of 4 mL/kg/h for nonabdominal–nonthoracic surgeries like ventriculoperitoneal shunt insertion and meningomyelocoele repair, 6 mL/kg/h for thoracotomy, and 10 mL/kg/h for laparotomy for replacement of evaporative loss during surgery. Fluid bolus of 1% DRL in dose of 10 mL/kg was given in event of hypotension (fall in Mean Arterial Pressure (MAP) by more than 30% of baseline). A total of 1 mL of blood loss was replaced with three ml of 1% DRL before exceeding the maximal allowable blood loss. Maximal blood loss was calculated by using following formula [MABL = {EBV * (HO-HI)/HO}] where Estimated Blood Volume (EBV) is estimated blood volume (90 mL/kg for term neonate), HO is starting hemoglobin, and HI is target hemoglobin (13 g for neonates). For any loss beyond Maximal Allowable Blood Loss (MABL) blood transfusion was given. Next blood glucose was monitored at hourly interval during intraoperative period and at the end of surgery (closure of surgical incision) with or without recovery from anaesthesia. Blood sample was also collected for measurement of serum electrolyte at the same time. If blood sugar at any point was recorded below 3.65 mmol/L, neonate would have been given 3 mL/kg of 10% dextrose intravenously followed by continuous infusion with blood sugar monitoring and would be excluded from study. After the end of surgery, neonates were given the standard maintenance fluid (Isolyte P) as per neonatal intensive care unit protocol. They were observed in neonatal intensive care room for first 24 h and any change in sensorium or convulsion was noted. Duration of surgery (from start of surgical incision to incision closure), total duration of procedure (from start of study i.e., first prick for blood sampling to incision closure), total amount of fluid received by neonate during surgery, amount of fluid bolus, amount of blood loss, and replacement of same was also recorded. Neonates were grouped based on total procedure duration (more than 120 min and less than 120 min), infusion rate (more than 10 mL/h and less than 10 mL/h) and requirement of fluid bolus as well as blood transfusion for analysis of result.

Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on mean ± SD (min–max) and results on categorical measurements are presented in number (%). Significance is assessed at 5% level of significance.

Student's t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups (intergroup analysis) on metric parameters. Significant figures are considered as follows, suggestive significance (P value: $0.05 < P < 0.10$), moderately significant (P value: $0.01 < P \leq 0.05$), and strongly significant (P value: $P \leq 0.01$) The statistical software namely SPSS 18.0, and R environment ver. 3.2.2 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc.

Results

We studied 100 neonates (53 female and 47 male) undergoing surgery under general anesthesia alone (72% of neonates) and along with caudal anesthesia (28% of neonates). Demographic data and other variables are given below [Table 1] A total of 42 neonates underwent thoracic surgery, 37 neonates underwent abdominal surgery, and 21 neonates underwent nonthoracic–nonabdominal surgery. We observed a consistent severe hyperglycemia in neonates having bladder dystrophy, cloachal dystrophy, and gastrochiasis preoperatively. Such six neonates were not included in the study in view of poorly optimized blood sugar levels. Average rate of intravenous fluid infusion was <20 mL/kg/h in 58% (58/100) of neonates and >20 mL/kg/h in 42% (42/100) of neonates during study.

Fluid bolus of 1% DRL in dose of 10 mL/kg was infused in 9% (9/100) of neonates. Packed red cells were transfused in 27% (27/100) of neonates.

After the infusion of 1% DRL during surgery, mean blood sugar levels were increased above the base line in all neonates at successive hourly interval. None of the neonates experienced hypoglycemia throughout surgery (blood sugar <3.6 mmol/L).

Comparison of blood sugar levels with respect to duration of procedure was suggestive of statistical significance after second hour of procedure and strongly significant after third hour of procedure [Table 2].

Comparison of blood sugar levels with respect to average infusion rate was suggestive of statistical significance after second hour of procedure [Table 3].

Hyperglycemia was observed in 92.6% and 87.7% of neonates receiving blood transfusion and not receiving blood transfusion, respectively. Statistical analysis revealed significant relationship ($P = 0.001$, Student's t test) for this observation [Table 4].

Table 1: Demographic data

	Min-Max	Mean±SD
Gestational age at birth (weeks)	36.2-40	37.37±0.95
Age (days)	3-28	6.28±5.03
Weight (kg)	2.1-3.8	2.47±0.33
Preoperative hemoglobin (g)	13.2-19.2	15.0±1.05
Estimated blood volume (mL)	189-342	222.62±29.52
Maximal allowable blood loss (mL)	2.80-72.65	28.55±13.62
Blood loss (mL)	10-90	25.85±17.39
Blood received (mL)	0-70	3.93±12.85
Total intravenous fluid received (mL)	27.20-214.90	102.98±35.38
Mean duration of surgery (min)	15-210	93.35±42.97
Mean total duration of procedure (min)	40-260	135.10±45.32

Table 2: Blood sugar levels (mmol/L) in relation to total duration of procedure at successive hourly interval

Blood sugar levels (mmol/L)	Duration of procedure (min)	Number of neonates	Mean±SD	P
First	>120	56	6.1±1.9	0.481
	<120	44	5.9±1.7	
Second	>120	56	9.3±2.2	0.026
	<120	44	8.3±2.2	
Third	>120	56	11.1±2.5	0.002
	<120	39	9.9±1.5	
Fourth	>120	55	11.8±1.9	NA
	<120	0		
Fifth	>120	15	13±1.8	NA
	<120	0		

Table 3: Comparison of blood sugar levels (mmol/L) in relation to average rate of Infusion

Blood sugar (mmol/L)	Average Infusion rate (mL/kg/h)		Total	P
	≤10	>10		
First blood sugar	1.00±0.16	1.08±0.32	6±1.1	0.718
Second blood sugar	1.91±0.05	1.59±0.4	8.9±0.6	0.292
Third blood sugar	2.40±0.62	1.91±0.4	10.7±2.2	0.091+
Fourth blood sugar	2.81±0.00	2.10±0.35	11.9±1.7	0.057+

Hyperglycemia was observed in 100% and 87.9% of neonates receiving fluid bolus and not receiving fluid bolus, respectively. Statistical analysis revealed significant relationship ($P = 0.023$, Student's t test) for this observation [Table 5].

Hyperglycemia was observed in all patients receiving general anesthesia and caudal anesthesia (GA + C) and general anesthesia alone (GA). Blood sugar levels were not influenced by caudal anesthesia and statistical analysis was not significant for above association [Table 6].

Serum sodium levels remained within physiological range in all neonates. None of the neonates experienced hyponatremia or hypernatremia. Mean preoperative and postoperative serum sodium concentration (mmol/L) were 139.52 ± 3.72 (min–max = 132.00–149.00) and 138.97 ± 4.07 (min–max = 131.00–149.00), respectively. None of the neonates had change in sensorium and convulsion for first 24 h postoperatively consistent with change in serum sodium levels.

Table 4: Blood sugar level (mmol/L) in neonates receiving blood transfusion and not receiving blood transfusion

Maximum blood sugar (mmol/L)	Blood received		Total
	No	Yes	
<8.3	9 (12.3%)	2 (7.4%)	11 (11%)
≥l8.3	64 (87.7%)	25 (92.6%)	89 (89%)
Total	73 (100%)	27 (100%)	100 (100%)
Mean±SD	195.05±39.18	228.37±55.45	204.05±46.31

Table 5: Blood sugar level (mmol/L) in neonates receiving fluid bolus and not receiving fluid bolus

Maximum blood sugar (mmol/L)	Fluid bolus received		Total
	No	Yes	
<8.3	11 (12.1%)	0 (0%)	11 (11%)
≥8.3	80 (87.9%)	9 (100%)	89 (89%)
Total	91 (100%)	9 (100%)	100 (100%)
Mean±SD	200.76±43.80	237.33±59.94	204.05±46.31

Table 6: Comparison of blood sugar level (mmol/L) in relation to caudal anesthesia

Blood sugar levels (mmol/L)	Type of anesthesia	*n*	Mean±SD	*P*
First	GA	72	6±1.6	0.59
	GA + C	28	6.2±2.2	
Second	GA	72	8.8±2.3	0.504
	GA + C	28	9.1±2.1	
Third	GA	67	10.5±2.3	0.833
	GA + C	28	10.6±1.8	
Fourth	GA	40	11.7±2.0	0.339
	GA + C	15	11.1±2.1	
Fifth	GA	12	13.0±2	0.411
	GA+C	3	13.9±1.5	

Discussion

There is no uniform consensus on the amount of glucose required during neonatal surgery. Also, there is a paucity of literature on the association between intraoperative hyperglycemia and various factors, such as average intravenous fluid infusion rate, fluid bolus, blood transfusion, use of neuraxial technique, and total duration of surgery.

Larsson *et al*. studied the use of only ringer acetate solution and ringer's acetate with 10% glucose (so as to provide glucose at the rate of 0.25–0.30 g/kg/h) in 30 neonates undergoing major surgery with infusion rate of 15–20 mL/kg during first hour followed by 10 mL/kg/h in both groups. They observed rise in blood sugar in both groups during surgery, more in glucose supplemented group. Hypoglycemia was noticed in only ringer acetate group, in few neonates who were younger than 48 h and during first hour of anesthesia.[6] Sandstorm *et al*. studied the use of ringer's acetate alone and ringer's acetate with 10% glucose in 14 neonates. They noticed rise in blood sugar in both groups and concluded that starved neonates without intraoperative glucose supply mobilized fat and thus maintained blood glucose concentrations.[7] In our study, we observed higher mean blood sugar values above the base line in all neonates at successive hourly interval after the infusion of 1% DRL. Hypoglycemia was not observed in any of the neonates. Rise in blood glucose is explained by metabolic and endocrine response to surgical stress resulting in an increase in counter-regulatory hormones.

Sumpelmann *et al*. studied use of 1% dextrose containing isotonic balanced salt solution in neonates undergoing major surgery at average infusion rate of 10 mL/kg/h. They observed that blood glucose levels were maintained within normal range without any hypoglycemia or hyperglycemia. Also, they did not notice any derangement in serum sodium concentration in postoperative period.[8] Datta *et al*. studied the use of 1% glucose containing ringer's lactate, 2% glucose containing ringer lactate, and 10% glucose in N/5 in 45 neonates undergoing primary repair of tracheoesophageal fistula at average infusion rate of 10 mL/kg/h. They observed rise in blood sugar level in all three groups without any significant difference in blood glucose and incidence of hyperglycemia among them during surgery. However, they also noticed that neonates receiving 1% glucose containing fluid had higher median blood glucose and higher incidence of hyperglycemia 24 hours after surgery, preoperative, and postoperative median blood glucose value being 3.8 (3.3–5.8) and 8.8 (7.2–10.1) mmol/L. This finding was attributed to highest glucagon: insulin ratio in this group which denotes the catabolic state. They also observed that serum sodium did not change significantly during the course of surgery in any of the group except in one neonate receiving 2% glucose in ringer lactate.[9] (sodium-128 mmol/L).

We observed that preoperative and postoperative serum sodium levels did not change significantly and were within physiological range in our study, this finding is comparable with their results but our neonates had high mean blood sugar concentrations throughout study. The first, second, third, fourth and fifth blood sugars were 5.8, 8.9, 10.6, 11.9, and 13 mmol/L, respectively. The difference in blood sugar concentrations could be explained on following basis. Neonates enrolled in study by Datta *et al*. underwent only one type of surgery (tracheoesophageal fistula repair), had average rate of infusion of 10.4 (10.0–10.9) mL/kg/h, exclusion of neonates receiving blood, and blood product transfusion intraoperatively. None of the neonates were given fluid bolus and use of morphine as a bolus and intermittently as required for analgesia. This was done to ensure uniformity in surgical duration and perioperative stress as these would have been major confounding factors in their results.

We enrolled neonates undergoing various thoracic, abdominal, nonthoracic–nonabdominal surgeries under general anesthesia alone and along with caudal anesthesia. We also included neonates receiving intravenous fluid infusion at variable rate, with variable duration of surgery and the one receiving fluid bolus as well as blood transfusion for variable amount of blood loss intraoperatively. Our institute is high volume center for neonatal surgery and we have to anesthetize neonates with above mentioned diverse variables, intraoperative fluid of choice remains dilemma in them. So, the present study was performed to know the more appropriate intraoperative intravenous fluid of choice so as not to result in overt change in blood glucose and serum sodium concentration. Secondary outcome of the study was to know the association between intraoperative blood sugar concentration and various factors, such as average intravenous fluid infusion rate, fluid bolus, blood transfusion, use of neuraxial technique, and total duration of surgery. We excluded neonates who were large for gestational age, small for gestational age, having low birth weight, sepsis, first 2 days of life, and requiring inotropes infusion preoperatively and intraoperatively as these would have been major confounding factors in our study.

Kanwal *et al.* observed that increasing severity of surgical stress (based on amount of blood loss, type of dissection, visceral trauma, and duration of surgery) in neonates is associated with greater and more prolonged changes in plasma catecholamine, blood glucose, and gluconeogenic substrates during and after operation.[10] Hence, neonates with prolonged duration of surgery, greater amount of blood loss, and moderate visceral dissection are associated with hyperglycemia. In our study, we also observed a statistical significant correlation between intraoperative hyperglycemia and intraoperative blood transfusion as well as prolonged duration of surgery.

Wolf *et al*. studied 40 children younger than 4 years undergoing elective abdominal surgery under general anesthesia supplemented with either systemic opioid or extradural analgesia. He found rise in blood sugar in both groups but significantly greater in opioid group as a result of greater suppression of stress response with extradural analgesia.[11] In our study, neonates who received caudal block had no significant changes in blood sugar concentrations compared to neonates who did not receive caudal block. Our findings are comparable with findings of Sumpelmann *et al*.[8]

Higher dose of opioid and deeper plane of anesthesia in neonates during surgery were associated with better attenuation of stress response, hence blood sugar level.[12,13] Dose of opioid required to ablate stress response of major surgery is much more than dose required to provide analgesia and may necessitates postoperative ventilation. This was impractical for most of our neonatal surgery in view of paucity of ventilators; hence, the dose of opioid was tailored so as it will allow postoperative extubation. Lack of Intermittent dosing with fentanyl may have contributed to hyperglycemia in our neonates.

We also monitored neonates for postoperative events like change in sensorium and convulsion for first 24 h postoperatively consistent with change in serum sodium levels. None of the neonates had these complaints. The problems of hyperglycemia are usually manifested due to increase in serum osmolality mainly osmotic diuresis, electrolyte disturbance, and intraventricular haemorrhage which usually appears at blood glucose level more than 13.9 mmol/L for longer duration. The risk of neonates developing osmotic diuresis is rare below a blood glucose level of 13.9 mmol/L because the neonate's relatively low glomerular filtration rate limits the filtered load of glucose.[14] Adverse effects of hyperglycemia are seen often with prolonged duration of hyperglycemia.

Strength of our study is that we studied neonates undergoing different kinds of surgeries of varying duration with variable amount of blood transfusion and intravenous fluid infusion rate in a large sample size. This study helps to understand that, intraoperative hyperglycemia is due to stress evoked by blood loss warranting fluid bolus as well as blood transfusion, prolonged duration of surgery and higher infusion rate. As the intraoperative hyperglycemia is the result of stress, it is a wise decision not to treat it. Our study also has some limitations. First, we did not keep follow up of trends in blood sugar level in distant postoperative period. If so, it would have helped us to know the duration of hyperglycemia if any which would have impact on outcome of procedure. And second we did not monitor the complications of hyperglycemia, if any postoperatively.

Under anesthesia, glucose requirement in term neonates varies widely due to stress induced glucose mobilization due to various factors and decreased metabolism. Highest and lowest rates of intravenous fluid infusion were 6.18 and 31.66 mL/kg/h in our neonates delivering appropriately exogenous glucose 61.8 and 316.6 mg/kg/h, respectively. This rate of glucose supplementation is less than the recommended rate of supplementation of 4–8 mg/kg/min.[1,2] Exogenous glucose supply should be adapted as needed by changing the glucose concentration of infusion and infusion rate. A careful intraoperative glucose monitoring is essential to detect hypoglycemia and hyperglycemia. Interruption of glucose in maintenance fluid may result in lipolysis, ketogenesis, hypercatabolism, and hyperglycemia. Glucose-free isotonic solution can be considered for giving fluid bolus as it will cut off the additional glucose load. Larger evidence based trials are necessary to know the role of dextrose supplementation in neonates intraoperatively and its influence on improvement in surgical outcome.

Conclusion

Use of 1% DRL in neonates undergoing surgery is effective in preventing hypoglycemia, hyponatremia and hypernatremia. Intraoperative hyperglycemia is more obvious with higher intravenous fluid infusion rate, prolonged duration of surgery, and requirement of fluid bolus as well as blood transfusion intraoperatively. Intraoperative blood sugar levels were not affected by use of neuraxial block.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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