Blood glucose monitoring in pediatric patients on cardio-pulmonary bypass

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ABSTRACT

Background: Meticulous blood glucose control during cardio-pulmonary bypass has received a lot of attention recently. Children are more vulnerable to adverse effects of cardio-pulmonary bypass (CPB) on glucose homeostasis. Objectives of the study were to find out changes in blood glucose due to cardio-pulmonary bypass and the Insulin requirements intra-operatively.

Methods: A single centre, prospective trial in 130 children undergoing cardiac surgery for congenital cyanotic/acyanotic heart disease, requiring cardio-pulmonary bypass. We administered dextrose IV 0.5g/kg/hr in pre bypass period to avoid hypoglycemia. Blood glucose levels were measured at various point of time [baseline, after 10 min and then every half hourly during bypass, 30 minutes after bypass and next during the immediate post-operative using a Hemo-cue glucometer]. To control blood glucose on cardio-pulmonary bypass pump, we used inj. Insulin as per study protocol. The statistical analysis was done using paired and unpaired t test & chi square test.

Results: We had examined 130 pediatric patients going on CPB for cardiac surgery. Blood glucose was monitored in patients who did not required inj. Insulin (Group II) on bypass for hyperglycemia (n=33) while 97 patients required insulin (Group I) on bypass because of hyperglycemia. 74% of patient required insulin on pump shows that cardio-pulmonary bypass significantly affects glucose homeostasis in children; most of the children (43%) required insulin 30 min after starting cardio-pulmonary bypass.

Conclusions: Blood glucose rise in children of congenital cardiac disease was significant after induction of anesthesia; on hypothermic CPB children of congenital cardiac disease may had rising blood glucose trend and the pre-operative blood glucose significantly affects the trend of blood glucose on CPB. The duration of CPB might not significantly affect insulin requirement of pediatric patients. CPB significantly affected glucose homeostasis in children. Hence it seems prudent to administer small amount of IV dextrose in prebypass period to avoid hypoglycemia but rate and dose of insulin should be adjusted as it may affect blood glucose level on CPB.

Keywords: Acyanotic heart disease, Hemo-cue glucometer, Insulin

INTRODUCTION

In 1971 S. P. Allison, et al was first to study “Changes in insulin secretion during open heart surgery” since then various studies has been done to know glucose homeostasis during cardiac surgery in adult. Recent emphasis is on good control of blood glucose intra-operatively. The effect of anesthesia and surgery are more pronounced during cardiac anesthesia because of more stress and exposure to extreme un-physiological conditions like Cardiopulmonary bypass (CPB).

Children are more vulnerable to adverse effects of CPB on glucose homeostasis. Uncontrolled blood glucose
intra-operatively has deleterious effects on the patients both intra operatively and post operatively. It can affect the emergence from anesthesia, produce fluid electrolyte imbalance, delay wound healing, hypoxic ischemic brain damage, spinal cord damage and increase post-operative morbidity and mortality. Therefore, monitoring of blood glucose levels on pump is an important factor in outcome of patient on CPB. We planned this trial with the aim to study blood glucose changes in pediatric population undergoing CPB; to control the blood glucose intra-operatively; to find out requirement of insulin on pump; to find correlation between duration of CPB and increase in blood sugar intra-operatively.

METHODS

The present research was single center, prospective study with the inclusion criteria as children between age group of 6 months and 12 years undergoing cardiac surgery for congenital heart diseases. The exclusion criteria for the present study was parents/ guardian refusal on behalf of patient; patients less than 6 months and more than 12 years; patients on steroids, anti-convulsant (phenytoin); children with hepatic/ renal failure, Cushing disease, thyroid disorder, sepsis, glomerulopathis; intravenous glucose or fluid intake within 4 hours before surgery and surgical procedures requiring total circulatory arrest.

History of any systemic medical diseases, history of any previous surgery and anesthesia, history of any drug intake and drug allergy was evaluated. A thorough preoperative assessment of the patient was done including all the systems as per hospital protocol. Nature of the study was explained to all the parents/ guardian of pediatric patients included in the study and written informed valid consent was taken from the parents/guardian of patient on separate consent form. With institutional ethics committee approval and written informed consent of parents, 130 children in age group of 6 month to 12 years and undergoing cardiac surgery were included in this prospective study.

Procedure

Baseline blood glucose was taken in Operation Theatre (OT). After fasting for 4 hours and children were pre medicated with inj. Midazolam 0.5 mg/kg and inj. Ketamine 5 mg/kg along with inj. Glycopyrrolate by oral route. The children over 5 years of age received inj. Midazolam 0.03 mg/kg and inj. Ketamine 0.5 mg/kg IV or inj. Ketamine 5 mg/kg IM children were monitored by electrocardiogram, pulse oximetry, and arterial pressure. The induction of anesthesia was performed with opioids (inj. Fentanyl 10 ug/kg) and benzodiazepines (inj. Midazolam 0.1mg/kg) inj. Pancuronium (0.1mg/kg) was used as muscle relaxant intubation was performed after adequate muscle relaxation with Pancuronium. In all children, additional monitoring included central venous pressure, rectal and nasal temperatures. Anesthesia was maintained with infusion of inj Midazolam 0.02 mg/kg/hr and inj Fentanyl 2 ug/kg/hr.

After the injection of 300 IU/kg of heparin, CPB was accomplished using a non-pulsatile pump with a membrane oxygenator. Core cooling was used in all patients, monitored by rectal and esophageal temperature. After CPB, reversal of heparin was accomplished with Protamine sulfate (1.3 mg/1 mg Heparin). No child received intravenous fluids before entering the operating room. Immediately after induction of anesthesia, a continuous infusion of Isolyte P was initiated at a rate of 10 mL/kg/hr.

Blood samples for blood glucose measurements were drawn after induction of anesthesia and before 30 min after induction of anesthesia (T1), 10 minutes after the beginning of CPB (T2) and half hourly till he/she was on bypass (T3-T7). Samples were taken from bypass machine. One sample was taken after 30 minutes of bypass (T8) and one sample was taken in the immediate post-operative period in the ICU (T9). At each point of time about ½ cc blood was taken as sample. Blood glucose was measured by HemoCue-beta-glucose photometer. Hypoglycemia was defined as a blood glucose concentration lower than 40 mg/dL and hyperglycemia greater than 200 mg/dL. Those who had blood glucose >200mg% had received inj. Insulin 5 units and those with >300mg% received 10 units on pump as per our hospital protocol and blood glucose was monitored.

Statistical analysis

The parametric data were analyzed by paired t test for intra group comparison (blood glucose trend) levels of significance and unpaired t test for inter group comparisons. Differences were significant when probability was less than 0.05 (p value). The results were expressed as mean ± Standard Deviation (SD) in the text and the tables. Chi square test was used for inferential data analysis of cyanotic and acyanotic children.

RESULTS

We had examined 130 pediatric patients going on CPB for cardiac surgery. Blood glucose was monitored in patients who did not required inj. Insulin (Group II) on bypass for hyperglycemia (n=33) while 97 patients required insulin (Group I) on bypass because of hyperglycemia. Table 1 shows demographic data in study population. There was significant difference (P<0.05) between age (month) of group I (51.21±43.55) and group II (73.91±46.18) and weight (kg) of group I (12.22±6.71) and group II (15.67±8.13) patients.

At the induction of anesthesia (preoperative blood glucose level = T0) there was significant statistical difference between in blood glucose level in two groups (133.27±37.35 vs 106.27±22.57mg %). This showed that
pre-operative blood glucose level may be strong determinant factor for rise in blood glucose on CPB. Similarly, insulin requirement on bypass is less likely to be affected by aortic clamp duration [group I (67.47±23.70) group II (60.06±31.60)].

Table 1: Demographic data in study population.

<table>
<thead>
<tr>
<th>Age (months)</th>
<th>Group I (insulin) n=97</th>
<th>Group II (no insulin) n=33</th>
</tr>
</thead>
<tbody>
<tr>
<td>56.78±44.84</td>
<td>51.21±43.55**</td>
<td>73.91±46.18*</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>13.09±7.23</td>
<td>12.22±6.71*</td>
</tr>
<tr>
<td>CPB Duration (min)</td>
<td>82.15±28.6</td>
<td>84.55±26.70</td>
</tr>
<tr>
<td>Clamp Duration</td>
<td>65.11±25.9</td>
<td>67.47±23.70</td>
</tr>
</tbody>
</table>

* Statistical significance (p <0.05)

As described in Table 2, the type of heart disease cyanotic/ acyanotic didn’t seem to affect hyperglycemia on CPB. After induction of anesthesia the rise in blood glucose levels from 106.27±22.57 mg% to 135.73±23.07 mg% was significant as shown in Table 3. After starting CPB the blood glucose levels showed statistically insignificant fall from (T1) 135.73±23.07 mg% to (T2) 131.6±19.7 mg% while from T2 (10 min on bypass) to T6 (120 min on bypass) there was significant rise at each point in blood glucose level [no patients in this group II were on bypass for 150 min (T7)]. The sample of blood glucose collected 30 min post bypass (T8) and after 10min in ICU (T9) shows significant lower (176.3±33.1mg% and 167.6±27.5mg%) glucose level than T6 (179.8±15.51mg%) (p<0.05).

Table 2: Distribution of patients according to their congenital heart disease.

<table>
<thead>
<tr>
<th>Cyanotic</th>
<th>Group I (Insulin) n=33</th>
<th>Group II (no insulin) n=22</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acyanotic</td>
<td>37</td>
<td>11</td>
</tr>
</tbody>
</table>

Table 3: Blood glucose level at different time on CPB.

<table>
<thead>
<tr>
<th>Sample collection time (T)</th>
<th>Blood glucose level (mg %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-operative (basal) (T0)</td>
<td>106.27±22.57</td>
</tr>
<tr>
<td>After induction (T1)</td>
<td>135.73±23.07*</td>
</tr>
<tr>
<td>On bypass 10 min (T2)</td>
<td>131.6±9.78</td>
</tr>
<tr>
<td>On bypass 30 min (T3)</td>
<td>158.8±23.29*</td>
</tr>
<tr>
<td>On bypass 60 min (T4)</td>
<td>164.2±18.88*</td>
</tr>
<tr>
<td>On bypass 90 min (T5)</td>
<td>171.2±17.52*</td>
</tr>
<tr>
<td>On bypass 120 min (T6)</td>
<td>179.8±15.51*</td>
</tr>
<tr>
<td>After bypass 30 min(T8)</td>
<td>176.3±33.11*</td>
</tr>
<tr>
<td>In ICU 10 min (T9)</td>
<td>166.7±27.52*</td>
</tr>
</tbody>
</table>

* Statistical significance (p <0.05)

The patients who required inj insulin on CPB required insulin at different time interval, once or frequently. Analysis of data showed that maximum patients (43%) required insulin 30 min on bypass (T3) first time, followed by 34% at 10 min on bypass (T2), whereas 22% received insulin first time 60 min on bypass and only 1% received insulin 90 min on CPB as depicted in Figure 1.

Figure 1: Distribution of patient requiring insulin at different point of time.

Only one patient required 25 u of insulin on CPB. The average insulin required on CPB was 11.08 IU/child. Figure 2 showed that maximum patients required 10 u of insulin and only one required 25 u.

Figure 2: Insulin requirement during cardio-pulmonary bypass.

DISCUSSION

Glucose homeostasis during anesthesia and cardiac surgery has been extensively studied and their correction during cardiac surgery has received increasing attention now a days. Hypoglycemia as well as hyperglycemia can induce neurological complications. During pediatric cardiac surgery, a large increase in blood glucose has been reported when exogenous glucose was added intraoperatively. However, when glucose was excluded, hypoglycemia occurred. Hypoglycemia (blood glucose <40mg %) in children during surgery can be deleterious. When severe and prolonged, it is accompanied by many functional disorders leading to irreversible neuronal damage. Hyperglycemia was also considered to be
deleterious because it can impair neurological recovery after an ischemic event.\textsuperscript{8,9}

Hyperglycemia (Blood glucose >200mg\%) during cardiac surgery results from a number of factors. These alterations in glucose metabolism are related, in part, to the metabolic response to surgical trauma but mostly to specific aspects of CPB, such as heparinization, hypothermia, and re-warming.\textsuperscript{10-12} The etiology of the disturbance of the plasma glucose-insulin relationship, which consistently occurs during CPB, includes inadequate insulin secretion.\textsuperscript{1} Hypothermic CPB increased catecholamines, cortisol, and glucagon which stimulate glycosis, hepatic gluconeogenesis, and glucose production, decrease total body glucose uptake enhance renal absorption of filtered glucose, and decrease exogenous insulin activity.\textsuperscript{12,17} High concentration of anti-insulin humoral factors also contribute to rise in blood glucose.\textsuperscript{15}

The degree and duration of hyperglycemia differ depending on the type of anesthesia, duration of CPB, degree of hemo dilution, and duration and depth of hypothermia.\textsuperscript{18,19} It may be due to hyperoxia as shown by Karim S. in animal studies.\textsuperscript{20} Various mechanisms by which hyperglycemia could affect clinical outcome have been suggested. Whether Intra operative hyperglycemia can affect neurological outcome in patients of cardiac surgery is still debatable. A study conducted by De Ferranti et al reported no adverse neurodevelopment at 1,4,8 year age group in children having intra operative hyperglycemia during CPB for cardiac surgery and Chaney, et al also failed to demonstrate even subtle neurological damage using S-100 and ck-BB as neurological damage marker.\textsuperscript{21,22} Hyperglycemia has been shown to worsen neurological injury after focal and global cerebral ischemia, probably because of anaerobic glycolysis induced conversion of glucose to lactate, which causes intracellular acidosis and impairment of cellular metabolism.\textsuperscript{7}

Hyperglycemia provokes numerous deleterious effects on myocardium subjected to ischemia-reperfusion process. In both diabetics and hyperglycemic dogs, the myocardial infarct size is strongly correlated with blood glucose concentration.\textsuperscript{23} Moreover, high blood glucose concentration abolishes ischemic preconditioning and amplifies reperfusion injuries.\textsuperscript{2,3} To perform a study with homogenous conditions, only children (between age group of 6 months to 12 years) operated under hypothermic CPB, without circulatory arrest, were included in our study. Procedures with total hypothermic circulatory arrest are mainly used on newborn children and induce a striking metabolic response to surgical stress.\textsuperscript{24} It was found that glucose withdrawal in this population can induce threatening hypoglycemia during the prebypass period. This risk was prevented by moderate intraoperative glucose intake (0.5gm/kg/hr) without any major hyperglycemia. Before induction of anesthesia no low blood glucose levels were recorded in 130 children in our study when no exogenous glucose was infused. Children were kept fasting for 6 hrs.

There was no incidence of hypoglycemia in our study, but previous studies show a trend to an increase of this incidence when glucose was excluded. Nicholson, et al have already reported similar results, suggesting that hypoglycemia in fasting children with congenital heart disease is not rare.\textsuperscript{7} This incidence depends on fasting duration, nutritional condition, and energy requirements. Because of their great metabolic needs and their higher oxygen consumption, infants with congenital heart disease are not able to maintain normal blood glucose during fasting. Their glycogen storage is relatively less than in adults and is exhausted more rapidly. Nishina, et al conducted a study in healthy infants during minor surgery, reported that during glucose-free infusion, a major lipid mobilization (lipolysis) occurred to maintain normoglycemia after fasting.\textsuperscript{25} In children with higher energy needs, this physiologic compensation is probably insufficient and hypoglycemia can occur. This emphasizes the necessity of the low rate of glucose infusion in this population. Our study data showed that preoperative blood glucose level may be a factor that significantly affects blood glucose level on CPB.

The children, in our study were premedicated as per hospital protocol. This was done to reduce the rise in blood glucose level due to induction as earlier reported by Aono J, et al.\textsuperscript{26} Their study observed that blood glucose values of crying and agitated children before induction were significantly higher than those of calm children during perioperative period. No previous study had been done in children showing any significant relationship between age and weight of child and blood glucose level on CPB. Our study findings were suggesting that the pediatric patients with higher age [gr. I (51.21 ± 43.55) and group II (73.91 ±46.18)] and weight have less increase of blood glucose on CPB.

The type of congenital heart disease cyanotic/ acyanotic does not found to affect blood glucose on CPB; no previous study data concluded the same. The patients were induced with high dose of opioids (inj. fentanyl 10 ug/kg) and benzodiazepines (0.1mg/kg) to reduce stress response.\textsuperscript{27,28} Inj. pancuronium was used as muscle relaxant. After induction there was significant increase in blood glucose level from 106.27+22.57 mg% to 35.73+23.07 mg% (p<0.05). This increase in blood glucose level was also attributable to inhibition of peripheral glucose uptake during anesthesia combined with elevated levels of plasma catecholamine, glucagon, and cortisol in response to surgical stress.\textsuperscript{11,12,17} However study performed by Jeanjacques L, et al noted no change in blood glucose levels after induction of anesthesia in adult patients.\textsuperscript{11}

The priming solution used contained no dextrose and volume is increased by ringer’s lactate solution and if required blood is added to maintain CPCV >25%.
Addition of blood to priming solution increases its glucose content as stored CPD blood contains 7 to 22 mmol/lit of glucose. Keidan I, et al showed that when stored CPD is added to priming solution, blood glucose level increases more with blood stored >5 days than that of stored <5 days in first 20 min of CPB. In our hospital we used only fresh (<5 days) blood. McKnight CK, et al in 1985 found that blood glucose concentration decreased by 36±9mg% immediately on the institution of CPB in 12 non-diabetic adult patients undergoing open-heart surgery with cardiopulmonary by-pass using priming fluids free of glucose. The blood glucose fall in our study is insignificant. The decrease in blood glucose can be explained by dilution of blood by prime fluid. The subsequent blood glucose reading showed increasing trend throughout bypass. The results were similar to previous studies. In our study the increase in blood glucose is neither significant with duration of bypass nor with the clamp duration. Similar result was obtained by Torsten Doenst in 2005.

The concept of tight blood glucose control or hyperinsulinemic normoglycemic clamp technique during cardiac surgery had shown to improve outcome of cardiac surgery in adult patients. But the recent studies completed in adults, concluded that intensive insulin therapy during cardiac surgery does not reduce perioperative death or morbidity rather there is increased incidence of death and stroke in the intensive treatment group. Another study reported that attempting to maintain normoglycemia during CPB with insulin may initiate postoperative hypoglycemia and intraoperative hyperglycemia during infant cardiac surgery, and was not associated with adverse neurodevelopmental outcomes at 1, 4, and 8 year. Finally the studies on blood glucose, insulin and perioperative period in cardiac surgery & intensive care suggested that the degree of intraoperative hyperglycemia may merely reflect the severity of underlying “stress”.

If so, prevention of hyperglycemia might not reduce perioperative complications, and the risks and costs of intensive intraoperative glycemic management may outweigh the benefits.

CONCLUSION

Blood glucose rise in children of congenital cardiac disease was significant after induction of anesthesia; on hypothermic CPB children of congenital cardiac disease may had rising blood glucose trend and the pre-operative blood glucose significantly affects the trend of blood glucose on CPB. The duration of CPB might not significantly affected insulin requirement of pediatric patients. CPB significantly affects glucose homeostasis in children. Hence it seems prudent to administer small amount of IV dextrose in pre bypass period to avoid hypoglycemia but rate and dose of insulin should be adjusted as it may affect blood glucose level on CPB.

Most of the previous studies were done in adult and there is need of more extensive study in pediatric population.

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REFERENCES


