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Hyperglycemia and its association with clinical outcomes in postsurgical neonates and small infants in the intensive care unit

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ABSTRACT

Purpose: The aim of the research was to investigate the association between postsurgical hyperglycemia of neonates and small infants (<6 months) during their stays in intensive care unit and clinical outcomes.
Methods: A retrospective study of 180 patients including neonates and small infants (<6 months) admitted to pediatric intensive care unit (PICU) after major abdominal and thoracic surgeries from July 2012 to December 2014 was performed. Clinical data including serum glucose levels, surgical procedures, PICU length of stays, total length of hospital stays, systemic infections and wound infections were recorded and analyzed. Surgical diagnosis and Pediatric Risk of Mortality III (PRISM III) score were analyzed as confounding factors.
Results: Maximum glucose values (Gmax) ranged from 4.8 to 32.9 mmol/L (median level: 8.4 mmol/L). Hyperglycemia was prevalent among this group of patients. 93.3% of them experienced hyperglycemia (>6.1 mmol/L) and 20% had severe hyperglycemia (>11.0 mmol/L). Both PICU length of stays and total hospital length of stays increased as Gmax increased ($P < 0.001$). This trend was still statistically significant when either surgical diagnosis or PRISM score had been controlled as confounding factors. Death rates and infectious rates were not significantly different among four groups of patients with different Gmax.
Conclusions: Hyperglycemia was prevalent in postsurgical neonates and small infants in PICU and was associated with increased PICU and hospital stays.

Studies showed that hyperglycemia had been associated with increased morbidity and mortality rates in critically ill pediatric patients. Several large randomized controlled trials designed to evaluate the effect of glycemic control in these patients had resulted in different outcomes [1–8]. The aim of this study was to investigate the association between postsurgical hyperglycemia of neonates and small infants (<6 months) during their PICU stays and their clinical outcomes.

1. Methods

1.1. Patient information

Data of 180 neonates and small infants (<6 months) admitted to PICU after surgical procedures had been collected from the database of West China hospital from July 2012 to October 2014. Surgical procedures included major thoracic and abdominal operations and the categories were listed in Table 1. We excluded patients with metabolic disorders (e.g. diabetes mellitus, congenital hyperinsulinism) or other medical conditions that influenced serum glucose levels. Children with previously diagnosed or existing infections were also excluded. This retrospective clinical study had been approved by the institutional research ethic committee at West China Hospital of Sichuan University.

1.2. Clinical data collection

Blood samples were taken immediately when the patient had entered PICU for both laboratory analysis (Cobas 8000 modular analyzer, Roche) and bed-side blood gas test (Compact 3, Roche). These tests were repeated at the 12th and 24th hours in the first day. Daily tests were performed from the second day until discharge from ICU. Insulin infusion would be initiated when serum glucose level was greater than 12 mmol/L and glucose levels were closely monitored until they went below the target. As insulin infusion influenced the hyperglycemia-associated clinical outcomes, we had only included glucose recordings of patients without insulin infusions or before receiving insulin infusions to analyze the associations between glucose levels and clinical outcomes.

Basic demographic information had been retrieved from medical records for each child. Data including diagnosis, surgical procedure, PICU length of stay (PICU LOS), total length of hospital stay (hospital

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Table 1
Patient demographics.

Total number of patients	180
Neonates	89 (49.4%)
Small infants (<6 months)	91 (50.6%)
Age, median (IQR), days	30 (3–57)
Weight, median (IQR), kg	4.8 (2.4–6.1)
Male sex	103 (57.2%)
Mechanical ventilation	173 (96.1%)
Maximum glucose level (median (IQR), mmol/L)	8.4 (7.2–10.4)
Maximum glucose level distribution	
<6.1 mmol/L	12 (6.7%)
6.1- 8.3 mmol/L	56 (31.1%)
8.3–11.1 mmol/L	76 (42.2%)
>11.1 mmol/L	36 (20.0%)
Incidence of hypoglycemia (Gmin) (<3.6 mmol/L)	44 (24.4%)
Surgical diagnostic category (number of patients and PRSIM score median (IQR))	

	Number	PRSIM core median (IQR)
All patients	180 (100%)	3 (5)
Thoracic procedures		2.5 (5.0)
Esophageal atresia	14 (7.8%)	
Pulmonary resections	6 (3.3%)	
Congenital diaphragmatic disorders	5 (2.8%)	
Gastrointestinal and biliary procedures		3.3 (4.3)
Hypertrophic pyloric stenosis	25 (13.9%)	
Duodenal obstructions	12 (6.7%)	
Small intestinal resections, enterostomy and anastomosis	29 (16.1%)	
Biliary reconstructions	16 (8.9%)	
Anorectal and colon procedures		3 (5.0)
Hirschsprung's diseases	22 (12.2%)	
Anorectal malformations	25 (13.9%)	
Other procedures		1.5 (3.0)
Incarcerated hernia	3 (1.7%)	
Retroperitoneal tumor excisions	14 (7.8%)	
Neural tube defect	3 (1.7%)	
Abdominal wall repairs and reconstructions	6 (3.3%)	

(Wilcoxon rank sum test on difference of PRISM scores among four surgical categories $Z = -1.017$, $P = 0.309$).

LOS), documented systemic infection, wound infection and clinical course were recorded.

We used the Pediatric Risk of Mortality III (PRISM III) score to evaluate disease severity of each patient in PICU [9]. As glucose level greater than 11.1 mmol/L (200 mg/dL) contributed two scores of the total scores of PRISM, we also calculated the modified PRISM score which did not include the item of glucose level.

1.3. Statistical analysis

Maximum serum glucose (Gmax) values of each neonate and infant during the PICU stay were categorized into <6.1 mmol/L (110 mg/dL), 6.1–8.3 mmol/L (110–150 mg/dL) 8.3–11.1 mmol/L (150–200 mg/dL) and >11.1 mmol/L (200 mg/dL). Hyperglycemia was defined as glucose level greater than 6.1 mmol/L while severe hyperglycemia was defined as glucose level greater 11.1 mmol/L [10,11]. We compared the PICU LOS, hospital LOS, infectious rates and death rates of each category with Wilcoxon rank sum test and Fisher exact probability method. Infections in ICU had all been proved by microbiological evidence. Both the surgical diagnosis and PRISM score of patient were important prognostic factors. Thus we used the multiple linear regression models to eliminate the confounding effects of these two factors in analyzing the effect of hyperglycemia on clinical outcomes. Surgical diagnoses were summarized into four major groups (thoracic procedures, gastrointestinal and biliary procedures, anorectal and colon procedures and others) for efficient analysis of the data. Statistical efficiency would not be achieved if too many kinds of diagnoses were included so we summarized them into four groups. PRISM III scores of these 4 groups had been compared with Wilcoxon rank sum test (Table 1).

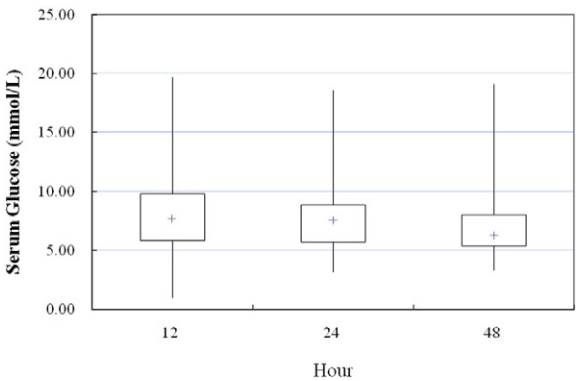

Fig. 1. Median serum glucose (mmol/L) trend within 48 h after surgery.

2. Results

Information of patients in our study had been presented in Table 1. About half of them were neonate (<28 days) and 57.2% were boys. The median PRSIM score was 3 (IQR 0–5). During the PICU stays of these children, maximum serum glucose (Gmax) values ranged from 4.8 to 32.9 mmol/L and the median Gmax was 8.4 mmol/L. Hyperglycemia was prevalent among this group of patients: 93.3% of them experienced hyperglycemia (>6.1 mmol/L) in ICU and severe hyperglycemia (>11.0 mmol/L) had been recorded in 20.0% of them. Incidence of hypoglycemia (<3.6 mmol /L) was 24.4%. PRISM scores were comparable among the four surgical diagnostic groups ($p = 0.309$) (Table 1). Fig. 1 illustrated the trend of median serum glucose levels within the 48 h after surgical procedures.

Maximum glucose values had been found to be associated with lengths of hospital stays. Both PICU length of stays and total hospital