RAPID COMMUNICATION

Hyperglycemia and postoperative outcomes in pediatric neurosurgery

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INTRODUCTION

Recent studies in adults have demonstrated the deleterious effects of hyperglycemia in intensive care patients and its substantial impact on crucial outcomes such as mortality. As a result, there is an increasing interest in the impact of this complication on the outcomes of critical illness in children.1

Hyperglycemia is prevalent among critically ill children and may be associated with poor outcomes and higher morbidity during hospitalization.2 Few prospective studies have analyzed the occurrence of hyperglycemia and the use of intensive insulin therapy in critically ill children. A recent single-center trial demonstrated the efficacy and safety of an insulin therapy protocol. The trial results indicated improved survival rates among the patients who received the treatment.3

A clear association between hyperglycemia and poorer outcomes has been demonstrated in some specific clinical situations, such as septic shock, cardiac surgery, and traumatic brain injury.4,5 However, hyperglycemia has yet to be fully studied in the context of pediatric surgery, and no pediatric neurosurgical studies have analyzed the association between hyperglycemia, morbidity, and mortality.

This study evaluated the postoperative glucose levels of children who underwent neurosurgical procedures for different indications and analyzed the association of these levels with lengths of mechanical ventilation, intensive care, and hospital stay.

MATERIAL AND METHODS

The study was conducted in the Pediatric Intensive Care Unit (PICU) of Santa Catarina Hospital, São Paulo, Brazil, a tertiary multidisciplinary hospital with 16 PICU beds. This retrospective cohort study evaluated all patients admitted to the PICU who underwent neurosurgical procedures from May 2004 to May 2009. Both plasma and capillary blood glucose values were collected from patients during their stay in the PICU and during their stay in the pediatric ward after transfer from the PICU. Hyperglycemia was defined as a blood glucose level ≥150 mg/dL. The three outcomes evaluated in the study were the durations of mechanical ventilation, PICU, and hospital stay. Hyperglycemia was studied along with other likely risk factors in these patients, such as fever, laryngitis, infection, hypothermia, packed red blood cells, and hormonal disorders. First, a univariate analysis was performed to identify the main risk factors associated with the three outcomes, and the statistically relevant risk factors were separated and analyzed in a multivariate analysis. The level of significance was set at 5%. Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) 18.0 (Chicago, Illinois). The study was approved by the Ethics in Research Committee of the institution where it was conducted.

RESULTS

The charts of 198 patients were analyzed during the study. The most frequent surgeries were brain tumor resection (37.4%), craniostenosis (31.3%), ventriculoperitoneal shunting (16.7%), craniotomy for craniofacial dysostosis (4.5%), spinal arthrodesis (4%), epilepsy surgery (2%), and brain revascularization for Moyamoya disease (1.5%).

A total of 139 glucose measurements were recorded for the patients included in the study. Hyperglycemia was diagnosed in 62.6% of the patients. The patient glucose level upon admission to the PICU and the highest glucose level noted in the first 24 hours post-admission were recorded. The mean glucose level was recorded following the 24-hour measurement. The results of the glucose measurements according to surgical diagnosis are listed in Table 1.

A univariate analysis identified a positive association between hyperglycemia and a prolonged duration of PICU stay (3.88 days vs. 2.46 days, p = 0.042). However, hyperglycemia was not associated with prolonged hospitalization or the duration of mechanical ventilation required (Table 2). The multivariate analysis did not identify any positive associations between hyperglycemia and any of the three outcomes studied (Table 3).
To the best of our knowledge, the present study is the first to analyze the effects and the incidence of hyperglycemia in a pediatric neurosurgery environment. The highest glucose levels were found in patients that underwent surgery for craniosynostosis, supratentorial tumor resection, and craniotomies; these procedures are more likely to involve longer surgical times and higher incidence of complications, such as bleeding and infection. These higher incidences of complications increase the risk of hyperglycemia. Univariate analysis indicated an association between hyperglycemia and prolonged duration of stay in the PICU. However, no association was found between hyperglycemia and the total duration of hospital stay or the length of mechanical ventilation time required. Multivariate analysis indicated no statistically relevant associations between hyperglycemia and any of the outcomes. The occurrence of severe hyperglycemia (above 300 mg/dL) was rare.

Hyperglycemia is common in critical illness as a consequence of organic stress and counter-regulatory hormones and is typically interpreted as a secondary event in critical care. Several studies have tried to identify an association between hyperglycemia and a worse prognosis in children, but their findings should be interpreted as markers of severe illness. As the patient’s condition improves, it is likely that their glucose levels will revert to the normal range. As a secondary event, patients with other complications that may affect glucose levels, either directly or indirectly, such as fever, infection or bleeding, are more likely to develop hyperglycemia and, consequently, worse outcomes such as a prolonged ICU stay. Such factors may explain why hyperglycemia was found to be associated with a prolonged stay in the PICU in the univariate but not in the multivariate analysis.

Up to 50% of pediatric patients who undergo neurosurgery may develop several postoperative complications, and hyperglycemia is an important event that may impact on their clinical course. Stress hyperglycemia is associated with insulin resistance and frequently affects adults and children. Some of the factors that may contribute to stress hyperglycemia are high glucose infusion rates, the increase in the production of endogenous glucose due to action of the counter-regulatory hormones (cortisol, glucagon, and catecholamine), and changes in glucose transport.

Changes in insulin counter-regulatory hormones due to surgical stress have not been clearly defined; therefore, the highest glucose level within the first 24 hours following surgery was analyzed separately from the glucose level at admission. There was a progressive reduction in glucose levels in all surgical groups during the course of hospitalization. Mild hyperglycemia was identified and its rapid progression to normal levels may be explained by the low preoperative morbidity of the population studied, as most procedures were elective and performed in patients with a low anesthetic risk. According to this hypothesis, the patients were more likely not to present the main consequences of severe hyperglycemia, such as osmotic diuresis, dehydration, and metabolic disorders. When considering the results of the entire study population, hyperglycemia was not severe enough in this scenario to cause adverse effects and outcomes related to this metabolic disorder.

It was not possible to evaluate the correlation between hyperglycemia and mortality because only two deaths occurred during the study. Nearly 59% of the patients received one or more doses of systemic corticosteroids during surgery or their ICU stay, while 93% of the patients who underwent brain tumor surgeries received them. There are no current recommendations regarding the routine postoperative use of corticosteroids, which are administered with the aim of reducing the brain edema associated with resection. Nevertheless, corticosteroids are well known to increase glucose levels, which may have contributed to our findings.

We did not identify a significant association between hyperglycemia and the three outcomes examined, which may be explained by the small sample size and the relatively few glucose measurements taken in the study population. As hyperglycemia was common in this group, special attention should be paid to it to prevent adverse events, especially because other studies with larger series of patients found a significant association between hyperglycemia and worse outcomes in surgical patients.

There were a few limitations associated with this study, particularly due to the retrospective analytical design and consequent lack of a previous protocol of glucose measurement. Moreover, some of the surgery subgroups contained few patients, which made it difficult to establish an association between glucose levels and outcomes.

The treatment of hyperglycemia in pediatric intensive care must be further analyzed, as there is no consensus on the benefits of several procedures, such as insulin therapy and strict glycemic control in these situations. In children, organic components such as beta cells, liver, kidneys, and muscles have not been exposed to oxidative, lipotoxic or...
Hyperglycemic stress for extended periods, and the effects of hyperglycemia on these patients may differ from those seen in adult populations. Therefore, changes in glucose levels that develop after neurosurgery should be better studied to outline preventive measures, such as determination of glucose infusion rates, prevention of unnecessary use of systemic corticosteroids, and early diagnosis of infection.

CONCLUSIONS

Hyperglycemia is frequent in children following neurosurgery and was not found to be associated with the durations of mechanical ventilation, PICU stay, or hospital stay in this sample of pediatric patients. In pediatric patients, glucose levels should be carefully and accurately controlled after surgery, as this may reduce morbidity and hospitalization time. Further studies are necessary to elucidate the role of hyperglycemia in pediatric neurosurgical patients.

Table 2 - Results of univariate analysis.

| Outcome          | Risk Factor | Median | SD  | N    | p-value |
|------------------|-------------|--------|-----|------|---------|
| PICU LOS         | Fever       | 2.7    | 1.9 | 138  | 0.006   |
|                  | No          | 5.08   | 8.11| 60   |         |
|                  | Yes         | 5.96   | 4.61| 138  | 0.001   |
|                  | MV time     | 5.83   | 8.49| 138  | <0.001  |
|                  | Yes         | 8.48   | 11.57| 60   |         |
| Hosp. LOS        | Use of PRBC | 3.13   | 2.94| 102  | 0.468   |
|                  | No          | 3.73   | 6.26| 96   |         |
|                  | Yes         | 7.23   | 6.79| 102  | 0.623   |
|                  | MV time     | 5.54   | 5.55| 102  | 0.017   |
|                  | Yes         | 7.8    | 12.43| 96   |         |
| Laryngitis       | PICU LOS    | 2.9    | 2.29| 168  | 0.027   |
|                  | No          | 6.33   | 10.89| 30   |         |
|                  | Yes         | 6.61   | 5.66| 168  | 0.001   |
|                  | MV time     | 6.21   | 8.83| 168  | 0.036   |
|                  | Yes         | 9.02   | 12.91| 30   |         |
| Coag. Disorders  | PICU LOS    | 3.32   | 4.82| 189  | 0.065   |
|                  | No          | 5.44   | 5.05| 9    |         |
|                  | Yes         | 7.08   | 7.95| 189  | 0.247   |
|                  | MV time     | 8.78   | 6.4 | 9    |         |
|                  | Yes         | 21.72  | 31.15| 9    |         |
| Inappropriate ADH| PICU LOS    | 3.4    | 4.87| 195  | 0.037   |
| Syndrome        | No          | 4.67   | 1.15| 3    |         |
|                  | Yes         | 7.4    | 7.41| 195  | 0.214   |
|                  | MV time     | 6.61   | 9.64| 195  | 0.022   |
|                  | Yes         | 8.33   | 1.15| 3    |         |
| Seizures         | PICU LOS    | 3.03   | 2.62| 190  | 0.003   |
|                  | No          | 12.63  | 19.33| 8    |         |
|                  | Yes         | 6.65   | 5.79| 190  | <0.001  |
|                  | MV time     | 6.56   | 9.75| 190  | 0.002   |
|                  | Yes         | 8.5    | 3.02| 8    |         |
| Hyperglycemia    | PICU LOS    | 2.46   | 1.43| 52   | 0.042   |
|                  | No          | 3.88   | 3.76| 87   |         |
|                  | Yes         | 5.15   | 2.02| 52   | 0.073   |
|                  | MV time     | 5.27   | 1.71| 52   | 0.078   |
|                  | Yes         | 9.74   | 15.6| 87   |         |
| CSF Leakage      | PICU LOS    | 3.24   | 4.72| 192  | 0.001   |
|                  | No          | 9.17   | 5.6 | 6    |         |
|                  | Yes         | 6.7    | 6.75| 192  | <0.001  |
|                  | MV time     | 6.32   | 8.49| 192  | 0.152   |
|                  | Yes         | 16.83  | 27.05| 6    |         |
| ICH              | PICU LOS    | 2.97   | 2.54| 189  | <0.001  |
|                  | No          | 12.78  | 17.95| 9    |         |
|                  | Yes         | 6.72   | 5.78| 189  | 0.011   |
|                  | MV time     | 6.49   | 9.67| 189  | 0.039   |
|                  | Yes         | 9.67   | 6.96| 9    |         |
| Infection        | PICU LOS    | 3.17   | 4.7 | 189  | <0.001  |
|                  | No          | 8.56   | 5.22| 9    |         |
|                  | Yes         | 6.58   | 6.74| 189  | <0.001  |
|                  | MV time     | 19.33  | 9.46| 9    |         |
| Use of PRBC      | PICU LOS    | 3.13   | 2.94| 102  | 0.468   |
|                  | No          | 3.73   | 6.26| 96   |         |
|                  | Yes         | 7.23   | 6.79| 102  | 0.623   |
|                  | MV time     | 5.54   | 5.55| 102  | 0.017   |
|                  | Yes         | 7.8    | 12.43| 96   |         |

Legend – PICU LOS – Pediatric Intensive Care Unit Length of stay, SD – standard deviation, MV – mechanical ventilation, PRBC – packed red blood cells, CSF – cerebrospinal fluid, ICH – intracranial hypertension, ADH – antidiuretic hormone.

Table 2 Cont.

| Outcome          | Risk Factor | Median | SD  | N    | p-value |
|------------------|-------------|--------|-----|------|---------|
| MV time          | Fever       | 6.18   | 8.8 | 189  | 0.001   |
|                  | No          | 16.17  | 18.15| 9    |         |
| Hypothermia      | PICU LOS    | 3.5    | 5.14| 166  | 0.65    |
|                  | No          | 7.37   | 7.8 | 166  | 0.365   |
|                  | Yes         | 4.06   | 4.28| 32   |         |
| Hosp. LOS        | MV time     | 7.05   | 10.38| 166  | 0.038   |
|                  | No          | 4.47   | 1.88| 32   |         |

Table 3 - Results of multivariate analysis.

| Outcome          | Risk Factor | Regression Analysis (Wald Test) |
|------------------|-------------|--------------------------------|
| PICU LOS         | Fever       | 7.72 <0.001                     |
| Laryngitis       | 9.13 0.003  |
| Hyperglycemia    | 3.2 0.062   |
| Coagulation disorders | 0.23 0.63 |
| Infection        | 4.1 0.043   |
| Use of steroids  | 2.96 0.085  |
| Fever            | 7.54 0.006  |
| Laryngitis       | 3.39 0.066  |
| Coagulation disorders | 0.31 0.576 |
| Infection        | 8.99 0.003  |
| Use of steroids  | 0.02 0.894  |
| Fever            | 48.24 <0.001 |
| Laryngitis       | 4.29 0.038  |
| Coagulation disorders | 5.27 0.022 |
| Infection        | 2.36 0.125  |
| Use of steroids  | 48.24 <0.001 |
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