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Bacterial respiratory tract infections are promoted by systemic hyperglycemia after severe burn injury in pediatric patients

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ABSTRACT

Background: Burns are associated with hyperglycemia leading to increased incidence of infections with pneumonia being one of the most prominent and adverse complications. Recently, various studies in critically ill patients indicated that increased pulmonary glucose levels with airway/blood glucose threshold over 150 mg/dl lead to an overwhelming growth of bacteria in the broncho-pulmonary system, subsequently resulting in an increased risk of pulmonary infections. The aim of the present study was to determine whether a similar cutoff value exists for severely burned pediatric patients.

Methods: One-hundred six severely burned pediatric patients were enrolled in the study. Patients were divided in two groups: high (H) defined as daily average glucose levels >75% of LOS >150 mg/dl), and low (L) with daily average glucose levels >75% of the LOS <150 mg/dl). Incidences of pneumonia, atelectasis, and acute respiratory distress syndrome (ARDS) were assessed. Incidence of infections, sepsis, and respiratory parameters were recorded. Blood was analyzed for glucose and insulin levels. Statistical analysis was performed using Student's *t*-test and chi-square test. Significance was set at $p < 0.05$.

Results: Patient groups were similar in demographics and injury characteristics. Pneumonia in patients on the mechanical ventilation (L: 21%, H: 32%) and off mechanical ventilation (L: 5%, H: 15%), as well as ARDS were significantly higher in the high group (L: 3%, H: 19%), $p < 0.05$, while atelectasis was not different. Patients in the high group required significantly longer ventilation compared to low patients ($p < 0.05$). Furthermore, incidence of infection and sepsis were significantly higher in the high group, $p < 0.05$.

Conclusion: Our results indicate that systemic glucose levels over 150 mg/dl are associated with a higher incidence of pneumonia confirming the previous studies in critically ill patients.

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1. Introduction

Critically ill patients and especially burn patients are at a high risk for infectious complications [1]. Severe infections are one of the leading cause in burn patients resulting in prolonged hospitalization [2,3] and worsened outcome [2]. One of the major infectious complications is pneumonia, which has been shown to increase burn mortality by 40% [4,5]. On the hand, severe thermally injured patients are particularly at risk for the development of pneumonia because of their vast hypermetabolic and inflammatory response, profound immune compromisation, prolonged bed rest, and need for mechanical ventilation [2]. Ventilation leads to impaired mucociliary clearance and excretion of pathogens with increased mucus content in the airways [6,7]. Not only does the amount of mucus affects infections, but it has also been shown in an in vitro experiment that increased glucose content in media promotes the bacterial growth [7–9]. Under physiologic conditions, glucose is not detectable in the airway fluids [10]. In a recent study, it was shown that systemic blood glucose levels greater than 8 mmol/l (144 mg/dl) lead to a marked increased glucose content in the airway system [11]. Increased glucose concentration in the mucus presents an excellent media for bacteria such as *Staphylococcus aureus* and *Pseudomonas aeruginosa* [12].

As aforementioned, a hallmark after severe burn injury is hypermetabolism associated with hyperglycemia and insulin resistance [13,14]. Increased pulmonary glucose levels with an airway/blood glucose threshold over 150 mg/dl lead to an overwhelming growth of bacteria in the broncho-pulmonary system, leading to increased risks of pulmonary infections [12]. Therefore, we determined whether this airway/blood glucose threshold can be translated to burn patients. The aim of this study was to determine whether systemic glucose levels over 150 mg/dl lead to increased pneumonia and pulmonary complications indicating bacterial growth promotion caused by the an existing airway glucose threshold.

2. Patients and methods

This cohort study used two-hundred eight severely burned pediatric (ages 0–17) patients with burns over 30% total burn surface area (TBSA). All individuals participated in a prospective randomized trial determining who consented to an IRB-approved experimental protocol between 2002 and 2008 determining the effects of tight glycemic control after severe burn injury were included in this study. Patients considered being futile at admission were excluded from the study. Patients were evaluated for their glycemic control according to their systemic glucose levels in responders and non-responders according the following criteria. A cut-off value of 150 mg/dl systemic blood glucose was used for the assessment of the success of glycemic control. Patients with good glucose control (at least for 75% of the length of stay below 150 mg/dl) were assigned to the low-glucose level group (L). All other subjects were stratified to the group with high glucose levels (H). A subset of 106 patients with continuous chest radiographic evaluation of the incidence of pneumonia was analyzed according to the incidence of pneumonia, atelectasis, and acute respiratory distress syndrome (ARDS) during the ICU stay. Furthermore, we determined the ratio of arterial partial oxygen pressure and fraction of inspired oxygen (P/F ratio), length of ventilation, and positive end expiratory pressures (PEEP). Lastly, burn wound infection and sepsis was prospectively determined.

At admission, patients received standardized burn care [15]. Patients were resuscitated according to the Galveston formula with 5000 cc/m^2 TBSA burned +2000 cc/m^2 TBSA lactated Ringer's solution given in increments over the first 24 h as necessary. Within 48 h of admission, all patients underwent total burn wound excision and their wounds were covered with autograft. Any remaining open areas were covered with homograft. After the first operative procedure, patients were taken back to the operation theater when donor sites were healed. This procedure was repeated until all open wound areas were covered with autologous skin. All patients underwent the same nutritional treatment according to a standardized protocol. Intake was calculated as 1500 kcal/m^2 body surface +1500 kcal/m^2 area burn as previously described [16–18]. The nutritional route of choice in our patient population was enteral nutrition via a naso-duodenal (Dobhoff) or nasogastric tube. Parenteral nutrition was only given in rare instances if the patient could not tolerate tube feeds. All patients received an antibiotic regimen at admission consisting of Vancomycin, Pip/Tazo and Fluoconazole. There was no difference between groups in the antibiotic regimen.

Patient demographics (age, date of burn and admission, gender, burn size and depth of burn), concomitant injuries such as inhalation injury, and outcomes (sepsis, morbidity, and mortality) were recorded. Inhalation injury was diagnosed by bronchoscopy along with a consistent history. Wound infection was defined as $>10^5$ colony forming units per gram tissue in a wound biopsy with the identification of a pathogen [19]. Repeated counts of the same bacteria in the same location were counted as the same infection. Sepsis and infection were diagnosed in accordance with the American Burn Association and Society of Critical Care Medicine guidelines [20,21]. Sepsis was defined as a positive blood culture or pathologic tissue identifying the pathogen during hospitalization or at autopsy, in combination with at least three of the following: leucocytosis or leucopenia (>12,000 or <4000/μl), hyperthermia or hypothermia (>38.5 or <36.5 °C), tachycardia (>20% above normal value), refractory hypotension (systolic BP < 20% below normal value), thrombocytopenia (platelets < 50,000/mm^3), hyperglycemia (serum glucose >240 mg/dl), and enteral feeding intolerance (residuals >200 cc/h or diarrhea >1 L/day) according the modified ACCP/SCCM criteria [20,21]. We further determined time between operations as a measure for wound healing and re-epithelization. Patient data was collected prospectively using the clinical information system Emtek by physicians, nurses and supportive staff. Data was processed and analyzed with Microsoft Access 2007®, Excel 2007®, Microsoft Corporation Inc. (Redmond, WA, USA).

2.1. Definitions

Pneumonia – The clinical diagnosis of pneumonia included the following: