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Adrenocortical status in infants and children with sepsis and septic shock☆

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KEYWORDS

Adreno-cortical state;
Corticosteroids;
Pediatric ICU;
Relative adrenal insufficiency;
Septic shock

Abstract *Background:* The benefit from corticosteroids remains controversial in sepsis and septic shock and the presence of adrenal insufficiency (AI) has been proposed to justify steroid use.
Aim: To determine adrenal state and its relation with outcome in critical children admitted with sepsis to PICU of Cairo University, Children Hospital.
Methods: Thirty cases with sepsis and septic shock were studied. Cortisol levels (CL) were estimated at baseline and after high-dose short ACTH stimulation in those patients and in 30 matched controls. Absolute AI was defined as basal CL < 7 μg/dl and peak CL < 18 μg/dl. Relative AI was diagnosed if cortisol increment after stimulation is < 9 μg/dl.
Results: Overall mortality of cases was 50%. The mean CL at baseline in cases was higher than that of controls (51.39 μg/dl vs. 12.83 μg/dl, $p = 0.000$). The mean CL 60 min after ACTH stimulation was higher than that of controls (73.38 μg/dl vs. 32.80 μg/dl, $p = 0.000$). The median of %rise in cases was lower than that of controls (45.3% vs. 151.7%). There was a positive correlation between basal and post-stimulation cortisol with number of system failure, inotropic support duration, mechanical ventilation days, and CO_2 level in blood. There was a negative correlation between basal and post stimulation cortisol with blood pH and HCO_3.
Conclusion: RAI is common with severe sepsis/septic shock. It is associated with more inotropic support and has higher mortality. Studies are warranted to determine whether corticosteroid therapy has a survival benefit in children with RAI and catecholamine resistant septic shock.

Introduction

Despite the advances in intensive care, septic shock and severe sepsis remain a major cause of morbidity and mortality. In fact, the incidence of septic shock and severe sepsis has been increasing over the past 30–40 years. It is estimated that in the USA there are about 750,000 new cases of severe sepsis every year.[1]

Patients with septic shock manifest an overwhelming inflammatory response to the infection; the body then regulates this response by producing anti-inflammatory cytokines which is manifested by a period of immune-depression.[2]

☆ The work was performed at PICU of New Children's Hospital, Cairo University's hospitals, Cairo, Egypt.

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Despite that the most common cause of adrenal insufficiency is sepsis and systemic inflammatory response syndrome (SIRS), there is a great controversy about using corticosteroids as one of the treatment options in children with sepsis and septic shock.[3] Some studies found that the use of corticosteroids produced no change in mortality rates or could even increase as a result of secondary infection.[4] On the other hand, many studies have reported better evolution when corticosteroids were used.[5]

Corticosteroids act by correcting a state of adrenal insufficiency, inhibiting synthesis of inducible nitric oxide synthase (iNOS) leading to reduced production of nitric oxide and hence lesser vasodilatation, restoring the sensitivity of vascular catecholamine receptors and decreasing the transcription of inflammatory cytokines. Steroids have been shown to improve blood pressure, reduce the prevalence of post-traumatic stress disorder and improve the emotional well-being of survivors of septic shock. Despite these potential advantages, still steroids are indicated in only those patients with septic shock who have failed to respond to vasopressors.[6]

Methodology

Objectives

We aimed in this work to assess the presence of clinical or subclinical adrenal insufficiency (evidenced by reduced cortisol and/or reduced responsiveness to Adreno-Corticotropin Hormone) in children with SIRS and septic shock.

Patients

This prospective clinical study was conducted in a tertiary pediatric intensive care unit, in Cairo University, children hospital.

The study included 30 patients with severe sepsis and 30 healthy controls of matching age for comparison.

Inclusion criteria

- Patients Aged between 2 months and 15 years suspected to have SIRS; meeting SIRS criteria are considered as having at least 2 of the following 4 clinical parameters abnormal[7]:
  (a) Body temperature (temperature >100.4 °F (38 °C) or temperature <96.8 °F (36 °C).
  (b) Heart rate (HR $>$ 90/min).
  (c) Respiratory rate [RR $>$ 20/min or PaCO2 $<$ 32 mmHg (4.3 kPa)].
  (d) Peripheral leukocytic count (WBC $< 4\times10^9$/L ($<$4000/mm^3), $>12\times10^9$/L ($>$12,000/mm^3), or 10% bands).

The International Pediatric Sepsis Consensus has proposed some changes to adapt these criteria to the pediatric population.[8]

In children, the SIRS criteria are modified in the following fashion:

- Heart rate is greater than 2 standard deviations above normal for age in the absence of stimuli such as pain and drug administration, or unexplained persistent elevation for greater than 30 min to 4 h. In infants, also includes Heart rate less than 10th percentile of age in the absence of vagal stimuli, beta-blockers, or congenital heart disease or unexplained persistent depression for greater than 30 min.
- Body temperature obtained orally, rectally, from Foley catheter probe, or from central venous catheter probe less than 36 °C or greater than 38.5 °C. Temperature must be abnormal to qualify as SIRS in pediatric patients.
- Respiratory rate greater than 2 standard deviations above normal for age or the requirement for mechanical ventilation not related to neuromuscular disease or the administration of anesthesia.
- White blood cell count elevated or depressed for age not related to chemotherapy, or greater than 10% bands plus other immature forms.[8]
- Or sepsis as defined by the presence of infection in association with criteria meeting SIRS.
- Or severe sepsis which is defined as evidence of end-organ dysfunction such as altered mental status, episode of hypotension, elevated creatinine or evidence of disseminated intravascular coagulopathy.
- Or septic shock as defined by persistent hypotension despite adequate fluid resuscitation or tissue hypo perfusion.[9]

Exclusion criteria

- Patients with Pre-existing condition associated with dysfunction of hypothalamo–pituitary–adrenal axis.
- Any use of corticosteroids during the 2 weeks preceding this episode.
- Patients with known primary immune deficiency disorders.

Patients were subjected to

(a) Clinical assessment including full history and thorough physical examination.
(b) Routine Laboratory tests (arterial blood gases, complete blood picture including differential count, C-reactive protein, liver function tests, renal function tests and coagulation profile).
(c) Assessment of the severity of the condition including:
- Presence or absence of mechanical ventilation.
- Level of inotropic support.
- Severity of illness in the 1st 24 h after diagnosis of septic shock as assessed by pediatric risk of mortality (PRISM) type3.
- Length of stay in pediatric intensive care unit

(d) Cultures from blood and from suspected site of infection.
(e) Radiography (chest X-ray) and others as needed according to infection site.

Specimen collection and intervention

(a) Blood samples were obtained within 24 h of admission for measurement of basal cortisol and adreno-corticotropin hormone by radio-immuno-assay, results were compared with those of normal controls.