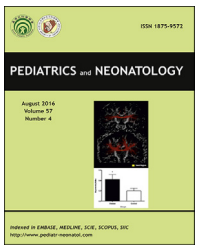
Pediatrics and Neonatology (2017) xx, 1–5

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: http://www.pediatr-neonatol.com



Original Article

Hyperdehydroepiandrosterone in Neonates With Hypoxic Ischemic Encephalopathy and Circulatory Collapse

Abdelmoneim Khashana [a,b,*], **Engy Ahmed** [c]

[a] *PEDEGO Research Center, Medical Research Center Oulu, University of Oulu, Oulu, Finland*
[b] *Department of Pediatrics and Neonatology, Suez Canal University Hospital, Ismailia, Egypt*
[c] *Epidemiology and Statistics, Health authority, Ismailia, Egypt*

Received Jan 22, 2016; received in revised form Apr 21, 2016; accepted Sep 29, 2016
Available online ■ ■ ■

Key Words
dehydroepiandrosterone;
hypoxia;
ischemia;
neonates;
vasopressor resistant hypotension

Background: Circulatory collapse is a very common complication of the critical illnesses in neonates including neonates with hypoxic ischemic encephalopathy; it can be the end result and cause of death of several conditions. Often, despite treatment with fluid resuscitation and vasopressor agents, circulatory collapse persist, and blood pressure can remain critically low, compromising adequate blood flow to vital organs and brain. Low blood pressure has been associated with increased mortality.
Method: To investigate adrenal function in newborn infants who suffer from circulatory collapse during hypoxic ischemic encephalopathy. A total of 30 infants were analyzed in the study: 15 neonates in group A (neonates had hypoxic ischemic encephalopathy with vasopressor resistant hypotension) and 15 neonates in group B (neonates with hypoxic ischemic encephalopathy without vasopressor resistant hypotension). All the studied patients were subjected to history, examinations and laboratory investigation including serum cortisol concentrations and cortisol precursor's levels.
Results: The cortisol concentrations did not differ significantly between the two groups: (12.9 ± 4.3) μg/dL and (12.1 ± 2.4) μg/dL in group A and group B, respectively. There are highly significant differences between groups A and B regarding Dehydroepiandrosterone (342.1 ± 101.3) μg/dL, (33.4 ± 16.5) μg/dL, respectively.
Conclusion: In this study, we noticed that cortisol concentrations did not differ between both groups in contrast to the expectation that neonates with critical illnesses should have higher cortisol concentrations than normal neonates. However, the marked increase in dehydroepiandrosterone DHEA may cause decrease cortisol function, so those neonates having accumulation

Abbreviations: DHEA, dehydroepiandrosterone; HPA axis, hypothalamic-pituitary-adrenal axis; 3β-HSD, 3-beta-hydroxysteroid dehydrogenase; HIE, hypoxic ischemic encephalopathy.

* Corresponding author. PEDEGO Research Center, Medical Research Center Oulu, University of Oulu, Oulu, Finland.
E-mail address: Abdelmoneim_khashana@hotmail.com (A. Khashana).

http://dx.doi.org/10.1016/j.pedneo.2016.09.010

of dehydroepiandrosterone may suffer from manifestation of adrenal insufficiency and vasopressor resistant hypotension in spite of normal cortisol level.

1. Introduction

Hypoxic ischemic encephalopathy (HIE) is a disease with neurological signs and symptoms that are induced by hypoxia and ischemia. Cardiac and vascular insult ultimately occurs when hypoxia is prolonged and results in hypotension.[1] In spite of major development in knowledge of fetal and neonatal pathologies, HIE still remains a serious condition, causing significant mortality and morbidity.[2]

Cerebral palsy may be attributed to perinatal asphyxia in case of metabolic acidosis in the cord blood (pH less than seven and base deficit more than 12 mmol/L), followed by encephalopathy within 24 h and a further neurological deficit in the form of spastic quadriplegia.[3]

In fetal life, since the arterial partial pressure of oxygen is normally low, the ensuing disturbances are primarily consequences of hypoperfusion. In spite of this, severe hypoxemia may be appear, leading to myocardial affection with subsequent cardiogenic shock and cerebral hypoperfusion or loss of cerebrovascular auto-regulation.[4] Current opinion suggests that as many as 70% of patients in intensive care units with septic or cardiogenic shock have relative adrenal insufficiency,[5] and corticosteroid therapy may be beneficial to some patients with septic shock.[6]

The acute stress response during critical illness is characterized by initiation of the hypothalamic pituitary adrenal axis (HPA axis), with increased production of cortisol and amplification of the translocation of the glucocorticoid receptors inside the cell nucleus. There is increasing evidence to show that in many patients with critical illnesses, this pathway may be impaired.[7] The prevalence of adrenal insufficiency in critically ill patients varies widely.[5,8] We found adrenal function impairment with circulatory collapse and refractory hypotension resistant to vasopressors in neonates with infections.[9]

The mechanisms leading to dysfunction of the HPA axis are complex and likely include decreased production of corticotropin-releasing hormone, ACTH, and cortisol and the dysfunction of their receptors.[10,11] Tissue corticosteroid resistance is a well-known manifestation of chronic inflammatory diseases.[12] It is therefore likely that acute inflammation, similar to chronic inflammation, may be associated with tissue corticosteroid resistance.[13] Endotoxin and proinflammatory cytokines have been shown to cause impairment in glucocorticoid nuclear translocation.[14]

Dysfunction of the HPA axis, critical illness related corticosteroid insufficiency (CIRCI), and is defined as an inadequate cellular corticosteroid activity for the severity of the patient's illness. It occurs as a result of a decrease in adrenal steroid production or tissue resistance to glucocorticoids.[15–17]

Therefore, we aimed to clarify whether the circulatory collapse in critically ill neonates with HIE was a result of insufficient cortisol production or whether it was due to the limited ability of their adrenal gland to increase cortisol synthesis to withstand critical illness.

2. Methods

A total of 30 infants were analyzed in the study: 15 neonates in group A (neonates had HIE with vasopressor resistant hypotension) and 15 neonates in group B (neonates with HIE without vasopressor resistant hypotension). Both groups were matched regarding the APGAR score at birth and the stage of HIE and all of them were in grade III. History, examinations and laboratory investigation of serum cortisol and its precursor's concentrations were done. The study is collaboration between Suez Canal University, Egypt and Oulu University, Finland in the period from 1st of April 2015 to the beginning of December 2015. Ethical approval was obtained for the study, the principles outlined in the Declaration of Helsinki were followed, and informed consent was obtained from the parents. The neonates were of 37 to 41 weeks of gestation, who were aged from four to 14 days and suffering from HIE. We assumed that by the fourth day of life, the direct influence of the maternal compartment had disappeared and by the 14th day of life the function of the adrenal gland may have stabilized.[18]

Refractory hypotension was defined as a mean blood pressure $<$10% percentile for age not responding to inotropes, including dopamine 15 μg/kg per minute or dobutamine ten μg/kg per minute.[19] Blood pressure values were recorded by digital intra-arterial or external blood pressure. The blood pressure values that are presented in this study represent the average of three recordings.

During the 48 hours before blood sampling, the following were used as exclusion criteria: major surgery in the preceding week or major stress induced by medical procedures,[18,20] a congenital anomaly, postnatal corticosteroid treatments before blood sampling, and a maternal history of endocrine disorders.[19] Neonates with septicemia were also excluded as, according to Khashana et al, as septic neonates with therapy-resistant hypotension had higher DHEA than those without hypotension. Moreover sepsis is the common etiology for neonatal shock and may contribute as a major confounding factor.[9]

Blood specimen of two milliliters was withdrawn from the venous line and serum was separated and frozen at −20 °C. The time of the day when the sample was collected was not expected to modify the results obtained due to the lack of circadian rhythm in neonates.[21] We gave oral glucose 30% during sampling to decrease pain and stress during sampling.

Please cite this article in press as: Khashana A, Ahmed E, Hyperdehydroepiandrosterone in Neonates With Hypoxic Ischemic Encephalopathy and Circulatory Collapse, Pediatrics and Neonatology (2017), http://dx.doi.org/10.1016/j.pedneo.2016.09.010