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Urinary Nitric Oxide in Newborns with Sepsis

Thesis Submitted for partial fulfillment of M. Sc degree in Pediatrices

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Urinary Nitric Oxide in Newborns with Sepsis

Key words

Nitric Oxide – Urine – Sepsis – newborns.

Abstract

Background: Neonatal Sepsis is a major problem in newborn nurseries because of the difficulty in early diagnosis and because of high morbidity and mortality.

The objective of this study was to investigate whether urinary nitric oxide (NO) level could be useful for the diagnosis of infected newborns.

Methods: Urinary NO are measured for newborns with sepsis on the 1st and on the 4th day who were group of study (group I) and compared with age matched healthy control (group II).

Results: Ninety percent of the septic group showed increase in the urinary NO level during sepsis, while in the control group there was decrease in the NO level, the mean of NO on the 1st day in group (I) was (67.13 ± 50.03) and was (78.52 ± 36.80) in group (II), the mean of NO on the 4th day was (97.49 ± 65.75) while in group (II) was (56.87 ± 29.62) and the percentage change from 1st day was (76.47 ± 103.33) in group I but was (-30.81 ± 25.77) in group II.

Conclusion: Urinary NO level which are quick and easy to measure are higher in the infected newborns as compared with controls. The sensitivity of the test is good and the serial measurements of NO is recommended to early detection of sepsis.

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List of Abbreviation

ADP = Adenosine diphosphate

ARDS = Acute respiratory distress syndrome

ATP = Adenosine triphosphate

BBs = Blood barriers

BH4 = Tetra hydroptein

BW = Birth weight
BW = Birth weight

CBC = Complete blood picture

cGMP = Cyclic guanosin monophosphate

CMV = Cyto megalo virus CMV = Cyto megalo virus

cNOS = Constitutive Nitric Oxide Synthase

CNS = Central nervous system

CONS = Coagulase negative staph

CRH = Cortico tropin releasing hormone

CRP = C - Reactive protein
CSF = Cerebro spiral fluid

DIC = Disseminated intravascular coagulopathy

DNA = **Dinucleic** acid

ECMO = Extra corporeal membrane oxygenation

EM = **Electron microscopy**

eNOS = Endothelial Nitric Oxide Synthase

ESR = Erythrocyte sedmintation rate

FAD = Flavin adenine dinucleotide

FDP = Fibrin degradation products

FMN = Flavin mono nucleotide

G -CSF = Granulacyte colony stimulation factor

GA = **Gestational age**

GBS = Group B streptococcus

Gh = **Growth hormone**

GnRH = Gonadotropin releasing hormone HIV = Human immuno deficiency virus

HSS = Hematological scoring system

HSV = Herps simplex virus HVS = High vaginal swab

IFA = Immun fluorescent antibody

IgA = Immunoglobulin A

IgE = Immunoglobulin E

IgG = Immunoglobulin G

IgM = Immunoglobulin M

IL-6 = Interlukein 6

iNOS = Inducible Nitric Oxide Synthase

IPPV = Intermittent positive pressure ventilation

IT = Immature neutrophils / total
IVIG = Intravenous immunoglobulins

LA = Latex particle agglutination

LBW = Low birth weight LBW = Low birth weight

MBC = Minimum bactericidal concentration
MIC = Minimum inhibitory concentration

mRNA = Messenger ribo nucleic acid

NB = Newborn

NEC = Necrotizing entero colitis NICU = Neonatal intensive care urite

NK = Natural Killer

nNOS = Neuronal Nitric Oxide Synthase

PCR = Polymerase chain reaction

 PGE_2 = Prostaglandins E_2

PGES = Prostaglandin endoperoxide synthase

PMNLs = Poly morpho nuclear leucocytes

PPHN = Persistant pulmonary hypertension

PRH = Prolacting releasing hormone

PROM = Premature rupture of membrane

PT = Prothrombin time

PTT = Partial thromboplastin time

RBCS = Red blood cells

RDS = Respiratory distress syndrom

rG-CSF = Recombinant granulacyte colony stimulation

factor

RSV = Respiratory suncytial virus

SGA = Small gestational age

SIRS = Systemic inflammatory response syndrome

TFA = Immuno – fluorescent – antibody

TLC = Total leucocytic count TNF = Tumous necrosis factor TNF α = Tumor necrosis factor- α

UTI = Urinary tract infection

VD = Vaginal delivery

VIQ = Ventilation perfusion matching

VLBW = Very low birth weight VLBW = Very low birth weight

WBCs = White blood cells

Correction sheet

Page		
2	isolation	Isolation
4	It occur	It occurs
27	Early Manifestations	Early manifestations
29	Late manifestations	Late manifestations
96	in 1 st day	on 1st day
	nitric oxide	Nitric Oxide
100	Hospital	hospital
103	cytomegal virus	cytomegalvirus
107	(forceps used)	removed

Chapter 1 Sepsis of Neonates

Sepsis of Neonates

Introduction:

Sepsis as either primary pathology or a complication of other illness, is a major cause of neonatal mortality and morbidity all over the world. The impact of infection can be reduced as international comparisons show, but even in the most technologically advanced countries, the contribution of a susceptible host, non specific clinical presentation and an ever changing population of pathogens makes for a great challenge (*Roberton et al.*, 1999).

Infection is responsible for approximately 2 million neonatal deaths per year in developing countries. In other industrialized countries, the mortality rate has decline to 5.1 per 1000 liver births due to progress in obstetrics and neonatal intensive care unit and improved survival particularly preterm and low birth weight neonates, which for the immunological state and the invasive therapies they are subjected to and extremely at risk for sepsis (*Lanari et al.*, 2001).

Definition:

Neonatal sepsis is defined as a clinical syndrome of bacteremia with systemic signs and symptoms of infection and a positive culture for central body fluid.

The National Neonatology Forum's definition for hospital is as follows:

(A) Probable sepsis:

Infants with clinical picture suggestive of sepsis with one or more of the following criteria:

a) Existence of predisposing factors: maternal fever or foul smelling liquor or prolonged rupture of membranes (>12hrs) or presence of gastric polymorphs.

- b) Positive septic screen (two of the four parameters namely, TLC $< 5000/\text{mm}^3$, band to total polymorph ratio of > 0.2, CRP > 6ug/ml, and ESR>10mm 1st hr).
- c) Radiological evidence of pneumonia.

(B) Proven sepsis:

Infants with clinical picture of sepsis with either

- Isolation of pathogens from blood, CSF and urine.
- Autopsy evidence.

(Guha et al., 2005)

Neonatal sepsis is resulting from the pathophysiological effect of local or systemic infection in the 1st month of life (*Behrman*, *1996*).

Sepsis is a set of acute physiologic responses to infection. It is defined by presence of two or more of the following manifestations; fever or hypothermia, tachycardia, tachypnea, and an abnormal white blood cells (WBCs) or increase in immature forms (*Gotoff*, 2000).

Incidence:

The incidence rate of neonatal sepsis varies from country to country, nursery to nursery and within the same nursery at different times (*Kliegman*, 1998).

The incidence of bacterial sepsis and meningitis, especially for *Gram negative enteric bacilli*, is higher in males than in females. Premature/ preterm infants have an increased incidence of sepsis. The incidence of sepsis is significantly higher in infants with very low birth weight (VLBW) <1000 gm at 76 per 1000 live births, than in infants with birth weight BW of 1000-2000 gm at 8 - 9 per 1000 live births.

The risk of death or meningitis from sepsis is higher with low birth weight (LBW) than full term neonates (*Guha et al.*, 2005).