Estimation Of some inflammatory markers in Neonatal Sepsis

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Abstract

Adhesion of leukocytes to vascular endothelium is an early step in the event leading to cellular extravasation and development of an inflammatory response. A number of molecules; including E-Selectin and ICAM-1 that mediates leukocytic endothelial adhesion have been identified.

Several studies have suggested that adhesion molecules could be useful in the early diagnosis of neonatal sepsis. The present study was performed to find out whether shedding of E-Selectin and ICAM-1 is an established component of the immune system and response to infection at birth. The aim of the study was to assess and compare soluble E-Selectin and ICAM-1 levels in the sera of 60 neonates (30 preterm, 30 full term) with clinically proven sepsis and 20 healthy neonates by ELIZA technique.

Key words:

Neonatal septicemia, adhesion molecules, E-Selectin, ICAM-1

List of Abbreviations

ADCC: Antibody dependant cell mediated cytotoxicity.
AMs: Adhesion molecules.
APCs: Antigen presenting cells.
BPD: Bronchopulmonary dysplasia.
CDC: Centre for disease control and prevention.
CMV: Cytomegalovirus.
CFRs: Case fatality rates.
CONs: Coagulase negative Staphylococci.
CTLs: Cytotoxic T Lymphocytes.
CNS: Central nervous system.
CFUs: Colony forming units.
CR: Complement repeats.
CRP: C-reactive protein.
DIC: Disseminated intravascular coagulopathy.
Desmolgein: Dsg.
Desmocollins: Dsc.
EOS: Early onset sepsis.
ELAM-1: E-Selectin.
EGF: Epidermal growth factor.
ECM: Extracellular matrix.
Fas: Factor for apoptotic signal.
GMP-140: P-Selectin.
GBS: Group B Streptococci.
G-CSF: Granulocyte colony stimulating factor.
GLYCAM-1: Glycosylated cell adhesion molecule-1.
GP: Platelet glycoprotein.
HEV: High endothelial venules.
HIV: Human Immunodeficiency virus.
HSV: Herpes Simplex virus.
IL 6: Interleukin 6.
IFNα: Interferon alpha.
IFN β: Interferon beta.
IFN γ: Interferon gamma.
ICAM-1: Intracellular adhesion molecules one.
I.T ratio: Immature/total neutrophil ratio.
IVIG: Intravenous Immunoglobulin.
IgSF: Immunoglobulin superfamily.

LAM-1: L-Selectin.
LECAM-1: L-Selectin.
LPA: Latex particle agglutination.
LFA-1: Leukocyte function adhesion 1.
LFA-2: Leukocyte function antigen 2.
LECAM-3: P-Selectin.
LPS: Lipo-polysaccharides.
MADCAM-1: Mucosal adressin cell adhesion molecule-1.
MRSA: Mecthicilin resistant staphylococcus aureus.
MPV: Mean platelet volume.
NICU: Neonatal Intensive Care Unit.
NK: Natural killer cells.
NNIS: National Nosocomial Surveilance system.
PROM: Premature rupture of membranes.
PMN: Polymorphnuclear leucocytes.
PCR: Polymerase chain reaction.
PADGEM: P-Selectin.
PSGL-1: P-Selectin glycoprotein ligand.
PE-CAM-1: Platelet-endothelial cell adhesion molecule-1.
STD: Sexually transmitted disease.
sLex: Sialyl Lewisx.
TNFα: Tumor necrosis factor alpha.
TLC: Total leukocyte count.
Th: T helper cells.
TCR: T cell receptor.
UTI: Urinary tract infection.
vWF: von Willebrand Factor.
VLBW: Very low birth weight.
VLA: Very late activation.
VCAM-1: Vascular adhesion molecule-1.

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Introduction & Aim of the work

Neonatal sepsis or sepsis neonatorum; are terms used to describe the systemic response to infection in newborn infant ***(Scharg , 2005)***.

In developed countries, infection is still one of the most common causes of mortality and hospitalization in pediatrics and newborn infants. The incidence of neonatal sepsis ranges from 1 to 10 cases for every 1,000 infants, with much higher values found in preterm, low birth weight newborn infants and generally in newborn infants admitted to neonatal intensive care units (NICU) ***(Bizzaro et al., 2005)***.

Clinical diagnosis of sepsis is not always easy, because symptoms and signs are not specific and a dramatic deterioration of clinical conditions can occur very rapidly even in asymptomatic newborn infants long before blood culture results are available ***(La Rosa., 2008).***

A number of diagnostic tests are currently used in assessing a neonate suspected of sepsis. Unfortunately, the sensitivity of those tests is very low in the early diagnosis of neonatal infection. Therefore, it is necessary to find biological markers that react rapidly after the onset of the inflammatory process in order to use them in the early diagnosis of neonatal sepsis ***(Sastre et al.,2007)***.

Adhesion of leukocytes to vascular endothelium is an early step in the events of sepsis leading to cellular extravasation and development of an inflammatory response ***(Washbourne et al., 2004)***.

A number of molecules that mediate leukocyte - endothelial adhesion has been identified, including E-selectin and ICAM-1.

Expression of adhesion molecules is strongly up regulated by cytokine activation ***(Hang., 2005).***

Increased levels of pro- inflammatory cytokines have been found in neonatal infection and accordingly up regulated shedding of soluble adhesion molecules may be precipitated ***(D'alquen., 2005).***

Since neonatal sepsis remains a major cause of mortality and morbidity in newborn infants, symptoms and signs are non specific, several studies have searched for early new diagnostic parameters.

The aim of the present study is to assess the level of inflammatory markers; ICAM-1 and E-selectin in neonates with sepsis to be used as an early diagnostic tool for detection of severe sepsis in preterm and full term neonates.

NEONATAL SEPSIS

Definition:

Neonatal sepsis or sepsis neonatorum is characterized by bacteraemia and clinical symptoms caused by microorganisms and their toxic products ***(Waheed et al., 2003)***. Neonatal sepsis is a term confined to infants less than three months old ***(Daniett et al., 2004).*** The criteria for neonatal sepsis should include documentation of infection in a newborn infant with a systemic illness in which non-infectious explanations for the abnormal patho-physiologic state are excluded or unlikely ***(Berham et al., 2000).***

CLASSIFICATION OF NEONATAL INFECTIONS

Neonatal infections are usually classified according to time and mode of onset into three categories:

i) Congenital infection, acquired in utero by vertical transmission with onset before birth.

ii) Early-onset neonatal infections, acquired by vertical transmission in the perinatal period, either shortly before or during the process of birth.

iii) Late-onset infections, acquired by horizontal transmission either in the community or nursery ***(Baltimore, 2003).***

Infants with very late-onset (late- late) onset sepsis are usually encountered in very low birth weight (VLBW) survivors who remain hospitalized for several weeks after birth. The major risk factor for sepsis in these infants is violation of anatomical barriers to infection by intravascular catheters or prolonged exposure to antimicrobial agents ***(Edward's & Baker ,2004).***