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New trend in management of neonatal septicemia

Essay

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الطرق الحديثة لعلاج العدوى الميكروبية في الأطفال حديثي الولادة

مقال

توطئة للحصول على درجة الماجستير في طب الأطفال

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وَأَنْزَلَ اللَّهُ عَلَيْكَ الْكِتَابَ وَالْحِكْمَةَ وَعَلَّمَكَ مَا

لَمْ تَكُنْ تَعْلَمُ وَكَانَ فَضْلُ اللَّهِ عَلَيْكَ عَظِيمًا



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To my Family

- *My father, My mother.*

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List of Contents

ITEM	PAGE
Introduction	1
Aim of the work	4
Review of Literature:	
Definitions and Classification of neonatal sepsis	5
Prevalence and Epidemiology	9
Modes of Transmission and Pathogenesis	11
Immune System of Newborn	15
Etiology&Risk Factors	29
Causative Organisms	34
Clinical Manifestation	45
Diagnosis and Investigation	49
Prevention&Mangement	79
Summary&Conclusion	92
References	96
Arabic Summary	1

List of Tables

ITEM	PAGE
Table(1) :Clinical Manifestations of Transplacental Infection	46
Table(2) :Septic shock definitions	49
Table (3):Serious Systemic Illness in Newborns: Differential Diagnosis of Neonatal Sepsis.	57
Table(4): Clinical symptoms and signs of severe neonatal illness including sepsis.	60
Table(5): Normal values of CSF in newborn period.	63
Table(6) : Hematological scoring system	67
Table(7) : Performance of scoring system in preterm and term infants for sepsis	68

List of Figures

Figures	PAGE
Figure (1):Pathogenesis of congenital and neonatal infections.	14
Figure(2):Suspected Neonatal Sepsis	87

List of Abbreviation

ITEM	ABBREVIATION
ADCC	Antibody-dependent cell-mediated cytotoxicity
APH	Ante partum hemorrhage
APPs	Active antimicrobial proteins and peptides
APR	Acute phase reactants
BPD	broncho pulmonary dysplasia
CMV	Cytomegalovirus
CNS	Central nervous system
CoNS	Coagulase-negative Staphylococcus
CRP	C-reactive protein
DC	Dendritic cells
EOS	Early onset sepsis
ESBL	extended spectrum beta-lactamase
ESR	Erythrocyte sedimentation rate
GBS	Group B streptococcal
GCSF	Granulocyte colony stimulating factor
GM-CSF	Granulocyte/ monocyte colony stimulating factor
GM-CSF	Granulocyte-Macrophage colony stimulating factor
GU	Genitourinary
HBV	Hepatitis B virus
HSV	Simplex virus
I/T	Immature to total neutrophil
IFN-γ	Interferon-gamma
Ig	Immunoglobulin
IL	Interleukin
IL	Interleukin
IVIG	Intravenous Immune Globulin

ITEM	ABBREVIATION
LBP	lipopolysaccharide-binding protein
LBW	Low birth weight
LOS	Late onset Sepsis
MAP	Mean arterial pressure
MRSA	Methicillin resistant staphylococcus aureus
MSAF	Meconium stained amniotic fluid
n- IMCI	Integrated Management of Childhood Illness
NEC	Necrotizing enterocolitis
NICHD	National Institute of Child Health and Development
NICUs	Neonatal intensive care units
NK	Natural killer
NNPD	National Neonatal Perinatal Database
NPVs	Negative predictive values
PCT	Procalcitonin
PET	Pre eclamptic toxemia
PIH	Pregnancy induced hypertension
PMNs	Polymorph nuclear cells
PROM	Premature rupture of membrane
RCTs	Randomized controlled trials
RDS	Respiratory distress syndrome
RES	Reticuloendothelial system
SAA	Serum a myloid A protein
SIRS	Systemic inflammatory response syndrome
TB	Tuberculosis
Th1	T helper 1
TLC	Total leukocyte count
TLR	Toll-like receptor
TLRs	Toll-like receptors

ITEM	ABBREVIATION
TLRs	Through toll-like receptor
TNF	Tumor necrosis factor
TNF-a	Tumor necrosis factor-alpha
TPN	Total parenteral nutrition
UTI	Urinary tract infection
VLBW	Very low birth weight
WBC	White blood cell
WHO	The World Health Organization

Introduction

Neonatal sepsis or septicaemia is a clinical syndrome characterized by systemic signs of circulatory compromise (e.g. poor peripheral perfusion, pallor, hypotonia, poor responsiveness) caused by invasion of the bloodstream by bacteria in the first month of life. In the pre-antibiotic era neonatal sepsis was usually fatal. Case fatality rates in antibiotic treated infants now range between 5% and 60% with the highest rates reported from the lowest income countries. (*Thaver and Zaidi, 2009*)

The World Health Organization (WHO) estimates that 1 million deaths per year (10% of all under-five mortality) are due to neonatal sepsis and that 42% of these deaths occur in the first week of life. (*Edmond and Zaidi, 2010*)

Among many risk factors the most important risk factor for neonatal sepsis is low birth weight. Other main risk factors are invasive procedures in the postnatal period and inadequate hand washing before and after handling babies. (*Chacko Betty and Sohi, 2005*)

Prematurity has got special challenge for clinicians and also other medical staff, such as microbiologists. Immature host defense mechanisms support early-onset sepsis, which can be very serious with very high mortality. While the past decade has been marked by a significant decline in early-onset group B streptococcal (GBS) sepsis in both term and preterm neonates, the overall incidence of early-onset sepsis has not decreased in many centers, and several studies have found an increase in sepsis due to gram-negative organisms. With increasing survival of these more fastidious preterm infants, late-onset sepsis or specially nosocomial bloodstream infection (BSI) will continue to be a challenging complication that affects other morbidities, length of hospitalization, cost of care, and mortality

rates. Especially the very low birth weight (VLBW) infants sensitive to serious systemic infection during their initial hospital stay. Sepsis caused by multiresistant organisms and *Candida* spp. are also increasing in incidence, has become the most common cause of death among preterm infant. ***(Kristóf et al., 2009)***

Maternal immunization is an important method of providing neonates with appropriate antibodies as soon as they are born. ***(Healy and Baker, 2007)***

A recent modeling study estimated that vaccination with *S. agalactiae* vaccine would prevent 4% of US preterm births and 60%–70% of neonatal *S. agalactiae* infection. ***(Sinha et al., 2005)***

The only intervention proven to decrease the incidence of early-onset neonatal sepsis is maternal treatment with intrapartum intravenous antimicrobial agents for the prevention of GBS infections. ***(Richard et al., 2012)***

New studies from Malawi and Nepal indicate that maternal antiseptic interventions such as vaginal chlorhexidine during labour may have a significant impact on rates of neonatal mortality and sepsis in developing countries. However, other studies from high-income countries have demonstrated little effect on rates of HIV or neonatal infection. ***(Edmond and Zaidi, 2010)***

Neonatal micronutrient supplementation trials of newborn vitamin A supplementation have shown encouraging reductions in neonatal mortality, and more trials are underway. ***(Gogi and Sachdev, 2009)***

As neonatal sepsis can be rapidly fatal if left untreated, highly effective antibiotic therapy must be used and delays in the provision of care must be minimized. Treatment must be effective against the causative pathogen,

safe for the newborn, and feasible to deliver reliably in the hospital or community setting.**(Edmond and Zaidi, 2010)**

Oral antibiotic therapy must be considered in settings where referral is not possible and there are no health care providers trained to give parenteral antibiotics.**(Darmstad et al., 2009)**

Recent data suggest an association between prolonged empirical treatment of preterm infants (≥ 5 days) with broad-spectrum antibiotics and higher risks of late onset sepsis, necrotizing enterocolitis, and mortality. To reduce these risks, antimicrobial therapy should be discontinued at 48 hours in clinical situations in which the probability of sepsis is low.**(Richard et al., 2012)**

The development of alternative anti-infection modalities has become one of the highest priorities of modern medicine and biotechnology.**(Vinodkumar et al., 2005)**

Results of studies evaluating IV immunoglobulin have been mixed, but a meta analysis found that Therapy with intravenous immune globulin had no effect on the outcomes of suspected or proven neonatal sepsis.**(Brocklehurst et al., 2011)**

Administering granulocyte-macrophage colony-stimulating factor (GM-CSF) increases neutrophil counts but does not reduce neonatal sepsis.**(Marlow et al., 2012)**

Pentoxifylline is an anti-inflammatory drug that may be able to reduce sepsis and complications from sepsis. Pentoxifylline in combination with antibiotics reduces mortality from sepsis in newborns without adverse effects. More research is needed on pentoxifylline and other anti-inflammatory drugs that might be used for sepsis in newborns. **(Haque and Mohan, 2011)**