MULTI–ORGAN DYSFUNCTION

IN NEONATES WITH

HYPOXIC-ISCHEMIC ENCEPHALOPATHY

A thesis

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Abstract

Introduction: Perinatal hypoxic-ischemic cerebral injury remains an important issue partly because it is the most clearly recognized cause of cerebral palsy. Multi-organ dysfunction (MOD) is one of four consensus based criteria for the diagnosis of intrapartum asphyxia. The theoretical concept behind MOD is the diving reflex.

Objectives: the aim of this study was to assess the patterns of involvement of each organ/system and combinations of involvement of these organs in infants with post-asphyxial hypoxic-ischemic encephalopathy (HIE).

Patients and methods: This is a retrospective study carried out on 100 hypoxic ischemic neonates who were admitted on their first day of life to the Neonatal Intensive Care Unit (NICU) in Kasr El Aini Hospital, Cairo University, Egypt.

Results: Multi-organ dysfunction (MOD) occurred in 74% of our patients with renal dysfunction the commonest to occur (64%). Two-organ dysfunction occurred in 49% of patients followed by one-organ dysfunction in 38% of patients with MOD. Mortalities increased as the number of organ dysfunction increased.

Conclusion: We found evidence in support of the MOD criterion in the definition of asphyxia, with renal dysfunction being the most commonly occurring dysfunction.

Key words: HIE, perinatal asphyxia, multi-organ dysfunction.

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List of abbreviations

AAP ..... American Academy of Pediatrics

ACOG..... American College Of Obstetrics And ynecology

ACTH ..... Adrenocorticotropic Hormones

ADP ..... Adenosine Diphosphate

aEEG..... Amplitude-Integrated Electroencephalogram

AFV..... Amniotic Fluid Volume

AIF..... Apoptosis-Inducing Factor

AMP ..... Adenosine Monophosphate

AMPA ..... Amino-3-Hydroxy-5-Methyl-4 Isoxazole Propionate

ANP ..... Atrial Natriuretic Peptide

APAF-1 ..... Apoptotic Protease-Activating Factor-1

ARF..... Acute Renal Failure

ATN ..... Acute Tubular Necrosis

ATP ..... Adenosine Triphosphate

BP..... Blood Pressure

BPM ..... Beat Per Minute

BPP..... Biophysical Profile

C4 ..... Complement 4

CA_1 ..... Cornu Ammonis 1

CA^{2}+ ..... Serum Ionized Calcium

CBF ..... Cerebral Blood Flow

CBFV..... Cerebral Blood Flow Velocity

CK-BB ..... Creatine Kinase Brain Isoenzyme

CNS..... Central Nervous System

CO ..... Cardiac Output

CP ..... Cerebral Palsy

CPAP..... Continuous Positive Airway Pressure

CPP ..... Cerebral Perfusion Pressure

CS ..... Cesarean Section

CSF ..... Cerebrospinal Fluid

CST ..... Contraction Stress Test

CT ..... Computed Tomograph

cTn ..... Cardiac Troponin

cTnI ..... Cardiac Troponin I

cTnT..... Cardiac Troponin T

DALYS..... Disability-Adjusted Life Years

V

DIC..... Disseminated Intravascular Coagulation

EAA ..... Excitatory Amino Acids

ECG..... Electrocardiogram

EEG..... Electroencephalogram

EFM ..... Electronic Fetal Monitoring

EGCG ..... Epigallocatechin Gallate

EGF..... Epidermal Growth Factor

ER ..... Endoplasmic Reticulum

FHR..... Fetal Heart Rate

FT_4 ..... Free Thyroid Hormone

GABA ..... Gamma Amino Butyric Acid

GFR..... Glomerular Filtration Rate

GH ..... Growth Hormone

GM1 ..... Monosialoganglioside

H_2 O_2..... Hydrogen Peroxide

HI ..... Hypoxic Ischemic

HIE..... Hypoxic Ischemic Encephalopathy

HOCL ..... Hypochlorous Acid

HR ..... Heart Rate

ICP ..... Intracranial Pressure

IDDM ..... Insulin-Dependent Diabetes Mellitus

IGF-1..... Insulin-Like Growth Factor 1

IL-18 ..... Interleukin 18

IL-1β ..... Interleukin 1-B

IUGR..... Intrauterine Growth Retardation

L-NAME..... Nω-Nitro-L-Arginine Methyl Ester

MRI ..... Magnetic Resonance Imaging

MRS ..... Magnetic Resonance Spectroscopy

MgSO4 ..... Magnesium Sulphate

MK-801 ..... [(+)-5-Methyl-10,11-Dihydro-5H-Dibenzo[A,D] Cyclohepten-5,10-Imine Maleate)]

MSAF..... Meconium-Stained Amniotic Fluid

mTAL..... Medullary Thick Ascending Limb

NE..... Neonatal Encephalopathy

NEC..... Necrotizing Enterocolitis

NICUs ..... Neonatal Intensive Care Units

NMDA ..... .N-Methyl-D-Aspartate

NO ..... Nitric Oxide

NOS ..... Nitric Oxide Synthase

NPO ..... Nothing Per Mouth

NSCs ..... Neural Stem Cells

NST ..... Non Stress Test

$O2^-$ ..... Superoxide Anion

OH ..... Hydroxyl Radical

PAF ..... Platelet-Activating Factor

PCA ..... Postconceptual Age

PDA ..... Patent Ductus Arteriosus

PG ..... Prostaglandins

PGE_2 ..... Prostaglandins E_2

PGI_2 ..... Prostaglandins I_2

PLIC ..... Posterior Limb of The Internal Capsule

PNA ..... Perinatal Asphyxia

PPHN ..... Persistent Pulmonary Hypertension

PVL ..... Periventricular Leukomalacia

PROM……Premature Rupture of Membranes

RDS..... Respiratory Distress Syndrome

ROS ..... Reactive Oxygen Species

SGPT ..... Serum Glutamic Pyruvic Transaminase

SIADH ..... Syndrome of Inappropriate Antidiuretic Hormone Secretion

SOGC ..... Society of Obstetricians And Gynaecologists of Canada

TGF-β1..... Transforming Growth Factor B1

TNF- α ..... Tumor Necrosis Factor A

TNF..... Tumor Necrosis Factor

US..... Ultrasound

VEGF ..... Vascular Endothelial Growth Factor

WHO ..... World Health Organization

Introduction And Aim of The Study

Introduction

Neonatal encephalopathy remains a major cause of neurodevelopmental disability in term infants, occurring in 1 to 2 per 1000 live term births. The term hypoxic-ischemic encephalopathy has also been used to describe this clinical condition, but it is misleading because many of the cases of neonatal encephalopathy have not experienced documented hypoxic-ischemic insult ***(Miller et al., 2004).***

The etiology of perinatal HIE includes those circumstances that can affect the cerebral blood flow in the fetus and newborn compromising the supply of oxygen to the brain. They may develop antepartum (20%), intrapartum (30%), intrapartum and antepartum(35%), or postpartum (10%). HIE develops in the setting of perinatal asphyxia, which is a multiorgan system disease (***Legido et al., 2000).***

Hypoxia and ischemia can cause damage to almost every tissue and organ of the body and various target organs involved have been reported to be kidneys in 50% followed by CNS in 28%, CVS in 25% and lungs in 23% cases ***(Gupta et al., 2005).***

Multi-organ dysfunction (MOD) is one of four consensus based criteria for the diagnosis of intrapartum asphyxia. The theoretical concept behind MOD is the diving reflex (conservation of blood flow to vital organs at the cost of non-vital organs) ***(Shah et al., 2004)***

Excessive stimulation of glutamate receptors appears to play an important role in the pathogenesis of neonatal brain injuries caused by lack of oxygen ***(Johnston, 2001).***