Ain Shams University

Faculty of Medicine

Department of Anesthesiology, Intensive care and Pain Management

PERIOPERATIVE ANESTHETIC PREVENTION OF NEUROLOGICAL INSULTS DURING PEDIATRIC CARDIAC SURGERIES

Essay

Submitted for the partial fulfillment of master degree in Anesthiology

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جامعة عين شمس
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الوقاية التخديرية من الإصابات العصبية خلال فترة ما حول جراحة القلب للأطفال

رسالة توطئة للحصول على درجة الماجستير في التخدير

مقدمة من

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List of Abbreviations

ACP	Antegrade Cerebral Perfusion
BDNF	Brain Derived Neurotrophic Factor
BIS	Bispectral Index Monitor
BP	Blood Pressure
CaO2	Arterial Oxygen Content
CBF	Cerebral Blood Flow
CBFV	Cerebral Blood Flow Velocity
CHD	Congenital Heart Disease
CK-BB	Creatine Kinase Brain Band
$CMRO_2$	Cerebral O_2 Metabolic Rate
CNS	Central Nervous System
CO	Cardiac Output
CO_2	Carbon Dioxide
CPB	Cardiopulmonary Bypass
CPP	Cerebral Perfusion Pressure
CSF	Cerebrospinal Fluid
CVR	Cerebrovascular Resistance
DHCA	Deep Hypothermic Circulatory Arrest
EEG	Electroencephalography
eNOS	Endothelial Isoform No Synthase
EPO	Erythropoietin
EPOR	Erythropoietin Receptor
FIO_2	Fractional Inspired Oxygen
GABA	Gamma-Aminobutyric Acid
GMH-IVH	Germinal Matrix Intraventricular Hemorrhage
HbO_2	Oxyhaemoglobin
HbO_2	Oxyhaemoglobin
HbT	Total Haemoglobin
Hbt	Total Haemoglobin
HCT	Hematocrit

HHb	Deoxy-Haemoglobin
HI/R	Hypoxic-Ischemic/ Reperfusion
HIF-1 A	Hypoxia Inducible Factor 1α
HITS	High-Intensity Transient Signals
ICH	Intracranial Hemorrhage
ICU	Intensive Care Unit
iNOS	Inducible Isoform
LCOS	Low Cardiac Output Syndrome
LFB	Low-Flow Cardiopulmonary Bypass
MCA	Middle Cerebral Artery
Nfκb	Nuclear Factor Kappa B
NIRS	Near-Infrared Spectroscopy
NMDA	N-Methyl-D-Aspartate
NO	Nitric Oxide
NSE	Neuron Specific Enolase
PAF	Platelet-Activating Factor
PGE1	Prostaglandins E1
PVL	Periventricular Leukomalacia
Q10	ratio of two metabolic rates separated by a 10°C
RCP	Retrograde Cerebral Perfusion
ROS	Reactive Oxygen Species
rSO2	Regional Oxygen Saturation
SCO_2	Cerebral Oxygen Saturation
$SjVO_2$	Jugular Venous Oxygen Saturation
TCD	Transcranial Doppler
VEGF	Vascular Endothelial Growth Factor
Vmca	Middle Cerebral Blood Flow Velocity

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Introduction

With advances in surgical techniques and medical care of pediatrics with congenital heart disease (CHD), mortality rates have significantly declined and more effort is being made toward preventing morbidity associated with pediatrics cardiac surgery. In particular, neurologic morbidity has been identified to be problematic in pediatrics with CHD ***(Bellinger et al., 2003)*.**

Although early postoperative central nervous system (CNS) sequelae such as stroke and seizures occur in a small percentage of pediatrics with CHD, the importance of more subtle neurologic findings at long-term follow-up is being increasingly recognized. These findings may include fine and gross motor impairments, speech and language delays, and disturbances in visual-motor and visual-spatial abilities, attention-deficit disorders, learning disorders, and impaired executive functioning ***(Menache et al., 2002).***

Mechanisms of (CNS) injury in infants undergoing cardiac surgery include: hypoxia-ischemia, emboli,

reactive oxygen species, and inflammatory microvasculopathy.

Preoperatively, the primary focus is on preventing hypoxic-ischemic injury and thromboembolic insults ***(Licht et al., 2004)***.

Modifiable intraoperative factors associated with (CNS) injury include: pH management, hematocrit during cardiopulmonary bypass, regional cerebral perfusion, and the use of deep hypothermic circulatory arrest ***(Shen et al., 2003).***

Postoperatively, secondary neurologic injury may be related to post-cardiopulmonary bypass alterations in cerebral autoregulation and additional hypoxic-ischemic insult, seizures, or other issues associated with prolonged intensive care unit stay ***(Dent et al., 2006).***

In addition to modifiable perioperative factors, prenatal, genetic and environmental factors are known to be important ***(Glauser et al., 1990).***

The heightened attention toward brain functioning and neurodevelopment has generated increased utility of neurologic monitors that are used for detection of cerebral hypoxia, perfusion abnormalities, and

electrophysiological derangements ***(Newman et al., 2001).***

The neuromonitors most commonly employed in the current era include near-infrared spectroscopy, transcranial doppler and continuous electroencephalography. These modalities, in conjunction with conventional physiologic intensive care monitoring, could enhance the ability to prevent injury that results from hypoxia ischemia, emboli, hypocarbia, hypotension and hyperthermia ***(Limperopoulos et al., 2002).***

Cerebral monitoring may improve neurologic outcome after pediatric cardiac surgery, reducing the burden that neurologic deficits pose to patients and families ***(Limperopoulos et al., 2002)***.

Chapter 1

Mechanisms of neurological insults in pediatrics with heart disease

Mechanisms of Neurological Insults In Pediatrics With Heart Disease

Injurious mechanisms were thought earlier to be confined to intraoperative. Nowadays, it is believed that such mechanisms coexist all through preoperative, intraoperative and postoperative periods ***(McQuillen et al., 2007).***

Before proceeding with the mechanisms of neurological injury it is necessary to indentify various presentations, both clinical and pathological, of neurological injuries which can be detected by neurological examination and or neuroimaging techniques preoperatively or postoperatively.

This chapter will discuss different mechanisms of neurological injuries and their clinical and pathological presentations trying to confine them to specific vulnerable periods (preoperative, intraoperative, and postoperative).

Clinical Presentations of Neurological Injury

Clinical presentations vary with different forms of congenital heart disease (CHD) and the incriminated mechanisms responsible for the neurological injury. Clinical presentations are going to be discussed before proceeding with the mechanisms of neurological.

Clinical presentation of brain injury abnormalities on neurological exam may be detected preoperatively or in the immediate post operative period. Neurobehavioral abnormalities prior to surgery were reported in greater than 50% of new-borns (<1 month at surgery) and 38% of infants (between 1 month and 2 years) with CHD. These abnormalities included hypotonia, motor asymmetry, absent suckling reflex, lethargy, restlessness/agitation , and autism like features . Abnormalities generally persisted or worsened postoperatively, with additional findings of cranial nerve abnormalities and choreoathetosis (***Limperopoulos et al., 2002)***.

Other researchers reported the incidence of an acute neurological event (defined as seizure, tone abnormality, or choreoathetosis) to be 25% within the first week after surgery and 56% after the first week. While, 17% of patients in these series presented with clinical findings preoperatively ***(Chock et al., 2006)***.

In other reports, the incidence of clinical post operative seizure is 4–11% and may be detected by continuous electroencephalography