Cereberal Protection Strategies following Cardiopulmonary Resuscitation

Essay

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Mohamed Essam Eldin

List of Contents

Page No.

List of Abbreviations

ACP : Advance Care Paramedic

ALS : Advanced Life Support

AMI : Acute Myocardial Infarction

APACHE : Acute Physiology and Chronic Health Evaluation

ARDS : Acute Respiratory Distress Syndrome

ATP : Adenosine Triphosphate

BLS : Basic Life Support

BTLS : Basic Trauma Life Support

CBF : Cerebral Blood Flow

cLMA : Classic Laryngeal Mask Airway

$CMRO_2$: Cerebral Metabolic Rate of oxygen consumption

COPD : Chronic Obstructive Pulmonary Disease

CPR : Cardiopulmonary Resuscitation

CSF : Cerebrospinal Fluid

CT : Computed Tomography

ECG : Electrocardiographic

EEG : Electroencephalographic

EMS : Emergency Medical Services

EMTs : Emergency Medical Technicians

$ETCO_2$: End-Tidal carbon dioxide

FOUR : Full Outline of Un-Responsiveness

FPR : False-Positive Rate

GCS : Glasgow Coma Scale

ICP : IntracranialPressure

ICU : Intensive Care Unit

IO : Intraosseous

IO : Intraosseous

IV : Intravenous

LMA : Laryngeal Mask Airway

LT-D : Disposable version of the Laryngeal Tube

MRI : Magnetic ResonanceImaging

NRCPR : National Registry of Cardiopulmonary Resuscitation

NSE : Neuron-Specific Enolase

OHCA : Out-of-Hospital Cardiac Arrest

OPALS : Ontario Prehospital Advanced LifeSupport Trial

PALS : Pediatric Advanced Life Support

PCI : Percutaneous Coronary Intervention

PEEP : Positive End-Expiratory Pressure

PHTLS : Pre-Hospital Trauma Life Support

QEEG : Quantitative EEG

ROSC : Return Of Spontaneous Circulation

SSEPs : Somatosensory-Evoked Potentials

STEMI : ST-Elevation Myocardial Infarction

TB : Tuberculosis

VF/VT : Ventricular Fibrillation/pulseless Ventricular Tachycardia

List of Figures

INTRODUCTION

Cardiac arrest may occur at the endpoint of many diseases. In all cases management has two priorities; rapid restoration of cardiopulmonary functions and minimization of ischemic damage to end organs **(Sulivan, 2011)**.

The pathphysiology of post-cardiac arrest syndrome is commonly complicated by persisting acute pathology that caused or contributed to the cardiac arrest itself **(Nolan et al., 2008)**.

Therapeutic hypothermia and treatment of the underlying cause of cardiac arrest impacts survival and neurological outcomes. Protocolized hemodynamic optimization and multidisciplinary early goal-directed therapy protocols have been introduced as part of a bundle of care to improve survival rather than single interventions **(Callaway et al., 2010)**.

Current recommendations suggest consideration of induced hypothermia for comatose adult patients with return of spontaneous circulation (ROSC) after in-hospital cardiac arrest of any initial rhythm or after out-hospital cardiac arrest (OHCA) with an initial rhythm of pulseless electric activity or a systole **(Holzer et al., 2005)**.

Mild therapeutic hypothermia (MTH) is the single most effective intervention and therefore the gold standard in post resuscitation care today. Therapeutic hypothermia had long been thought to unfold its cytoprotective properties simply via unspecific inhibition of Catabolic processes throughout the organism during the reperfusion period **(Holzer et al., 2005)**.

A novel development was the introduction of targeted cooling of cerebral structures instead of whole body cooling. Targeted cooling has been shown to gain effectiveness similar to whole body cooling while reducing nursing efforts during MTH **(Tsai et al., 2008)**.

Xenon's organ-protective properties have been shown in several models of neurologic injury including stroke, traumatic brain injury, and hypoxic-ischemic encephalopathy. Xenon may also be effective within a prolonged time frame after ROSC, ranging from 10 minutes up to 5 hour **(Fries et al., 2008)**.

Several systematic reviews evaluated predictors of poor outcome, including clinical circumstances of cardiac arrest and resuscitation, patient characteristics, neurological examination, electrophysiological studies, biochemical markers, and neuroimaging **(Wijdicks et al., 2006)**.

The most studied neuroimaging modalities are Magnetic Resonance Imaging (MRI) and Computed Tomography (CT) of the brain. Extensivecortical and subcortical lesions on MRI are associated withpoor neurological outcome **(Wijman et al., 2009)**.

AIM OF THE WORK

- The aim of this study is to review pathophysiology of post cardiac arrest syndrome and highlight cerebral resuscitation strategies and outcome of cardiac arrest survivors.

CEREBRAL BLOOD FLOW

The normal cerebral blood flow (CBF) is approximately 50ml/100g/min. This represents the average blood flow for the whole brain. Blood flow to the grey matter is higher at 80ml/100g/min, whereas flow to the white matter averages 20ml/100g/min **(Fields and Bhardwaj, 2011)**.

This represents about 14% of the cardiac output. There are critical thresholds for the cerebral blood flow. At about 20 ml/100g/min, loss of conciousness and electroencephalographic (EEG) slowing occurs **(Nortje and Menon, 2004)**.

Below 18ml/100g/min, ionic homeostasis is impaired and neurons converts to anaerobic metabolism and the EEG becoms flat. Loss of membrane intergity with massive calcium influx and irreversible damage occur at a cerebral blood flow of 10 ml/100g/min. The neuronal events caused by reduction in the cerebral blood flow is also time dependent **(Nortje and Menon, 2004)**.

At a flow of 18 ml/100g/min, infarction occurs at about 4 hours; at 15 ml / 100 g/ min it occurs in about 3.5 hours; at 10 ml /100 g /min it occurs at about 3 hours and at 5 ml/ 100g/ min at about 30 minutes **(Nortje and Menon, 2004)**.

Cerebral perfusion pressure (CPP):

The perfusion pressure (i.e arteriovenous pressure gradient) in the brain is more complex than that of other organs because it is confined within an uncompressible vault. It is dependent on the pressure difference between mean arterial pressure (MAP) measured at the brain level and the intracranial pressure (ICP).

This pressure difference is known as cerebral perfusion pressure. The normal CPP is 70 - 80 mmHg and the threshold for critical ischemia is 30- 40 mmHg. As seen from the equation below, even at normal MAP the elevated ICP above 20 mmHg will compromise CPP and therefore reduce cerebral blood flow.

$$CPP = MAP – ICP$$

$$MAP = Pd + 1/3 (Ps – Pd)$$

CPP: cerebral perfusion pressure

Map: mean arterial blood pressue

ICP: intracranial pressure

Pd: diastolic pressure

Ps: systolic pressure **(Taylor and Hirsch, 2010)**

Factors affecting CBF:

Various mechanisms exist that allow adequate basal CBF to supply the substrate demands of the brain. However, in addition, local regulatory mechanisms direct blood flow to regions that are particularly active (i.e blood flow is coupled to local mtabolic needs). Furthermore, the physiological variable influence CBF **(Tylor and Hirsch, 2010)**.

Flow – metabolism coupling and local chemical regulators:

Local neuronal activity causes increase in cerebral metabolic requirment of oxygen and glucose and is accompained by increased regional CBF to match glucose and oxygen use with delivery **(Nortje and Menon, 2004)**.

The parallel changes in CBF with cerebral metabolic requirment of oxygen and glucose is known as flow – metabolism coupling. There is evidence to suggest that CBF may be modulated by changes in glucose consumption rather than oxygen consumption under hypoxic conditions **(Paulson, 2002)**.

The regulatory changes involved in flow – metabolism coupling have a short latency (about 1 second), where transient changes in the concentration of local metabolic mediators seem to determine the fine control of regional CBF by affecting the muscle tone **(Nortje and Menon, 2004)**.

Vasoconstriction occurs by the action of free calcium ions, thromboxane (a product of arachnoid acid/ endo-peroxidase metabolism) and endothelin (secreted by endothelial cells). Some calcium channel blockers blunt hypoxic vasodilatation and prevent adenosine release **(Paulson, 2002)**.

Potent vasodilators include perivascular pottasium (released in high concentration during siezures, hypoxia and electrical stimulation), adenosine (an ATP metabolite in response to arterial hypotension and hypoxia), prostaglandins (e.g PGE 2 and prostcyclin), lactate, acetylcholine, serotonin, substance P and nitric oxide. Nitric oxide is synthesized by endothelial cells and then diffuses into the smooth muscle layer inducing cyclic guanosine monophosphate (GMP) production leading to smooth muscle relxation and hence cerebral vessel vasodilatation. There is evidence to suggest that it is released in response to exitatory amino acid release, hypercapnoea, ischemia, subarachnoid hemorrhge and volatile anaesthetic agents **(Tylor and Hirsch, 2010)**.

Autoregulation:

Autoregulation is the ability of the cerebral circulation to maintain cerebral blood flow at a relatively constant level in the face of wide fluctuations in CPP by altering cerebrovascular resistance. In normal circumstances, as both ICP and cerebral