Neuron-specific Enolase, Serum100 B, Electroencephalography as Indicators of Extent of Brain Damage in Post Cardiac Arrest Patients

Thesis

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I dedicate this work to the memory of my beloved mother, for whom I owe all blessings in my life.

To my father, my sisters for their continuous support, care and love.

Sondos Ahmed Salaheldin

Dedication

To:

My parents

for their endless love, support,

and continuous care

&

My Family

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List of Abbreviations

Abb.	Full term
CPR	*Cardiopulmonary resuscitation*
EEG	*Electroencephalogram*
ICU	*Intensive care unit*
IHCA	*In hospital cardiac arrest*
NSE	*Neuron-specific enolase*
OHCA	*Out hospital cardiac arrest*
ROSC	*Return of spontaneous circulation*
S100B	*Serum100B*

Introduction

Post cardiac arrest syndrome occurs after return of spontaneous circulation (ROSC) following cardiorespiratory arrest. It reflects a state of whole-body ischemia and subsequent reperfusion. It is often super-imposed on the underlying condition, which caused the cardiac arrest, the pre-existing comorbidities, and other complications of resuscitation. Its severity depends on the duration, cause of cardiac arrest and the quality of resuscitation process ***(Binks et al., 2010).***

Post cardiac arrest syndrome is a unique and complex combination of pathophysiological processes, including post-cardiac arrest brain injury, post-cardiac arrest myocardial dysfunction, systemic ischemia /reperfusion response and the unresolved pathological process that caused the cardiac arrest ***(Neumar et al., 2008)***.

Cardiac arrest causes a primary and secondary brain injury. The primary injury occurs at the time of arrest and is non-reversible, and the secondary injury follows return of spontaneous circulation (ROSC) and subsequent cerebral reperfusion and is potentially reversible ***(Temple et al., 2012).***

The brain is exquisitely sensitive to hypoxia. Within 20 seconds of circulatory arrest, neuronal oxygen stores are used up leading to unconsciousness. After 5 minutes, glucose and

adenosine triphosphate (ATP) stores are depleted. This leads to disruption in calcium homeostasis, free radical formation, and the activation of harmful protease cascades and cell death signaling mechanisms. This causes the primary cerebral injury ***(Temple et al., 2012).***

After restoration of cerebral blood flow, ATP is regenerated which leads to devastating free radical formation and the secondary cerebral injury. Cell death continues by both apoptosis and necrosis ***(Temple et al., 2012).***

Cardiac arrest is a devastating event; overall survival from out-of-hospital cardiac arrest is 6.4% (children 9.1%, adolescents 8.9%, and infants 3.3%) Survival rates for in-hospital cardiac arrest ranged from 16 to 38% in different studies published in the last decade ***(Manole et al., 2009).***

Brain injury was the cause of death in 68% after out-of hospital cardiac arrest and in 23% after in-hospital cardiac arrest. The unique vulnerability of the brain is attributed to its limited tolerance of ischemia as well as its unique response to reperfusion ***(Neumar et al., 2008).***

Serum brain-specific biomarkers e.g. Neuron-specific enolase (NSE) and serum 100B (S100B) have the potential to assist in the early detection and quantification of the severity of brain injury, response to therapeutic interventions, and prediction of outcome after cardiac arrest ***(Fink et al., 2014).***

The rationale of dosing markers of neuronal injury in the blood of resuscitated patients is that higher levels of biomarkers correlate with a higher extent of brain damage and consequently lower chances of recovery ***(Sandroni et al., 2015).***

S100B is secreted by astrocytes or can spill from injured cells and enter the extracellular space or bloodstream. Serum levels of S100B increase in patients during the acute phase of brain damage ***(Michetti et al., 2018).***

Electroencephalography has been studied extensively as a tool for evaluating the depth of coma and extent of damage after cardiac arrest. Many malignant EEG patterns have been associated with poor functional outcome, the most reliable of which appear to be generalized suppression to<20μV, burst-suppression pattern with generalized epileptiform activity, and generalized periodic complexes on a flat background ***(Neumar et al., 2008).***

Aim of the Work

To study the levels of Neuron-specific enolase, Serum 100B, Electroencephalogarm patterns in post cardiac arrest pediatric patients and to correlate these findings with cardiac arrest circumstances and patients' outcome.

Chapter 1

Cardiac Arrest and Post Cardiac Arrest Syndrome

Definition:

Cardiac arrest is one of the greatest medical emergencies. It is characterized by absent or inadequate cardiac contraction resulting in circulatory failure. Unless cardiac arrest is quickly corrected by resuscitation techniques, it is fatal ***(Stoppler et al., 2016).***

Advancement in resuscitation techniques has resulted in development of new disease entity termed 'Post cardiac arrest syndrome'. A term that was first used by Vladimir Negovsky in the 1960s ***(Geocadin et al., 2008).***

Post cardiac arrest syndrome is defined as a unique and complex combination of pathophysiological processes resulting from Cardiac arrest, it is composed of:

1. Post cardiac arrest brain injury,
2. Post cardiac arrest myocardial dysfunction,
3. Systemic ischemia /reperfusion response,
4. The unresolved pathological process that caused the cardiac arrest ***(Geocadin et al., 2008).***