International Emergency Nursing 24 (2016) 66–70

Contents lists available at ScienceDirect

International Emergency Nursing

journal homepage: www.elsevier.com/locate/aaen

REVIEW

The science of reperfusion injury post cardiac arrest – Implications for emergency nurses

Edward Baker MSc (Senior Charge Nurse) [a,*], Geraldine Lee PhD, MPhil (Lecturer in Nursing) [b]

[a] Emergency Department, King's College Hospital NHS Trust, Denmark Hill, London SE5 9RS, United Kingdom
[b] King's College London, James Clerk Maxwell Building, 57, Waterloo Road, Waterloo, London SW1 8WA, United Kingdom

ARTICLE INFO

Article history:
Received 24 February 2015
Received in revised form 4 June 2015
Accepted 5 June 2015

Keywords:
Resuscitation
Hypothermia
Extracorporeal membrane oxygenation
Reperfusion injury
Emergency nurse

ABSTRACT

Survival following cardiac arrest in the developed world remains below 10%. In those who survive the initial cardiac arrest, prognosis remains poor due to the onset of multi-organ failure with both significant cardiac and neurological dysfunction. Nurses have demonstrated good understanding of cardiac arrest/post arrest guidelines and have good technical skills but deficits remain in their understanding of pathophysiological processes involved in post cardiac arrest syndromes.

This article aims to provide an overview of these pathophysiological processes involved in the post cardiac arrest phase, potential treatment options and the nursing interventions that may be required within the emergency department setting. This article will focus emergency nurses to become more involved in patient management at this critical phase of treatment and highlight potential early signs of deterioration.

Although return of spontaneous circulation (ROSC) is crucial in the process of recovery from cardiac arrest, it is only the first of many complex stages. Given the complexity of post cardiac arrest syndrome and its impact on the patient, healthcare professionals need to understand the cellular changes associated with reperfusion injuries in order to improve outcomes. It is only through effective nursing care and medical management that improved outcomes will become more common in the future.

1. Introduction

Cardiac arrest remains a significant public health problem both out-of-hospital and in-hospital and is associated with high rates of mortality and significant morbidity. In the United Kingdom, there are on average 30,000 out-of-hospital cardiac arrests every year and the predicted survival to hospital discharge is 8.3% (Resuscitation Council (UK), 2014). In those who survive the initial cardiac arrest, prognosis remains poor in immediate survivors due to the onset of multi-organ failure with both significant cardiac and neurological dysfunction after circulation has been restored. These processes are widely known as reperfusion injuries or Post Cardiac Arrest Syndrome (Nolan et al., 2008).

For those who arrive at the emergency department (ED), ED nurses are regularly involved in the management of patients in the early post cardiac arrest phase. Like many health care professionals, ED nurses develop an understanding of the physiological and pharmacological protocols used in both the peri-arrest and post-arrest phases through standardized resuscitation training programs (Hamilton, 2005). Often these courses do not provide education surrounding the cellular pathophysiology of cardiac arrest which may result in nurses having deficits in knowledge (Gass and Curry, 1983; van Soeren et al., 2000). The primary aim of this paper is to provide emergency nurses an overview of the pathophysiological changes and cellular dysfunction seen in post cardiac arrest patients. The secondary aim is to highlight treatment options that may be available in the clinical environment and potential management options available. By describing the pathophysiological changes that occur in cardiac arrest, ED nurses will gain the detailed physiological knowledge that allows them to appreciate the complexities of post cardiac arrest treatments and be able to apply the theory to their practice.

2. Physiology of normal cellular energy production

To understand cellular dysfunction post cardiac arrest, it is important to understand the normal metabolic pathways that exist in the cell for energy production. This primarily involves the cellular organelle called the mitochondria which function to produce an energy form that can be utilized by the cell to perform normal function, a process called aerobic respiration. It is often referred to as the powerhouse of the cell and in the past 20 years, electron microscopy has greatly increased our understanding of its vital

* Corresponding author. Emergency Department, King's College Hospital NHS Trust, Denmark Hill, London SE5 9RS, United Kingdom. Tel.: +44(0)2078483444; fax: +44(0)2078483444.
E-mail address: edwardbaker@nhs.net (E. Baker).

http://dx.doi.org/10.1016/j.ienj.2015.06.009
1755-599X/

functions. The presence of oxygen is required for this process of aerobic respiration to occur. This functional energy form is called adenosine tri-phosphate (ATP) and is formed through two metabolic processes; the citric acid cycle (Krebs cycle) and oxidative phosphorylation (Mannella, 2006).

The Krebs cycle is a cyclic process resulting in a small amount of ATP production but more importantly produces the functional products required for oxidative phosphorylation to occur. The primary product from the Krebs cycle is nicotinamide adenine dinucleotide (NADH). Oxidative phosphorylation is a metabolic process occurring in the mitochondrial membrane where electrons are passed down a transport chain by a number of proton donors and acceptors using the chemical processes of oxidation and reduction (redox reactions). The primary electron donor is NADH and the primary electron acceptor is oxygen (Ayoub et al., 2008).

As NADH donates an electron into the electron transport chain, this leaves NAD + H^+. This hydrogen ion is an acid (a proton) which is able to travel across the inner mitochondrial membrane creating a concentration gradient and allowing a process of chemiosmosis that continues to power the chemical redox reactions down the electron transport chain. The final electron transfer combined with movement of protons (H^+ = acids) across the organelle membrane via chemiosmosis generates the phosphorylation of adenosine diphosphate (the spent cellular fuel) to adenosine tri-phosphate (active fuel which the cell can utilize) (Dimroth et al., 2000). Cells need ATP and oxygen to function and any changes to the biochemical processes in the body's cells can have a potentially lethal impact on the body's organs, in particular the heart and the brain.

3. Cellular energy production intra-cardiac arrest

Cardiac arrest is probably the most catastrophic event that affects oxygen delivery and therefore cellular respiration. With a significantly reduced oxygenated blood flow to the cells in all the vital organs and surrounding tissues (ischaemia), aerobic respiration and ATP production therefore comes to a halt. The cells are forced to change their energy production to an ineffective process of energy production – anaerobic respiration. This process of glycolysis results in limited ATP production and large amounts of waste products are produced that cannot be removed/metabolized due to the lack of perfusion of oxygenated blood to the cells. The process itself is very similar to fermentation in yeast cells which produce alcohol and carbon dioxide as by-products which in turn kill the yeast cells when in high enough concentrations. Extrapolating the process to humans in cardiac arrest, the major waste products seen in anaerobic respiration are lactic acid and carbon dioxide. This also has an effect on cellular pH and overall function and results in cell death in high enough concentrations (Sharma et al., 2007). For clinicians treating a patient who presents with cardiac arrest, arterial blood gases are a good indicator of the cellular damage and the pH reflects the level of acidosis.

4. Pathophysiology of reperfusion injuries

Restoring the circulation with oxygenated blood as quickly as possible and returning the cardiac rhythm to sinus rhythm has been the aim of cardiac arrest treatment. One of the hypotheses of cardiac arrest management was that the restoration of the circulation was the primary goal with a paucity of research describing what happened to cells after the circulation was restored. It is now known that when oxygenated blood is delivered post-arrest to cells, as the intra and extra cellular metabolic pathways are restored, there is a massive movement of ions across cell membranes and unfortunately this activity results in cellular dysfunction and cell death. We now know that these disordered processes are referred to as reperfusion injuries or cardiac arrest syndrome.

Much of our understanding regarding the cellular changes that occur as a consequence of cardiac arrest has been gained from animal based experiments. In a study involving rodents, cardiac arrest was simulated prior to commencing resuscitation and the investigators noted that the neurons in the brain continued to die for twenty-four hours after the circulation was restored (Jia et al., 2008). This led to further investigation into reperfusion injury and poor neurological outcome that led to the discovery of what we now understand as cardiac arrest syndrome (Nolan et al., 2008). Prior to this, it was believed that duration of hypoxia during cardiac arrest was solely responsible for poor outcome after return of circulation. Reperfusion injuries can now be reproduced in animal models following periods of resolved ischaemia. Reperfusion injuries were often seen post myocardial infarction with changes seen on 12-lead ECGs and arrhythmias often observed. The mechanism was poorly understood until research demonstrated micro-cellular changes seen in transplanted organs after a prolonged period of hypoperfusion (Lemasters and Thurman, 1997).

5. Inflammatory response

The mechanism of reperfusion injury has now been researched and is known to involve a number of different processes which in combination result in cell death. There is an almost instant inflammatory response where interleukins are produced by affected tissues and the endothelial cells of the local capillary vasculature. This process of chemical signalling results in white blood cells being attracted to the affected areas and attaching themselves to the endothelial lining of the capillaries which are only wide enough to allow one haemoglobin molecule past at a time. This results in blockage of the capillaries and further ischaemia to the affected tissues. This inflammatory process has been demonstrated in the neurons of the brain to result in increased intracranial pressure which increases cell death after traumatic brain injury (TBI). This poor outcome associated with the inflammatory response has also been demonstrated post myocardial infarction in cardiac cells (myocytes) (Adrie et al., 2002).

6. Free radical production and oxidative stress

At the point of reperfusion, when oxygen delivery is restored to the cells, there is an increase in oxidative stress demonstrated through an exponential increase in the production of reactive oxygen species (ROS) or free radicals (FR). These free radicals are highly reactive and therefore very dangerous oxygen based molecules with an unpaired electron. Electrons, which normally orbit the nucleus of an atom in pairs, become separated and are highly charged (Rosenfeldt et al., 2013). This process of FR production occurs normally as a by-product of oxidative phosphorylation in very small quantities. In these minute quantities, the cells' normal production of antioxidants is sufficient to prevent the damaging effects of these reactive molecules. This is no longer possible after the extreme oxidative stress post cardiac arrest. Oxidative stress has been demonstrated across a wide range of clinical conditions and procedures including orthopedic and cardiac surgery (Fig. 1) (Rosenfeldt et al., 2013).

Free radicals are responsible for excessive cellular aging and DNA mutation. These reactive molecules also attack the proteins, lipids and glycoglucoamines of the cellular and organelle membranes. Without normal membrane function cellular function will become disordered. The presence of excessive quantities of FR also results in a form of redox signalling which can result in the stimulation of a process of apoptosis (cell death) (Marchi et al., 2012).

Apoptosis is defined as the process of structured and commanded cell death. This is the opposite of necrosis which is a traumatic cell death results in de-nucleation of the cell with