HELDA
HELSINGIN YLIOPISTO
HELSINGFORS UNIVERSITET
UNIVERSITY OF HELSINKI

UNIVERSITY OF HELSINKI

https://helda.helsinki.fi

Seize the day and seize seizures after cardiac arrest

Skrifvars, Markus B.

2018-02

Skrifvars , M B & Hästbacka , J 2018 , ' Seize the day and seize seizures after cardiac arrest ' , Resuscitation , vol. 123 , pp. A3-A4 . https://doi.org/10.1016/j.resuscitation.2017.12.009

http://hdl.handle.net/10138/298245
https://doi.org/10.1016/j.resuscitation.2017.12.009

publishedVersion

Downloaded from Helda, University of Helsinki institutional repository.

This is an electronic reprint of the original article.

This reprint may differ from the original in pagination and typographic detail.

Please cite the original version.

Resuscitation 123 (2018) A3–A4

Contents lists available at ScienceDirect

Resuscitation

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

Editorial

Seize the day and seize seizures after cardiac arrest

Upon admission to the ICU after cardiac arrest, second hit of the cardiac standstill-related hypoxic brain injury evolves, an important contributor to both mortality and poor neurologic outcome [1,2]. There are few effective treatment interventions [3]. The pathophysiology is highly complex but studies have suggested the contribution of decreased cerebral blood flow, cerebral vasoconstriction, inadequate oxygen delivery, and decreased oxygen utilization [4,5]. Known determinants of oxygen delivery to the brain include cerebral perfusion pressure as well as the oxygen and carbon dioxide content of arterial blood [6]. Targeting mild hypercapnia is one promising option that has been shown to improve oxygen delivery to the brain after cardiac arrest and has been shown to be associated with better long-term outcome [7,8].

One ominous sign of most types of brain injury are the presence of seizures and epileptic activity seen on the EEG [9]. There are limited data in cardiac arrest patients but a recent observational study on patients with subarachnoid hemorrhage by Witsch and colleagues showed a clear temporal association between epileptic periodic discharges and reduction in brain tissue oxygen [10]. Whilst this does not provide clear evidence of causality, it raises the possibility that epileptic discharges might result in a hypermetabolic state with even further hypoxia. This would ultimately result in a vicious circle increasing the occurrence of epileptic discharges.

A logical question that follows is whether an increase in oxygen delivery to the brain could decrease the likelihood of epileptic activity? This was the hypothesis of Moonen and colleagues, a group that has done some important work in this area [11,12]. In a retrospective two-centre study they evaluated associations between epileptic activity seen on the EEG with global hemodynamics, oxygen and carbon dioxide levels during the first 48 h of ICU care [13]. The authors could not confirm any association between time-weighted estimations of relative hypoxia, hyperoxia, hypocapnia, hypercapnia, hypotension or hypertension with the occurrence of epileptic activity. It needs to be stated that a clear limitation of this study was that EEGs were not performed systematically but on clinician request instead, and they were performed at various times even up to five days from the cardiac arrest. As rightfully acknowledged by the authors, given the highly temporal association between epileptic discharges and decreases in brain tissue oxygen, an EEG obtained between day three and day five may not accurately reflect brain oxygenation on day one and two.

Interestingly, the incidence of epileptic activity in the study by Moonen and colleagues was similar to what was seen in a post-hoc study of the TTM trial and occurred in almost 30% of the patients [9]. Noteworthy is also that the true incidence may be higher during if monitored with continuous EEG. The main predictors of the presence of seizure activity were initial rhythm and no-flow time, which also are well known determinants of the severity of hypoxic brain damage [14]. This study also shows that even though patients with epileptic discharges have a much worse outcome than those without epileptic activity, the outcome is not always futile. Despite the lack of high class evidence on how to treat of seizures after cardiac arrest, short treatment efforts with generally accepted antiepileptic agents appear motivated in selected cases [15].

The authors also rightfully suggest the imminent need for further trials in the area. The Neuroprotect post CA trial is underway, comparing whether hemodynamic optimization with higher MAP reduces cerebral ischaemia after cardiac arrest [16]. We have recently finished the recruitment of patients with bystander witnessed ventricular fibrillation into the factorial COMACARE study. We have enrolled 120 patients undergoing TTM, to compare the effect of high and low oxygen, carbon dioxide and MAP targets with oxygen delivery, epileptic activity on continuous EEG, laboratory markers of brain injury and long-term functional outcome [17]. Both these trials are pilot trials and are not expected to provide definitive evidence regarding effects on patient centered long-term outcomes. The TAME study, on the other hand, is a large phase three randomized controlled trial that over the next few years aim to enroll 1700 cardiac arrest patients into treatment targeting mild therapeutic hypercapnia or normocapnia during the first 24 h of ICU care [18]. All these trials will give important evidence on how to modulate brain oxygen delivery after cardiac arrest and whether that can decrease the occurrence of epileptic activity and ultimately also improve patient outcomes.

Conflict of interest

None.

References

[1]. Sekhon MS, Ainslie PN, Griesdale DE. Clinical pathophysiology of hypoxic ischemic brain injury after cardiac arrest: a two-hit model. Crit Care 2017;21:90.
[2]. Laver S, Farrow C, Turner D, Nolan J. Mode of death after admission to an intensive care unit following cardiac arrest. Intensive Care Med 2004;30:2126–8.
[3]. Kirkegaard H, Soreide E, de Haas I, Pettila V, Taccone FS, Arus U, et al. Targeted temperature management for 48 vs 24 h and neurologic outcome after out-of-Hospital cardiac arrest: a randomized clinical trial. JAMA 2017;318:341–50.

https://doi.org/10.1016/j.resuscitation.2017.12.009
0300-9572/© 2017 Elsevier B.V. All rights reserved.

[4]. Buunk G, van der Hoeven JG, Meinders AE. Prognostic significance of the difference between mixed venous and jugular bulb oxygen saturation. Resuscitation 1999;41:257–62.
[5]. Edgren E, Enblad P, Grenvik A, Lilja A, Valind S, Wiklund L, et al. Cerebral blood flow and metabolism after cardiopulmonary resuscitation. Resuscitation 2003;57:161–70.
[6]. Rosenthal G, Hemphill 3rd JC, Sorani M, Martin C, Morabito D, Obrist WD, et al. Brain tissue oxygen tension is more indicative of oxygen diffusion than oxygen delivery and metabolism in patients with traumatic brain injury. Crit Care Med 2008;36:1917–24.
[7]. Eastwood GM, Schneider AG, Suzuki S, Peck L, Young H, Tanaka A, et al. Targeted therapeutic mild hypercapnia after cardiac arrest: A phase II multi-centre randomized controlled trial (the CCC trial). Resuscitation 2016;104:83–90.
[8]. Vaahersalo J, Bendel S, Reinikainen M, Kurola J, Tiainen M, Raj R, et al. Arterial blood gas tensions after resuscitation from out-of-hospital cardiac arrest: associations with long-term neurologic outcome. Crit Care Med 2014;42:1463–70.
[9]. Lybeck A, Friberg H, Aneman A, Hassager C, Horn J, Kjaergaard J, et al. Prognostic significance of clinical seizures after cardiac arrest and target temperature management. Resuscitation 2017;114:146–51.
[10]. Witsch J, Frey HP, Schmidt JM, Velazquez A, Falo CM, Reznik M, et al. Electroencephalographic periodic discharges and frequency-Dependent brain tissue hypoxia in acute brain injury. JAMA Neurol 2017;74:301–9.
[11]. Ameloot K, Genbrugge C, Meex I, Jans F, Boer W, Vander Laenen M, et al. An observational near-infrared spectroscopy study on cerebral autoregulation in post-cardiac arrest patients: time to drop 'one-size-fits-all' hemodynamic targets? Resuscitation 2015;90:121–6.
[12]. Ameloot K, Meex I, Genbrugge C, Jans F, Boer W, Verhaert D, et al. Hemodynamic targets during therapeutic hypothermia after cardiac arrest: a prospective observational study. Resuscitation 2015;91:56–62.
[13]. Moonen C, Lemmens R, Van Paesschen W, Wilmer A, Eertmans W, Ferdinande B, et al. The impact of global hemodynamics, oxygen and carbon dioxide on epileptiform EEG activity in comatose survivors of out-of-hospital cardiac arrest. Resuscitation 2018;123:92–7.
[14]. Oksanen T, Tiainen M, Skrifvars MB, Varpula T, Kuitunen A, Castren M, et al. Predictive power of serum NSE and OHCA score regarding 6-month neurologic outcome after out-of-hospital ventricular fibrillation and therapeutic hypothermia. Resuscitation 2009;80:165–70.
[15]. Nolan JP, Soar J, Cariou A, Cronberg T, Moulaert VR, Deakin CD, et al. European resuscitation council and european society of intensive care medicine 2015 guidelines for post-resuscitation care. Intensive Care Med 2015;41:2039–56.
[16]. Ameloot K, De Deyne C, Ferdinande B, Dupont M, Palmers PJ, Petit T, et al. Mean arterial pressure of 65 mm Hg versus 85–100 mm Hg in comatose survivors after cardiac arrest: rationale and study design of the Neuroprotect post-cardiac arrest trial. Am Heart J 2017;191:91–8.
[17]. Jakkula P, Reinikainen M, Hastbacka J, Pettila V, Loisa P, Karlsson S, et al. Targeting low- or high-normal Carbon dioxide, Oxygen, and Mean arterial pressure After Cardiac Arrest and REsuscitation: study protocol for a randomized pilot trial. Trials 2017;18:507.
[18]. Parke RL, McGuinness S, Eastwood GM, Nichol A, Nielsen N, Dankiewicz J, et al. Co-enrolment for the TAME and TTM-2 trials: the cerebral option. Crit Care Resusc 2017;19:99–100.

Markus B. Skrifvars *
Johanna Hästbacka
Division of Intensive Care, Department of Anaesthesiology, Intensive Care and Pain Medicine, Helsinki University Hospital and University of Helsinki, Finland

* Corresponding author.
E-mail address: markus.skrifvars@hus.fi
(M.B. Skrifvars)

5 December 2017