Resuscitation 102 (2016) 11–16

Contents lists available at ScienceDirect

Resuscitation

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

Clinical paper

Cerebral oxygenation in mechanically ventilated early cardiac arrest survivors: The impact of hypercapnia☆

Glenn M. Eastwood[a,b,c,*], Aiko Tanaka[a,d], Rinaldo Bellomo[a,b]

[a] Department of Intensive Care, Austin Hospital, Melbourne, VIC, Australia
[b] Australian and New Zealand Intensive Care Research Centre, Melbourne, VIC, Australia
[c] School of Nursing and Midwifery, Faculty of Health, Deakin University, Melbourne, Australia
[d] Department of Anesthesiology and Intensive Care, Osaka University Graduate School of Medicine, Suita, Osaka, Japan

ARTICLE INFO

Article history:
Received 14 August 2015
Received in revised form 21 January 2016
Accepted 6 February 2016

Keywords:
Cardiac arrest
Cerebral oxygenation
Hypercapnia
Normocapnia
Mechanical ventilation

ABSTRACT

Background: Optimal cerebral oxygenation is considered fundamental to cerebral protection in cardiac arrest (CA) patients. Hypercapnia increases cerebral blood flow and may also improve cerebral oxygenation. It is uncertain, however, whether this effect occurs in mechanically ventilated early survivors of CA.

Methods: We enrolled mechanically ventilated resuscitated patients within 36 h of their cardiac arrest. We performed a prospective double cross-over physiological study comparing the impact of normocapnia ($PaCO_2$ 35–45 mmHg) vs. mild hypercapnia ($PaCO_2$ 45–55 mmHg) on regional cerebral tissue oxygen saturation ($SctO_2$) assessed by near infrared spectroscopy (NIRS).

Results: We studied seven adult CA patients with a median time to return of spontaneous circulation of 28 min at a median of 26 h and 30 min after CA. During normocapnia (median $EtCO_2$ of 32 mmHg [30–41 mmHg] and $PaCO_2$ of 37 mmHg [32–45 mmHg]) the median NIRS-derived left frontal $SctO_2$ was 61% [52–65%] and the right frontal $SctO_2$ was 61% [54–68%]. However, during mild hypercapnia (median $EtCO_2$ of 49 mmHg [40–57 mmHg] and $PaCO_2$ of 52 mmHg [43–55 mmHg]) the median left frontal $SctO_2$ increased to 69% [59–78%] and the right frontal $SctO_2$ increased to 73% [61–76%])($p = 0.001$, for all comparisons).

Conclusion: During the early post-resuscitation period, in mechanically ventilated CA patients, mild hypercapnia increases cerebral oxygenation as assessed by NIRS. Further investigations of the effect of prolonged mild hypercapnia on cerebral oxygenation and patient outcomes appear justified.

Introduction

Cardiac arrest (CA) causes hypoxic brain injury that results in acute neurological injury and exerts a profound effect on the long-term neurological outcome of CA survivors.[1,2] Following return of spontaneous circulation (ROSC) optimal cerebral oxygenation is considered fundamental to cerebral protection in these patients.[3,4] However, in the early post-resuscitation period, cerebrovascular auto-regulation is thought to be deranged.[5,6] Impaired auto-regulation may, in turn, affect the impact of arterial carbon dioxide tension ($PaCO_2$) on cerebral perfusion and, consequently, cerebral oxygenation.

The potential impact of $PaCO_2$ on cerebral perfusion and oxygenation may be important in the setting of CA. In this regard, $PaCO_2$ is emerging as a modifiable and potentially therapeutic intervention for resuscitated CA patients.[1,7] $PaCO_2$ is a potent regulator of cerebrovascular tone and hypercapnia increases cerebral blood flow.[8] The rapid vasodilatory effect of hypercapnia appears related to changes in arterial pH and cerebral vascular resistance.[6,8] Its effect on cerebral tissue oxygenation in mechanically ventilated early survivors of CA, however, remains uncertain.

Cerebral oximetry using near infrared spectroscopy (NIRS) provides a form of non-invasive regional cerebral tissue oxygen saturation ($SctO_2$) monitoring and an estimate of tissue oxygen levels.[9] The normal adult $SctO_2$ range is 60–70% and correlates with jugular bulb oxygen saturation ($SjbO_2$) as a measure of cerebral oxygenation.[9] Observational studies involving NIRS during CA resuscitation[10] and post-CA resuscitation care have demonstrated

☆ A Spanish translated version of the summary of this article appears as Appendix in the final online version at http://dx.doi.org/10.1016/j.resuscitation.2016.02.009.

* Corresponding author at: Department of Intensive Care, Austin Hospital, 145 Studley Road, Heidelberg, Melbourne 3084, VIC, Australia. Fax: +61 3 9496 3932.
E-mail addresses: glenn.eastwood@austin.org.au (G.M. Eastwood), aiko.tanaka@austin.org.au (A. Tanaka), rinaldo.bellomo@austin.org.au (R. Bellomo).

http://dx.doi.org/10.1016/j.resuscitation.2016.02.009
0300-9572/

the feasibility of NIRS monitoring.[3,11] In addition, a statistically significant association between lower $SctO_2$ values and lower survival rates has been shown in resuscitated CA patients (median $SctO_2$ 63% vs 69%, $p < 0.01$) at 24 h[11] and lower $SctO_2$ values have been reported during the application of therapeutic hypothermia (TH).[3,12] Such NIRS technology, therefore, offers an opportunity to non-invasively assess the cerebral oxygenation impact of increasing $PaCO_2$ in mechanically ventilated CA patients in the first one to two days after ROSC.

Accordingly, we performed a prospective double cross-over physiological study in such patients to assess the impact of increased $PaCO_2$ on NIRS-derived $SctO_2$.

Methods

Study design, setting and population

We performed a prospective double cross-over physiological efficacy study. We enrolled seven non-traumatic adult CA patients admitted to the intensive care unit (ICU) of our tertiary teaching hospital between February, 2014 and April, 2015. The Austin Health human research ethics committee provided prospective approval with a waiver of informed consent as the $PaCO_2$ levels were within reported values in such patients (HREC approval number LNR/14/Austin/555).

Patient management and study procedures

After excluding patients with a short time to ROSC (<5 min) who showed signs of rapid awakening and responsiveness upon ROSC, our unit protocol for the management of resuscitated CA patients during the study period was applied to all suitable CA patients (i.e. those patients with a primary CA and for active treatment) to provide circulatory support, normalise physiological derangements and achieve and maintain target temperature. Eligible CA patients were those patients without suspected or confirmed raised intra-cranial pressure and who were within their first 36 h of ICU admission.

For each patient, ventilation-controlled targeting of $PaCO_2$ values was guided by end-tidal carbon dioxide ($EtCO_2$). The target $PaCO_2$ range for normocapnia was a $PaCO_2$ of 35–45 mmHg. The target range for mild hypercapnia was a $PaCO_2$ of 50–55 mmHg. The assessment order was: (i) normocapnia, (ii) mild hypercapnia, (iii) normocapnia, and (iv) mild hypercapnia.

We recorded baseline $SctO_2$, $EtCO_2$ and $PaCO_2$ measurements. The respiratory rate of the ventilator was decreased to move the patient into the mild hypercapnic range using $EtCO_2$ readings as a guide. Then, following a period of 30 min, a second set of $SctO_2$, $EtCO_2$ and $PaCO_2$ measurements was recorded. The respiratory rate was the increased to return the patient back into the normocapnia range, again guided by $EtCO_2$ readings. The process was then repeated during the third and fourth study periods with the measurements also obtained 30 min following the respiratory rate change. Positive end expiratory pressure (PEEP) was kept constant throughout to avoid any of its confounding effects. For each patient, at completion of the final study period, all ventilator settings were returned to pre-study settings and the $EtCO_2$ and $PaCO_2$ target ranges were subsequently determined by the patient's treating Intensivist.

All patients received mechanical ventilation (MV) with an Evita 4 or Evita XL (Drägerwerk AG, Lübeck, Germany) or an AVEA ventilator (CareFusinon, Yorba Linda, CA). Bilateral cerebral (frontal) oxygen saturation was measured with near using NIRS (INVOC—In Vivo Optical Spectroscopy, The INVOS System, Somanetics, Troy, MI, USA). $PaCO_2$ was monitored via arterial blood gas (ABG) sampling with analysis performed by the ABL800 FLEX (Radiometer, Copenhagen, Denmark) using the alpha-stat strategy. Finally, $EtCO_2$ concentration readings were displayed in real time by IntelliVue MP70 monitors (Philips Healthcare, Eindhoven, Netherlands).

Data collection and analysis

Along with $SctO_2$, $EtCO_2$, and $PaCO_2$ measurements, we obtained the following variables: demographic features (age, gender, body weight), CA characteristics (initial monitored cardiac rhythm, location of CA, time to ROSC; suspected CA cause), time from CA event to assessment and ICU care processes during the study intervention (temperature control, sedation use, analgesic use and vasopressor use), severity of illness score (acute physiology and chronic health evaluation (APACHE) III) score and Simplified Acute Physiology Score (SAPS) II), as well as vital status at ICU and hospital discharge.

All analyses were performed using SPSS version 19.0 (SPSS Inc., Chicago, IL, USA). Categorical data are reported as numbers with proportions and continuous data are expressed as medians with inter-quartile range [IQR] and compared by using Wilcoxon rank sum test. Changes of $SctO_2$, $EtCO_2$, and $PaCO_2$ from the end of the targeted normocapnia periods to the end of the targeted mild hypercapnia periods were assessed. Due to the lag effect of cerebral hypoperfusion during the immediate post-resuscitation period as well as the impact of cooling on arterial gases.[13] We performed a sensitivity analysis to compare arterial oxygen tension (PaO_2), body temperature, mean arterial pressure (MAP), FiO_2, PEEP and pressure support (PS) during targeted normocapnia and targeted mild hypercapnia for the entire sample as well as a cohort of patients excluding those very early in their ICU admission (approximately 6 h post-CA) or studied while being actively cooled. A $p < 0.05$ was considered statistically significant.

Results

Patient characteristics

Seven adult CA patients (six male patients) with a median time to ROSC of 28 min [IQR 22–38 min] and median time of 26 h 30 min [IQR 21 h 30 min–28 h 8 min] from CA event to assessment were studied. Of these, three patients (43%) were receiving TH and the remaining four patients (57%) were receiving strict normothermia during the study period. The demographic characteristics, process of care at the time of assessment and outcomes for the study patients are shown in Table 1. Comparison of body temperature, MAP, FiO_2, PEEP and PS during targeted normocapnia and targeted mild hypercapnia are shown in Table 2.

Cerebral oximetry changes

At the end of the normocapnia periods, the median left frontal $SctO_2$ was 61% [52–65%] and the right frontal $SctO_2$ was 61% [54–68%] corresponding to a median $EtCO_2$ of 32 mmHg [30–41 mmHg] and a median $PaCO_2$ of 37 mmHg [32–45 mmHg].

There was a significant increase ($p = 0.001$) in all $SctO_2$ values at the end of the hypercapnia periods, with the median left frontal increasing to 69% [59–78%] and the right frontal increasing to 73% [61–76%] corresponding to a median $EtCO_2$ of 49 mmHg [40–57 mmHg] and a median $PaCO_2$ of 52 mmHg [43–55 mmHg].

The % increases from baseline in the left and right frontal $SctO_2$ from normocapnia to mild hypercapnia were 17% (13–23%) and 15% (10–19%), respectively. Correspondingly, there was an increase in $EtCO_2$ of 30% (21–39%) and $PaCO_2$ of 24% (16–41%).

Changes in the (a) left frontal $SctO_2$ and (b) right frontal $SctO_2$, and the corresponding changes in (c) $PaCO_2$ and (d) $EtCO_2$ in a