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Clinical paper

Using the relationship between brain tissue regional saturation of oxygen and mean arterial pressure to determine the optimal mean arterial pressure in patients following cardiac arrest: A pilot proof-of-concept study☆

Mypinder S. Sekhon[a], Peter Smielewski[b], Tahara D. Bhate[a], Penelope M. Brasher[c], Denise Foster[a], David K. Menon[b], Arun K. Gupta[b], Marek Czosnyka[d], William R. Henderson[a], Kenneth Gin[e], Graham Wong[e], Donald E. Griesdale[a,c,f,*]

[a] Division of Critical Care Medicine, Department of Medicine, Vancouver General Hospital, University of British Columbia, Vancouver, BC, Canada
[b] Neurocritical Care Unit, Addenbrooke's Hospital, Cambridge University Hospitals Trust, Cambridge University, Cambridge, United Kingdom
[c] Centre for Clinical Epidemiology and Evaluation, Vancouver Coastal Health Research Institute, Vancouver, BC, Canada
[d] Brain Physics Lab, Division of Neurosurgery, Cambridge University Hospitals Trust, Cambridge University, Cambridge, United Kingdom
[e] Division of Cardiology, Department of Medicine, Vancouver General Hospital, University of British Columbia, Vancouver, BC, Canada
[f] Department of Anesthesiology, Pharmacology and Therapeutics, University of British Columbia, Vancouver, BC, Canada

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ABSTRACT

Introduction: Prospectively assess cerebral autoregulation and optimal mean arterial pressure (MAP_{OPT}) using the dynamic relationship between MAP and regional saturation of oxygen (rSO_2) using near-infrared spectroscopy.
Methods: Feasibility study of twenty patients admitted to the intensive care unit following a cardiac arrest. All patients underwent continuous rSO_2 monitoring using the INVOS® cerebral oximeter. ICM+® brain monitoring software calculates the cerebral oximetry index (COx) in real-time which is a moving Pearson correlation coefficient between 30 consecutive, 10-s averaged values of MAP and correspond rSO_2 signals. When rSO_2 increases with increasing MAP (COx $\geq$0.3), cerebral autoregulation is dysfunctional. Conversely, when rSO_2 remains constant or decreases with increasing MAP (COx <0.3), autoregulation is preserved. ICM+® fits a U-shaped curve through the COx values plotted vs. MAP. The MAP_{OPT} is nadir of this curve.
Results: The median age was 59 years (IQR 54–67) and 7 of 20 were female. The cardiac arrest was caused by myocardial infarction in 12 (60%) patients. Nineteen arrests were witnessed and return of spontaneous circulation occurred in a median of 15.5 min (IQR 8–33). Patients underwent a median of 30 h (IQR 23–46) of monitoring. COx curves and MAP_{OPT} were generated in all patients. The mean overall MAP and MAP_{OPT} were 76 mmHg (SD 10) and 76 mmHg (SD 7), respectively. MAP was outside of 5 mmHg from MAP_{OPT} in 50% (SD 15) of the time. Out of the 7672 5-min averaged COx measurements, 1182 (15%) were at 0.3 or above, indicating absence of autoregulation. Multivariable polynomial fractional regression demonstrated an increase in COx with increasing temperature ($P = 0.008$).
Conclusions: We demonstrated the feasibility to determine a MAP_{OPT} using cerebral oximetry in patients after cardiac arrest.

Abbreviations: AHA, American Heart Association; CCU, coronary care unit; COx, correlational coefficient between MAP and rSO_2; CPP, cerebral perfusion pressure; FVd/FVm, flow velocity diastolic/mean; HIBI, hypoxemic ischemic brain injury; ICP, intracranial pressure; ICU, intensive care unit; IQR, interquartile range; MAP, mean arterial pressure; MAP_{OPT}, optimal mean arterial pressure; ONSD, optic nerve sheath diameter; ROSC, return of spontaneous circulation; rSO_2, regional saturation of oxygen; SD, standard deviation; TBI, traumatic brain injury; TCD, transcranial Doppler.

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* Corresponding author at: Critical Care Medicine, Vancouver General Hospital, Room 2438, Jim Pattison Pavilion, 2nd Floor, 855 West 12th Avenue, Vancouver, BC V5Z 1M9, Canada.
E-mail address: donald.griesdale@vch.ca (D.E. Griesdale).

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Introduction

Hypoxemic-ischemic brain injury (HIBI) is the major cause of death in patients following cardiac arrest.[1] Furthermore, approximately half of those who survive will be left with an unfavorable neurologic outcome.[2] HIBI is characterized by cerebral edema with elevated intracranial pressure (ICP) and dysfunctional cerebral autoregulation.[3] In healthy individuals, cerebral autoregulation attempts to maintain constant cerebral blood flow (CBF) over a wide range of mean arterial pressure (MAP). In HIBI, autoregulation is impaired, with the plateau becoming narrowed and right-shifted.[4] This may have consequences for targeting a specific MAP threshold in these patients. If the MAP is below the autoregulatory threshold, additional ischemia can result, leading to further brain injury. Conversely, if the MAP above the autoregulatory threshold, excessive perfusion may lead to increased cerebral edema and worsening brain injury.

The American Heart Association recommends keeping MAP at 65 mmHg or above in all patients following cardiac arrest.[5] However this "one size fits all" philosophy clearly does not take into consideration intra-subject variability and, moreover, any possible disruption in a patient's cerebral autoregulation capacity. Recently, there has been interest in using the dynamic fluctuations in MAP on brain regional saturation of oxygen (rSO_2) using near-infrared spectroscopy (NIRS).[6,7] If MAP and rSO_2 trend in the same direction (e.g. decreasing MAP leads to equal reductions in rSO_2), then effective cerebral autoregulation is likely severely compromised. Conversely, if rSO_2 remains constant during changes in MAP then autoregulation is likely intact. Over time, a moving correlation coefficient (a value between −1 and +1) between MAP and rSO_2 can be repeatedly calculated. This is termed the cerebral oximetry index (COx). A positive or negative COx indicates dysfunction or intact cerebral autoregulation, respectively.[8] The MAP_{OPT} can then be identified at the point with the lowest COx.[7] This approach has been applied to two studies in patients after cardiac arrest using differing definitions of intact autoregulation.[6,9] We thus conducted a single center proof-of-concept study to determine if we could prospectively determine MAP_{OPT} in a cohort of patients admitted after cardiac arrest. In addition, we wanted to determine additional feasibility outcomes: patient recruitment rates, duration of monitoring and adequacy of data capture. We also sought to assess the percentage of time of intact autoregulation and the ability to determine MAP_{OPT}.

Methods

This is a single-center feasibility proof-of-concept study. The Research Ethics Board at the University of British Columbia (H14-02405) approved the protocol and written informed consent was obtained from patients in a deferred manner.

Patient inclusion

We included patients 16 years or older who were admitted following a cardiac arrest who had a post-resuscitation Glasgow Coma Score of 8 or less. Patients had to be enrolled within 36 h of their cardiac arrest and had more than 20 consecutive minutes of spontaneous circulation following resuscitation. We excluded patients with a past history of cardiac arrest, traumatic brain injury, intracerebral hemorrhage or ischemic stroke. We also excluded patients where there was no commitment to ongoing support by the medical team.

Patient management

All patient care decisions were at the discretion of the treating team. As per institutional protocol, patients who have a cardiac arrest from a presumed cardiac cause undergo targeted temperature management to either 33 °C or 36 °C, at the discretion of the attending physician. This is undertaken with surface cooling using the Artic Sun® Temperature Management System (Bard Medical, Murray Hill, NJ, USA). During the time of the study, there was no institutional temperature management protocol for cardiac arrest from a presumed non-cardiac cause (e.g. hypoxemia).

Study site

Affiliated with the University of British Columbia, the intensive care unit (31 beds) and coronary care unit (14 beds) manage all of the post cardiac arrest patients at Vancouver General Hospital. The ICU and CCU are staffed by fellowship trained intensive care physicians and cardiologists, respectively.

Neurophysiologic monitoring

We monitored brain regional saturation of oxygen (rSO_2) bilaterally using the INVOS® cerebral oximeter (Covidien, Ireland) on the day of admission and continued for up to 48 h after the cardiac arrest. Invasive blood pressure and rSO_2 data were captured in real-time using ICM+® brain monitoring software (Division of Neurosurgery, Cambridge University). Daily during the study, two investigators (DG, MS) measured MCA flow velocity using TCD.

Statistical methods

Categorical data are summarized as count (percent) and continuous data are summarized as mean (standard deviation) or median and interquartile range (25th–75th percentile) if the data were skewed. We used Stata 10.0 (StataCorp, TX, USA) for all analyses. All tests were two-sided and a p-value <0.05 was considered statistically significant. As this was a proof-of-concept study, no formal sample size calculation was performed. Twenty patients represented the maximum number of patients we could recruit with the available resources. TCD was used to estimate CPP using the following formula: $CPP = MAP \times FVd/FVm + 14$.[10] A non-invasive ICP was then estimated as $ICP = MAP - CPP$.

Determination of COx and MAP_{OPT}

ICM+® brain monitoring software calculates both COx and MAP_{OPT}. COx is a moving Pearson correlation coefficient between 30 consecutive, 10-s averaged values of MAP and corresponding rSO_2 signals (with 80% overlap of data).[11] For the purposes of analysis, we averaged the rSO_2, MAP and COx over a 5-min time period.[8] To calculate MAP_{OPT}, ICM+® divides MAP into bins of 5 mmHg and then discards the first and last MAP bins. MAP bins which contain <2% of data points are also discarded.[12] ICM+® then fits a U-shaped curve through the COx values plotted vs. MAP.[13] The MAP_{OPT} is the nadir of this curve. MAP_{OPT} was calculated for each 6 h time period. Fig. 1 demonstrates data capture (MAP, rSO_2 and COx) and the generation of MAP_{OPT} in an individual patient. We then calculated the difference between the patients' actual average MAP (on an hourly basis) and the MAP_{OPT}. Presence of cerebral autoregulation was defined a priori as a COx <0.3.[8,14]

Modeling of COx with MAP and temperature

The relationship was assessed visually by plotting COx vs. MAP and COx vs. temperature for each individual. For the relationship between COx and MAP, the median and IQR for COx was calculated for each 5 mmHg bin of MAP of each individual. For the relationship between COx and temperature, we overlaid the scatter plot with a locally weighted scatter plot smoothing function conditioned on the individual. In order to visually assess the relationship between COx and temperature across all patients, we used restricted cubic