Clinical Article

Phase shift and correlation coefficient measurement of cerebral autoregulation during deep breathing in traumatic brain injury (TBI)

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Summary

Background. Impairment of cerebral autoregulation is known to adversely affect outcome following traumatic brain injury (TBI). The phase shift (PS) method of cerebral autoregulation (CA) assessment describes the time lag between fluctuations in arterial blood pressure (ABP) and cerebral blood flow velocity (CBFV) in the middle cerebral artery. An alternative method (Mx-ABP) is based on the statistical correlation between ABP and CBFV waveforms over time. We compared these two indices in a cohort of severely head injured patients undergoing controlled, 6-breaths-per-minute ventilation.

Methods. PS and Mx-ABP were calculated from 33 recordings of CBFV and MAP in 22 patients with TBI. Spearman’s correlation coefficient was used to assess the agreement between PS and Mx-ABP. The relationship between ICP slow wave amplitude, MAP slow wave amplitude and mean ICP was also examined.

Findings. Mean values for Mx-ABP and PS were 0.44 ± 0.27, and 49 ± 26 (degrees), respectively. PS correlated significantly with Mx-ABP ($r = -0.648$, $p < 0.001$). A Bland-Altman plot of normalised Mx-ABP and Phase Shift values showed no significant bias or relationship (mean difference = 0.0004, $r = -0.037$, $p = 0.852$). During the test procedure, ICP fluctuated in an approximately sinusoidal fashion, with a mean amplitude of 4.96 ± 2.72 mmHg (peak to peak). The magnitude of ICP fluctuation during deep breathing correlated weakly but significantly with mean ICP ($r = 0.391$, $p < 0.05$) and with the amplitude of ABP fluctuations ($r = 0.625$, $p < 0.0005$).

Conclusions. Phase shift and Mx-ABP in TBI are well correlated. Deep breathing presents as an effective tool with which to assess autoregulation using the phase shift method.

Keywords: Cerebral autoregulation; intracranial pressure; cerebral perfusion pressure; transcranial doppler ultrasound; head injury.

Introduction

The classical definition of cerebral autoregulation (CA) describes the brain’s intrinsic ability to maintain adequate blood flow despite alterations in cerebral perfusion pressure (CPP) [27, 44]. Cerebral autoregulation assessment techniques used clinically typically assess responses in cerebral blood flow (CBF) and cerebral blood flow velocity (CBFV) to changes in arterial blood pressure (ABP) alone [31].

The Mx index, an index of cerebral autoregulation first described by Czosnyka et al. and subsequently studied by a number of authors [8, 23, 39] correlates slow changes in CPP with slow changes in middle cerebral
artery blood flow velocity (CBFV) [8]. This index has demonstrated prognostic value in head injury, with high Mx (>0.3) indicating disturbed autoregulation and predicting poor outcome [10]. Lang et al. subsequently reported a modified Mx index (Mx-ABP), correlating ABP rather than CPP with CBFV [22]. This study found a strong correlation between the two indices and outcome in head injury, in addition to a significant correlation between the indices themselves.

The phase shift method of autoregulation assessment measures the time lag between fluctuations in MAP and CBFV at specific frequencies of interest [11, 36, 46]. This method has been validated by a number of authors and can be applied without applying any external stimulus, whereby the relationships between spontaneous oscillations in MAP and CBFV are analysed to provide an index of autoregulation [12, 17, 30, 36]. An alternative approach to the method is to perform fixed rate deep breathing during CBFV recordings, such that a more pronounced fluctuation in MAP and CBFV occurs at the frequency of respiration. This method has been applied in both healthy volunteers and patients suffering from cerebrovascular pathology, and has also been validated as a measure of autoregulation [11, 21].

A number of comparative studies exist which have investigated the relationships between dynamic CA testing methodologies [22, 23, 37–39, 42, 45] however no comparisons between phase shift and Mx indices have been reported in severe TBI. In order to provide insights into the utility of phase shift during 6 per minute deep breathing as a continuous measure of autoregulation in this patient group and to add to the body of comparative literature on this topic, we performed a comparison between phase shift and Mx indices in 22 severely head injured patients receiving 6 breaths per minute ventilation.

Materials and methods

Patients

We studied 22 severely head-injured patients, defined as a Glasgow Coma Scale (GCS) score of 8 or less after initial resuscitation or who deteriorated to this level during the first 12 h of treatment. The mean admission GCS was 9, average age was 41 ± 18 years. There were 3 female and 19 male patients (Table 1).

Management of these patients consisted of aggressive surgical and medical therapy including immediate evacuation of intracranial mass lesions, mechanical ventilation, and control of intracranial pressure, using a protocol consistent with the guidelines for the management of severe head injury [4]. Monitoring and data collection was approved by the University of Kiel institutional review board.

Data recordings

At least one TCD examination was performed on all 22 patients between days 1 and 5 post injury. Eleven of these patients received a second recording between days 6–10. Blood pressure recordings were obtained with a radial artery fluid-coupled system (pvb Critical Care, Kirchseeon, Germany). Intracranial pressure (ICP) was measured with an intraparenchymal sensor (Camino V420®, San Diego, CA, U.S.A. or Spiegelberg Brain-Pressure Monitor®, Spiegelberg KG, Hamburg, Germany). Intraparenchymal ICP sensors were placed on the side of injury, or in the right frontal area if there was diffuse injury or multiple contusions. Middle cerebral artery blood flow velocities (CBFV) were recorded bilaterally using transcranial Doppler (TCD) ultrasound equipment (Multi-Dop X2®, DWL, Singen, Germany). All TCD studies were consistently performed by one examiner (EWL). The frequency response differences between the Camino and Spiegelberg monitors did not impact on our analysis, as the differences lie outside the frequency range we studied.

Patients were ventilated at 6 breaths per minute for a short period of time to induce fluctuations in mean arterial pressure (MAP) and cerebral blood flow velocity (CBFV). Ventilator settings were adjusted to keep minute volume unchanged by increasing tidal volume and decreasing respiratory rate. Due to the short duration of this manoeuvre we did not draw serial arterial blood samples but monitored end-tidal CO₂ on the ventilator, which stayed within normal limits throughout. The procedure did not lead to a net increase in ICP. Prior to and during the test procedure, nursing and pharmacological interventions were avoided to minimise any influence on the recorded signals. There were no complications associated with this procedure. MAP, ICP and CBFV signals were recorded with a sampling rate of 57.4 Hz and

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<th>Table 1. Patient demographics (n = 22)</th>
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Mean admission GCS includes those patients whose GCS deteriorated to 8 or less within 24h of admission.