BJA

British Journal of Anaesthesia, 0 (0): 1–9 (2017)

doi: 10.1093/bja/aex333
Clinical Investigation

CLINICAL INVESTIGATION

Novel method for intraoperative assessment of cerebral autoregulation by paced breathing

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Abstract

Background. Cerebral autoregulation (CA) is the mechanism that maintains constancy of cerebral blood flow (CBF) despite variations in blood pressure (BP). Patients with attenuated CA have been shown to have an increased incidence of peri-operative stroke. Studies of CA in anaesthetized subjects are rare, because a simple and non-invasive method to quantify the integrity of CA is not available. In this study, we set out to improve non-invasive quantification of CA during surgery. For this purpose, we introduce a novel method to amplify spontaneous BP fluctuations during surgery by imposing mechanical positive pressure ventilation at three different frequencies and quantify CA from the resulting BP oscillations.

Methods. Fourteen patients undergoing sevoflurane anaesthesia were included in the study. Continuous non-invasive BP and transcranial Doppler-derived CBF velocity (CBFV) were obtained before surgery during 3 min of paced breathing at 6, 10, and 15 bpm and during surgery from mechanical positive pressure ventilation at identical frequencies. Data were analysed using frequency domain analysis to obtain CBFV-to-BP phase lead as a continuous measure of CA efficacy. Group averages were calculated. Values are means (SD), and $P<0.05$ was used to indicate statistical significance.

Results. Preoperative *vs* intraoperative CBFV-to-BP phase lead was 43 (9) *vs* 45 (8)°, 25 (8) *vs* 24 (10)°, and 4 (6) *vs* −2 (12)° during 6, 10, and 15 bpm, respectively (all P=NS).

Conclusions. During surgery, cerebral autoregulation indices were similar to values determined before surgery. This indicates that CA can be quantified reliably and non-invasively using this novel method and confirms earlier evidence that CA is unaffected by sevoflurane anaesthesia.

Clinical trial registration. NCT03071432.

Key words: anaesthetics, inhalation; cerebrovascular circulation; intraoperative neurophysiological monitoring

Editorial decision: July 20, 2017; **Accepted:** August 22, 2017

Editor's key points

- Cerebral autoregulation (CA) maintains cerebral blood flow by altering cerebral vascular tone in the face of changing perfusion pressure.
- If CA is impaired, patients exposed to hypotension are at risk of perioperative stroke.
- There is no simple and non-invasive method for intraoperative assessment of CA during anaesthesia.
- A novel technique using assessment of cerebral blood flow velocity changes during mechanical ventilation is proposed.

Cerebral autoregulation (CA) is a physiological mechanism that maintains constant cerebral blood flow (CBF) despite variations in blood pressure (BP) and therefore safeguards cerebral metabolic needs during hypotension.[1] If the efficacy of CA is compromised, the risk of cerebral hypoperfusion increases when BP is lower, for example during anaesthesia.[2] Indeed, attenuated CA, as found in patients with diabetes,[3] hypertension,[4] vascular disease,[5 6] or previous cerebral infarction,[7] has been demonstrated to be associated with an increased incidence of perioperative stroke.[8–10] Nevertheless, studies that quantify CA efficacy in perioperative patients are scarce because a standardized non-invasive measurement technique is lacking.

Studies of CA efficacy involve assessment of the CBF response to a BP modification, and in such studies, CBF is usually assumed to correlate closely with CBF velocity (CBFV), which is more easily measured. After a sudden BP change provoked by the release of inflated thigh cuffs[11 12] or vasoactive medication,[13] CBFV,[14] measured with a transcranial Doppler system, returned to baseline within a few seconds. This latency has been used as a measure of CA efficacy, and using these techniques, several studies demonstrated that sevoflurane anaesthesia does not affect CA.[15–17] To eliminate the need to induce a BP modification, an alternative non-invasive method quantifies CA from the CBFV response to spontaneous BP fluctuations originating from short-term BP control by the sympathetic nervous system.[18–20] Unfortunately, this method is inappropriate in anaesthetized patients because sevoflurane suppresses sympathetic outflow[21] and thus the necessary spontaneous BP oscillations.[22] Indeed, the only study attempting to quantify CA during surgery using this method shows obliteration of BP oscillations with sufficient amplitude.[23] This renders intraoperative non-invasive CA quantification effectively impossible.

In the present study, we set out to improve non-invasive CA quantification during surgery. For this purpose, we introduce a novel method to amplify spontaneous BP fluctuations by imposing mechanical positive pressure ventilation at three different frequencies. Intraoperative CA efficacy determined from the resulting imposed BP oscillations was then compared with preoperative values during paced breathing at identical frequencies. We hypothesized that CA indices determined with this novel method are unaffected by sevoflurane anaesthesia.

Methods

The study was approved by the Institutional Ethics Committee of the Academic Medical Centre AMC Amsterdam (reference: MEC 2016_116) and registered with ClinicalTrials.gov (ref: NCT03071432). Oral and written informed consent were obtained before inclusion.

Patients and study design

A total of 18 patients were included in this prospective study. Two patients were excluded because of preoperative insufficient adherence to the protocol and another two because exclusion criteria were met (no transcranial window and cardiac arrhythmia during surgery, respectively). The remaining 14 patients [four male (29%); mean age 58 (range 43–73) yr, weight 73 (range 57–99) kg, and height 172 (range 158–185) cm] completed the protocol both before and during surgery. Exclusion criteria were laparoscopic procedures, known diabetes mellitus, Parkinson's disease, cardiac arrhythmia, central or peripheral autonomic neuropathy, Shy-Drager syndrome, cardiomyopathy (known), and the inability to detect transcranial Doppler signals because of anatomical variances.

Frequency domain analysis of CA

In awake subjects, BP, and consequently CBFV, fluctuate spontaneously around two predominent frequencies. The low frequency (LF; ~0.1 Hz or a wavelength ~10 s) is attributable to baroreflex-mediated sympathetic nervous system activity,[18 19] and the high frequency (HF; ~0.25 Hz or a wavelength of ~4 s) is attributable to respiration (Fig. 1A and B). Using 'frequency domain' analysis,[24 25] the relative power (or amplitude) of these fluctuations can be calculated and analysed in order to determine CA efficacy. Given that CA is a mechanism that requires ~5 s[7] to react to BP disturbances, HF BP oscillations pass unaltered into CBFV oscillations.[20] In contrast, LF BP oscillations are counter-regulated and damped by CA. Therefore, LF oscillations in CBFV are out of phase with LF oscillations in BP, and the phase lead of CBFV to BP in the LF domain (expressed in degrees, °) is the main measure for CA efficacy. When CA is intact, this is reflected as a ~50° LF phase lead, whereas impaired CA is characterized by a ~30° LF phase lead.[3 7]

Coherence

The squared coherence function reflects the fraction of CBFV variation that can be linearly attributed to BP variation. In a similar manner to a correlation coefficient, it varies between zero and one and must be sufficiently high to be able to calculate the BP–CBFV relationship (i.e. CA). In awake subjects, spontaneous LF BP oscillations are of sufficient magnitude (Fig. 1A and B), expressed as power. During anaesthesia, however, the power (or amplitude) of LF BP fluctuations is extremely low,[23] owing to suppression of the autonomic nervous system by anaesthetic agents,[21] and remaining BP variation is solely attributable to the intrathoracic pressure effects of mechanical positive pressure ventilation (Fig. 1C and D).[22] Any LF oscillation still present is considered 'noise'; hence, coherence is low. This presents the researcher with a problem and with a possible solution. When LF BP oscillations are desired for CA calculation, they might be imposed by adjusting mechanical ventilation to different frequencies (Fig. 1E and F). In the present study, we created consistent BP oscillations of a sufficient power at 6, 10, and 15 bpm or 0.1, 0.17, and 0.25 Hz, respectively, and determined the CBFV-to-BP relationship for each breathing frequency. These breathing frequencies may not always be within the physiological range for mechanical ventilation or respiratory rate. Indeed, they are not intended to examine the effects of respiratory rate *per se*, but these breathing frequencies are imposed to induce an