Continuous monitoring of cerebrovascular autoregulation: a validation study

E W Lang, H M Mehdorn, N W C Dorsch, M Czosnyka

Background: Continuous monitoring of dynamic cerebral autoregulation, using a moving correlation index of cerebral perfusion pressure and mean middle cerebral artery flow velocity, may be useful in patients with severe traumatic brain injury to guide treatment, and has been shown to be of prognostic value.

Objective: To compare an index of dynamic cerebral autoregulation (Mx) with an index of static cerebral autoregulation (sRoR).

Methods: Mx was validated in a prospective comparative study against sRoR, using 83 testing sessions in 17 patients with traumatic brain injury. sRoR and Mx were calculated simultaneously during pharmacologically induced blood pressure variations.

Results: Mx was significantly correlated with sRoR ($R = -0.78$, $p < 0.05$). Nine patients were found to have failure of cerebral autoregulation, with an sRoR value $< 50\%$. If an Mx value of 0.3 was used as the cut off point for failure of cerebral autoregulation, this index had $100\%$ sensitivity and $90\%$ specificity for demonstrating failure of autoregulation compared with the sRoR. An increase in cerebral blood flow velocity correlated significantly with Mx ($R = 0.73$, $p < 0.05$) but not with cerebral perfusion pressure ($R = 0.41$).

Conclusions: Dynamic and static cerebral autoregulation are significantly correlated in traumatic brain injury. Cerebral autoregulation can be monitored continuously, graded, and reliably assessed using a moving correlation analysis of cerebral perfusion pressure and cerebral blood flow velocity (Mx). The Mx index can be used to monitor cerebral blood flow regulation. It is useful in traumatic brain injury because it does not require any external stimulus.

Cerebral pressure autoregulation is an intrinsic ability of the brain to maintain a stable blood flow in the face of changes in arterial blood pressure or cerebral perfusion pressure. It is a major self defence mechanism against secondary ischaemic insults after traumatic brain injury and subarachnoid haemorrhage. Impairment of cerebral autoregulation has been shown to affect prognosis. Cerebral autoregulation involves both a response to slow changes in arterial blood pressure or cerebral perfusion pressure, known as “static autoregulation,” and a response to rapid changes in arterial blood pressure or cerebral perfusion pressure, called “dynamic autoregulation.” For patients with severe traumatic brain injury it would be desirable to be able to monitor cerebral autoregulation without recourse to mechanical manipulation of the blood pressure—for example, by the carotid compression and release manoeuvre, sudden head tilt manoeuvres, or leg cuff deflation tests—because these may cause undesirable increases in intracranial pressure, while pharmacological blood pressure manipulations are difficult and time consuming to perform.

With this in mind, one of our group (MC) has developed a cerebral autoregulation monitoring algorithm, known as “Mx”, which is based on the continuous analysis of slow, spontaneous fluctuations of cerebral perfusion pressure and cerebral blood flow velocity measured by transcranial Doppler ultrasound. Because there have been only a few studies assessing the inter-test agreement of cerebral autoregulation tests, and because Mx has so far only been compared with the leg cuff deflation test, which is also an index of dynamic cerebral autoregulation, we have now compared Mx with a well established index of static cerebral autoregulation, the static rate of regulation (sRoR).

Both Mx and sRoR can serve as indices to express the stability of cerebral blood flow during changes in cerebral perfusion pressure. The main difference is that the Mx index is usually derived from comparatively small and spontaneous fluctuations of cerebral perfusion pressure and cerebral blood flow velocity, while the sRoR index requires somewhat larger and pharmacologically induced blood pressure variations. In this protocol, calculating Mx from pharmacologically induced blood pressure variations had a twofold purpose: first, to use an identical dataset for comparison of both indices, and second, to validate the use of Mx as an index of the stability of cerebral blood flow velocity during large variations in cerebral perfusion pressure.

METHODS

Patients

Our patient group comprised two women and 15 men. Their mean (SD) age was 43 (15) years. All the patients had a Glasgow coma scale of less than 9 after initial resuscitation on admission, or it deteriorated to that level within the first 12 hours. Further details are shown in table 1.

Blood pressure recordings were obtained using a radial artery fluid coupled system (pvb, Kirchseeon, Germany). Intracranial pressure was measured with an intraparenchymal sensor (Intracranial Pressure Express®, Codman, Bracknell, UK; or Camino V420®, San Diego, California, USA). Intracranial pressure sensors were placed on the side of the injury, or in the right frontal area when there was diffuse injury or multiple contusions.

Cerebral blood flow velocities were recorded bilaterally using transcranial Doppler ultrasound (Multi-Dop X2®, DWL, Sipplingen, Germany), and the calculated mean blood flow velocity from both sides for all testing sessions was used. Obtaining a comparable transcranial Doppler signal source on different monitoring occasions was achieved by using a small...
arterial blood pressure and intracranial pressure. The same
were closely observed; ventilator settings and the levels of
the minimum cerebral perfusion pressure at each test session was that obtained
by decreasing the routine infusion of noradrenaline gradually
to zero, or to a point where the perfusion pressure fell to 55
mm Hg; the noradrenaline infusion was then gradually
increased until the perfusion pressure reached approximately
100 mm Hg, after which it was cut back to maintain a
desirable level. The protocol required about 35 to 50 minutes to
complete.
Throughout these manipulations, all physiological variables
were closely observed; ventilator settings and the levels of
sedation (midazolam) and analgesia (fentanyl) were main-
tained constant during the study. Arterial PaO₂ was main-
tained between 4.7 and 5.1 kPa. No additional treatment
aimed at controlling intracranial pressure—such as mannitol
or barbiturates—was given from 45 minutes before the study
until after its completion. In all cases blood pressure manipu-
lations were achieved according to the protocol. During one
blood pressure elevation we observed cardiac arrhythmias, but
these resolved spontaneously after decreasing the noradren-
aline infusion rate.
All analogue signals were recorded, averaged, and stored
digitally using a Neurox® multimodality data acquisition sys-
tem (GMS, Kiel-Mielkendorf, Germany). Fifteen second
time-averaged values of arterial blood pressure, mean cerebral
blood flow velocity, and mean intracranial pressure were cap-
tured and stored on disk for analysis. The cerebral perfusion
pressure was calculated on-line as the difference between
arterial blood pressure and intracranial pressure. The same
data sample was used for the calculation of both Mx and sRoR.
The number of testing sessions varied depending on the time
of presentation, the evolution of the injury, and the patient’s
clinical course in the intensive care unit. In order to avoid
potential bias caused by different numbers of test sessions, all
sessions for each patient were averaged.
This study was performed with the approval of the local
university ethics committee, which waived the need for
informed consent because varying the cerebral perfusion
pressure was considered to be an individual therapeutic trial.

**METHODS**

Our protocol involved manipulating arterial blood pressure
with noradrenaline (norepinephrine; Arterenol) to achieve
cerebral perfusion pressure changes between approximately
50 and 100 mm Hg. Eighty three cerebral autoregulation test
sessions involving blood pressure variations were undertaken
in 17 patients with traumatic brain injury. The minimum cer-
erebral perfusion pressure at each test session was that obtained
by decreasing the routine infusion of noradrenaline gradually
to zero, or to a point where the perfusion pressure fell to 55
mm Hg; the noradrenaline infusion was then gradually
increased until the perfusion pressure reached approximately
100 mm Hg, after which it was cut back to maintain a
desirable level. The protocol required about 35 to 50 minutes to
complete.

Table 1: Demographic details of the patients

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (years)</th>
<th>Sex</th>
<th>Injury</th>
<th>Monitoring day*</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>46</td>
<td>M</td>
<td>EDH, bilateral contusions</td>
<td>4, 5, 6, 7, 9, 10, 11, 12, 13</td>
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<tr>
<td>2</td>
<td>37</td>
<td>M</td>
<td>EDH, SDH, bilateral contusions</td>
<td>5, 6, 7, 8, 12, 13</td>
</tr>
<tr>
<td>3</td>
<td>41</td>
<td>M</td>
<td>SDH</td>
<td>2, 3, 4, 7</td>
</tr>
<tr>
<td>4</td>
<td>28</td>
<td>M</td>
<td>Bilateral SDH; EDH</td>
<td>5, 7</td>
</tr>
<tr>
<td>5</td>
<td>73</td>
<td>M</td>
<td>SDH, unilateral contusion</td>
<td>2, 3, 5, 6, 8, 10</td>
</tr>
<tr>
<td>6</td>
<td>26</td>
<td>M</td>
<td>Multiple contusions</td>
<td>2, 3, 5, 6, 8, 10</td>
</tr>
<tr>
<td>7</td>
<td>38</td>
<td>M</td>
<td>EDH</td>
<td>3, 5, 6, 9</td>
</tr>
<tr>
<td>8</td>
<td>61</td>
<td>M</td>
<td>Multiple contusions; SDH</td>
<td>3, 4, 7</td>
</tr>
<tr>
<td>9</td>
<td>56</td>
<td>F</td>
<td>SDH, multiple contusions</td>
<td>2, 3, 5, 6, 7, 9, 10</td>
</tr>
<tr>
<td>10</td>
<td>45</td>
<td>M</td>
<td>Unilateral contusion</td>
<td>0, 1, 3, 4</td>
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<tr>
<td>11</td>
<td>26</td>
<td>M</td>
<td>EDH</td>
<td>2, 3, 4, 7, 8, 9, 10, 15</td>
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<tr>
<td>12</td>
<td>22</td>
<td>M</td>
<td>EDH, SDH, unilateral contusion</td>
<td>1, 2, 4, 5, 6, 8, 10</td>
</tr>
<tr>
<td>13</td>
<td>53</td>
<td>M</td>
<td>SDH, unilateral contusion</td>
<td>2, 4, 6</td>
</tr>
<tr>
<td>14</td>
<td>22</td>
<td>M</td>
<td>EDH</td>
<td>1, 2, 3, 4, 6</td>
</tr>
<tr>
<td>15</td>
<td>59</td>
<td>M</td>
<td>Bilateral contusions</td>
<td>1, 3, 5, 7</td>
</tr>
<tr>
<td>16</td>
<td>46</td>
<td>F</td>
<td>Multiple contusions</td>
<td>2, 3, 5, 8, 9, 11</td>
</tr>
<tr>
<td>17</td>
<td>53</td>
<td>M</td>
<td>SDH, multiple contusions</td>
<td>3, 6, 7</td>
</tr>
</tbody>
</table>

*Day post-injury.
EDH, epidural haematoma; SDH, acute subdural haematoma.

**Static rate of regulation (sRoR)**

This index describes the change in cerebrovascular resistance
(CVR) determined from the relation between cerebral blood
flow velocity (CBFV) and changing cerebral perfusion
pressure (CPP). It is calculated as

\[ \text{sRoR} = \frac{100 \times (\text{ΔCPP})}{(\text{ΔCVR})} \]

where CVR = CPP/CBFV.²

An sRoR of 100% or more indicates completely intact
autoregulation where cerebral blood flow velocity is independent
of cerebral perfusion pressure, similar to the plateau phase
of cerebral autoregulation; 0% indicates complete loss of
cerebral autoregulation, with cerebral blood flow purely
dependent on and linearly related to cerebral perfusion
pressure. A value of 50% is considered the cut off for failure of
autoregulation. Thus sRoR is an index expressing quantita-
tively the stability of changes in cerebral blood flow when
arterial blood pressure (or cerebral perfusion pressure) varies.

rigid head frame (the “Arthur Lam transcranial Doppler probe
holder”), which attaches at the nasion and the ears and on
which transcranial Doppler probes can be firmly mounted and
maintained in a fixed position. Having ensured positional sta-
bility in this way, we used the same settings for depth, power,
sample volume, and gain at each test session.
The management of these patients consisted of aggressive
surgical and medical treatment including immediate evacua-
tion 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.¹
Continuous cerebrovascular autoregulation monitoring

Table 2  Mean values and standard deviations of cerebral perfusion pressure (CPP) and cerebral blood flow velocity (CBFV)

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPP [mm Hg]</td>
<td>60 (10)</td>
<td>95 (12)</td>
</tr>
<tr>
<td>CBFV [cm/s]</td>
<td>61 (20)</td>
<td>79 (17)</td>
</tr>
</tbody>
</table>

Values are mean (SD).

RESULTS

Table 1 gives information on the patients. During blood pressure variations, cerebral perfusion pressure (mean (SD)) increased from 60 (10) to 95 (12) mm Hg. Mean cerebral blood flow velocity increased from 61 (20) to 79 (17) cm/s (table 2).

The Mx index showed a significant correlation with sRoR ($R = -0.78; p < 0.05$; fig 1). Nine patients were found to have failure of cerebral autoregulation, with sRoR values of < 50%, indicated by the points below the horizontal line. When a value of 0.3 was selected as the cut off point for failure of cerebral autoregulation using the Mx index—indicated by the points to the right of the vertical line—this index had 100% sensitivity and 90% specificity for showing failure of cerebral autoregulation compared with the sRoR.

At the same time an increase in the cerebral blood flow velocity correlated significantly with the Mx ($R = 0.73$, $p < 0.05$; fig 2) but not with cerebral perfusion pressure ($R = 0.41; p = 0.08$, NS). This shows that the greater the increase in blood flow velocity during cerebral perfusion pressure changes, the greater the value of Mx.

DISCUSSION

Our study shows that cerebral autoregulation can be monitored continuously, graded, and reliably assessed using a correlation analysis of slow cerebral blood flow velocity waves and cerebral perfusion pressure, known as Mx. Although measured for the purposes of this study at the same time as sRoR, the Mx index does not normally require any external mechanical or pharmacological stimuli. Mx serves to indicate and quantify the stability of cerebral blood flow regulation during blood pressure changes. This interpretation is based on a physiological model in which intact cerebral autoregulation is indicated by an autoregulatory plateau phase, whereby changing the cerebral perfusion pressure has little effect on cerebral blood flow velocity. Our study also shows that dynamic and static assessments of cerebral autoregulation are significantly correlated in patients with traumatic brain injury.

Continuous cerebral autoregulation monitoring

While previous comparative studies required repeated testing sessions, this study used identical datasets for simultaneous assessment of static and dynamic cerebral autoregulation. Subsequent or repeated cerebral autoregulation testing may have influenced the results to an unknown extent in previous studies. So far only the leg cuff deflation test has been shown to yield stable results on repetition. The Mx monitoring protocol allows continuous monitoring of cerebral autoregulation, while other tests offer only intermittent “snapshot” monitoring. It was pointed out by Lewis et al that autoregulatory disturbance precedes autoregulatory failure. Continuous Mx monitoring in patients with traumatic brain injury could thus identify disturbances of cerebral autoregulation in time to achieve successful treatment. The use of continuous cerebral autoregulation monitoring as part of a head injury treatment protocol is supported by Mascia et al, who reported that management of cerebral perfusion pressure with vasopressor agents was safe so long as autoregulation was preserved. They stressed that “the assessment of pressure autoregulation should be considered as a guide for arterial pressure oriented therapy after head injury.”

We have also confirmed that Mx serves as an indicator of the stability of cerebral blood flow regulation during blood pressure changes, being significantly correlated with the sRoR index. The sRoR, however, requires pharmacological induction of blood pressure variations and it is thus more difficult and time consuming to perform. Figure 2 shows the relation between Mx and cerebral blood flow velocity changes: a high Mx signifies a marked change in cerebral blood flow velocity during variation in blood pressure, indicating compromised cerebral autoregulation or complete failure of autoregulation.

Comparative studies

Inter-test agreement has been examined in only six studies to our knowledge—in traumatic brain injury, in traumatic brain injury with subarachnoid haemorrhage, in normal subjects during anaesthesia with propofol followed by isoflurane, in patients with occlusive cerebrovascular disease, in acute ischaemic stroke, and in healthy volunteers at different levels of ventilation. It appears from these studies that there is demonstrating failure of cerebral autoregulation compared with the sRoR.
at least some similarity between tests that assess dynamic cerebral autoregulation and those that assess static autoregulation.

Smielewski et al reported a significant correlation between the transient hyperaemic response test and the dynamic cerebral autoregulation index, based on a moving correlation analysis between cerebral perfusion pressure and systolic cerebral blood flow velocity in patients with traumatic brain injury (the “Sx” index, contrasted with the mean velocity in our Mx index). There is also evidence that metabolic cerebral autoregulation correlates well with dynamic cerebral autoregulation assessed by the Valsalva manoeuvre. Steinmeier et al, however, found no correlation between the orthostatic hypotension test, the cuff deflation test, and the transient hyperaemic response test in a combined subarachnoid haemorrhage-traumatic brain injury group, although there was good agreement between the orthostatic hypotension test and a cross correlation analysis. In a series of 61 patients with acute stroke, Dawson et al reported that dynamic but not static cerebral autoregulation was impaired.17

Piechnik et al compared the Mx and Sx indices at different CO2 levels with the cuff deflation test in healthy volunteers, and reported a “...reasonably good correlation” between both Mx and Sx and the cuff deflation test. They stressed that all indices of dynamic cerebral autoregulation depended on the degree of ventilation, hyperventilation causing impairment of autoregulation; this was also shown in the original cuff deflation study. For intensive care management this finding emphasises the importance of maintaining a constant mild to moderate degree of hyperventilation, which was done in all patients in our study.

Tiecks et al have shown that in normal human subjects measurements of dynamic autoregulation yield similar results to static testing during both intact and pharmacologically impaired autoregulation. They also suggested that static cerebral autoregulation may be less vulnerable than dynamic autoregulation because of different control mechanisms and centres. Our study shows that in patients with traumatic brain injury dynamic and static cerebral autoregulation are equally affected, which does not allow any conclusions to be drawn about possible control mechanisms.

Conclusions

Our study provides further insight into the correlation between static and dynamic cerebral autoregulation in severely head injured patients. It confirms the feasibility and value of the Mx index for continuous and reliable monitoring of cerebral autoregulation. Further comparative studies are needed to determine whether static and dynamic cerebral autoregulation are equally affected in other critical neurological conditions such as subarachnoid haemorrhage or spontaneous hypertensive intracerebral haemorrhage.

ACKNOWLEDGEMENTS

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REFERENCES


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