Clinical study

Cerebral blood flow and dynamic cerebral autoregulation during ethanol intoxication and hypercapnia

Martin Blaha MD, Rune Aaslid PhD, Colleen M. Douville BA, Reinaldo Correra RVT, David W. Newell MD,
Department of Neurological Surgery, School of Medicine, University of Washington, Seattle, WA, USA

Summary More than one-third of patients diagnosed with head injury are intoxicated with ethanol. Most clinical and animal studies have shown alcohol to have a deleterious impact in the setting of cerebrovascular trauma; however, there are also data showing neuroprotective effects in low ethanol doses. Human studies using imaging modalities suggest that small doses of alcohol produce cerebral vasodilatation and higher doses cerebral vasoconstriction. The aim of this study was to investigate the effect of ethanol intake on dynamic cerebral autoregulation and velocities in the middle cerebral arteries, and compare these changes with the effects of hypercapnia. Dynamic cerebral autoregulation and cerebral blood flow velocities were analysed before and after alcohol intake (1.1 g/kg of body weight) in six adult volunteers. Cerebral blood flow velocities in both middle cerebral arteries were monitored continuously by transcranial Doppler. A value for dynamic cerebral autoregulation was calculated from the rate of increase in middle cerebral artery velocities after a rapid-step decrease in arterial blood pressure. A sudden decrease in blood pressure was achieved by the release of previously inflated large blood pressure cuffs around the subject’s thighs. Three volunteers were also tested before alcohol intake with CO₂ challenge (breathing 6% CO₂) during the autoregulation procedure. Blood alcohol level reached 90 mg/dl approximately 60 min after ethanol ingestion. Cerebral blood velocities increased by 8% from baseline for uncorrected end-tidal (et) CO₂ and by 24% for correction to et CO₂ = 40. Dynamic cerebral autoregulation measured as an autoregulation index decreased from 4.3 ± 1.3 to 2.9 ± 1.1 (p = 0.089), which did not reach statistical significance. During hypercapnic conditions, dynamic cerebral autoregulation dropped from 4 ± 0.8 to 0.9 ± 0.9. In conclusion, mild alcohol intoxication caused cerebral vasodilatation with a subsequent increase in cerebral blood flow of 8–24%. Dynamic cerebral autoregulation was not found to be significantly impaired by ethanol. Hypercapnia almost completely destroys the physiological autoregulatory mechanism. A mild hyper-ventilation to etCO₂ = 34–36 may be a compensatory contra-measure for ethanol-induced vasodilatation in the setting of head trauma © 2003 Elsevier Science Ltd. All rights reserved.

Keywords: alcohol, autoregulation, cerebral blood flow, head injury, hypercapnia, transcranial Doppler ultrasonography

INTRODUCTION

Of the 2657 patients admitted with blunt or penetrating trauma from the emergency room in our regional level I trauma center, 47% had a positive blood alcohol level (BAL) and 35.8% were intoxicated (BAL > 100 mg/dl) on admission. In a group of 520 patients diagnosed with brain injury, 36.7% were intoxicated with ethanol. To adequately treat this significant subpopulation of intoxicated head injury patients, animal and clinical studies have previously been conducted to investigate acute and chronic effects of ethanol on cerebral hemodynamics, metabolism, outcome from head trauma, and the risk of associated complications. Most clinical studies have found alcohol intoxication associated with increased mortality and morbidity. Interestingly, further stratification of patients has shown that acute intoxication alone did not increase mortality or risk of complication, in contrast to an intoxicated population with evidence of chronic alcohol use, which had a twofold increased risk of complications. Three-fourths of acutely intoxicated patients admitted with trauma in our institution had evidence of chronic alcoholism (positive Short Michigan Alcohol Screening Test) and 30% had bio-chemical evidence of chronic alcohol abuse.

The deleterious impact of ethanol intoxication in the setting of head injury has also been demonstrated in animal studies. Other data have demonstrated the neuroprotective effect of low doses of ethanol (1–2.5 g/kg), given prior to traumatic brain injury, due to a decreased degree of uncoupling between glucose metabolism and cerebral blood flow. Human studies on cerebral blood flow suggest that small doses of alcohol produce cerebral vasodilatation and higher doses produce cerebral vasoconstriction. Chronic alcoholism was associated with a reduction of cerebral blood flow and cerebral metabolism. Regional changes in cerebral blood flow were studied using the 133Xe inhalation technique or 99mTc SPECT (single-photon emission computed tomography), and showed a vasodilatory effect in prefrontal and temporal regions. The aim of this study was to investigate the effect of ethanol intake on dynamic cerebral autoregulation and compare these changes with the effects of hypercapnia. A second target was to evaluate the changes in velocities from the middle cerebral arteries and correlate them with changes in cerebral blood flow.

MATERIALS AND METHODS

The study was approved by the University of Washington Human Subject Review Committee. Written informed consent was obtained from each volunteer.

Subjects

Six healthy adult volunteers (five males and one female) with no history of alcohol abuse participated in this study. Their ages were between 27 and 39 years (mean 32.5 ± 4.1) and they described themselves as social drinkers. We advised them to not drink any alcohol for 24 h prior to testing and to avoid caffeine-containing beverages for 6 h prior to the test.

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Correspondence to: Dr Martin Blaha, Neurosurgery Department, Royal Perth Hospital, Box X2213 GPO, Perth, WA 6847, Australia. Tel.: +61-08-9224-2596; Fax: +61-08-9224-8099; E-mail: drmartinblaha@yahoo.com

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Alcohol source and blood alcohol level measurement

As a source of ethyl alcohol, Wild Turkey whisky, 50% alcohol, was used. Blood alcohol level (BAL) was measured with a breath analyzer (BAC Datametr, National Patent Analytical Systems, OH, USA).

Hemodynamics measurement

A headband was placed onto the subject’s head allowing secure attachment of a left and right transducer over the temporal windows. Velocities from both middle cerebral arteries were continuously monitored at a depth providing the best signal (50–54 mm) using TCD equipment (MultidopX, DWL, Sipplingen, Germany). Non-invasive continuous blood pressure and heart rate were recorded with a tonometric sensor (CBM-7000, Colín, San Antonio, TX, USA) placed over the right radial artery and a pneumatic calibration cuff placed on the right upper arm. End-tidal (et) CO2 concentration was intermittently measured with a CO2 analyzer (Datex 223, Puritan-Bennett, Tewksbury, MA, USA).

Dynamic cerebral autoregulation

Large blood pressure cuffs were placed around both thighs of the subject. The cuffs were attached to an inflation device (E-20 Rapid cuff inflator, Hokanson, Bellevue, WA, USA) and inflated to 30 mmHg above systolic blood pressure for 3–4 min. The sudden release of these cuffs caused a rapid-step decrease in arterial blood pressure, which remained lowered for approximately 20 s and then gradually returned to baseline values. A drop in arterial blood pressure, which remained lowered for approximately 20 s and then gradually returned to baseline values. The etCO2 at the same time dropped from 40.7 ± 2.2 to 36.7 ± 2.6 mmHg. To correct these etCO2 changes for measured velocities, we recalculated allVmca at et CO2 level of 40 mmHg. A value of 3.4% change in Vmca per 1 mmHg of etCO2 was used.14 The corrected mean velocity increased by 76% from 62.0 to 77.3 cm/s (p = 0.002). Pulsatility index (PI) was also averaged from both middle cerebral arteries for every subject. Compared to a value of 0.86 ± 0.13 before alcohol ingestion, PI decreased to 0.77 ± 0.16 during the highest blood alcohol level. We did not use any PI correction for etCO2 changes due to a lack of supportive data in the literature.

Mean ARI with a BAL = 0 was 4.5 ± 1.1. A second measurement during alcohol intoxication (BAL = 90.3 ± 19.9) showed decreased ARI to 3.6 ± 1.2. For CO2 correction we used our data from autoregulation testing with CO2 challenge, which showed an 8.2% decrease in ARI for every 1 mmHg of etCO2 increase. Recalculated ARI for etCO2 = 40 mmHg was 4.2 before alcohol ingestion and 2.9 with BAL = 90.3 ± 19.9. Neither the uncorrected nor corrected ARI decrease was statistically significant (paired t test, p = 0.136 and or 0.078, respectively). When dynamic cerebral autoregulation was tested with CO2 challenge, ARI decreased from 4 ± 0.75 to 0.9 ± 0.9.

RESULTS

The results of our study are summarized in Table 1. No volunteer had significant side differences in middle cerebral artery velocities, so we averaged these numbers for every subject. Mean velocity in the MCA increased during alcohol ingestion from baseline 63.5 ± 9.7 to 68.5 ± 8.4 cm/s (p = 0.015) during alcohol blood levels of 90.3 ± 19.9 mg/dl. This represents a 7.9% increase from baseline values. The etCO2 at the same time dropped from 40.7 ± 2.2 to 36.7 ± 2.6 mmHg. To correct these etCO2 changes for measured velocities, we recalculated allVmca at et CO2 level of 40 mmHg. A value of 3.4% change in Vmca per 1 mmHg of etCO2 was used.14 The corrected mean velocity increased by 76% from 62.0 to 77.3 cm/s (p = 0.002). Pulsatility index (PI) was also averaged from both middle cerebral arteries for every subject. Compared to a value of 0.86 ± 0.13 before alcohol ingestion, PI decreased to 0.77 ± 0.16 during the highest blood alcohol level. We did not use any PI correction for etCO2 changes due to a lack of supportive data in the literature.

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Table 1  Results of ethanol intoxication

<table>
<thead>
<tr>
<th>Alcohol level (mg/dl)</th>
<th>Baseline</th>
<th>20 min</th>
<th>40 min</th>
<th>60 min</th>
</tr>
</thead>
<tbody>
<tr>
<td>etCO2 (mg/Hg)</td>
<td>0</td>
<td>45.4 ± 12.4</td>
<td>87.5 ± 19.4</td>
<td>90.3 ± 19.9</td>
</tr>
<tr>
<td>Vmca (cm/s)</td>
<td>63.5 ± 9.7</td>
<td>68.5 ± 9.9</td>
<td>67.8 ± 11.6</td>
<td>68.5 ± 8.4</td>
</tr>
<tr>
<td>Vmca corrected to etCO2 = 40 mmHg (cm/s)</td>
<td>62.0 ± 7.7</td>
<td>67.0 ± 8.2</td>
<td>71.4 ± 11.6</td>
<td>77.3 ± 6.4</td>
</tr>
<tr>
<td>PI</td>
<td>0.86 ± 0.13</td>
<td>0.75 ± 0.22</td>
<td>0.77 ± 0.12</td>
<td>0.77 ± 0.16</td>
</tr>
<tr>
<td>HR (beats/min)</td>
<td>63.7 ± 14.4</td>
<td>68 ± 13.6</td>
<td>72.7 ± 16.4</td>
<td>66 ± 13.0</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>114.7 ± 9.0</td>
<td>119.2 ± 14.1</td>
<td>116.7 ± 17.3</td>
<td>116 ± 9.3</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>58.8 ± 6.2</td>
<td>67.0 ± 9.1</td>
<td>62.2 ± 10.1</td>
<td>60.7 ± 7.5</td>
</tr>
<tr>
<td>ARI</td>
<td>4.5 ± 1.1</td>
<td>43 ± 1.3</td>
<td>3 ± 1.2</td>
<td>2.9 ± 1.1</td>
</tr>
</tbody>
</table>

etCO2, end-tidal etCO2; Vmca, velocity in the middle cerebral artery; PI, pulsatility index; HR, heart rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; ARI, autoregulation index.

DISCUSSION

Cerebral blood flow

In our study we used transcranial Doppler to non-invasively assess cerebral hemodynamics. This method does not measure absolute cerebral blood flow but is able to provide reliable data about relative changes in CBF based on the assumption that the MCA diameter does not change and, therefore, changes in middle cerebral artery velocity are directly related to changes in cerebral blood flow. This assumption was confirmed by Newell et al. comparing intraoperative flow in the internal carotid artery versus transcranial velocities in the MCA.

The present study shows increased mean velocities in the middle cerebral arteries from 63.5 ± 9.7 to 68.5 ± 8.4 cm/s (+7.9%). The paired Student’s t test was used to analyze these data and showed statistical significance (p = 0.015). Cerebral blood flow and Vmca are very sensitive to changes in CO2 levels. Markwalder et al. showed that for every 1 mm increase (decrease) in CO2, Vmca increased (decreased) by 3.4%. Because of unequal values of etCO2 during our Vmca measurements, we corrected all measured values to an etCO2 = 40 mmHg using an index of 3.4%/l mmHg CO2. The corrected Vmca values showed a steady increase from 62.0 ± 7.7 to 77.3 ± 6.4 cm/s (+24.6%). This difference was statistically significant (p = 0.02). This increase in middle cerebral arteries is caused by vasodilatation in the peripheral cerebral vessels caused by alcohol and results in increased cerebral blood flow during mild alcohol intoxication. The index for CO2 correction was calculated for sudden changes in CO2 with subsequent immediate measurement of changes in Vmca. In our study CO2 changes were slow during the 60 min interval and vascular tone may have had time to adapt to a new CO2 level. There are no data to precisely adjust this time factor. We can say that mild alcohol intoxication increased cerebral blood flow by 8–24% as a function of increased velocities in both MCAs. This finding is consistent with studies using 133Xe or 99mTc SPECT to measure CBF which showed a 12–14% increase compared to baseline. Hypocapnia decreases CBF by approximately 13.6–20.4% and vasodilatation with BAL around 90 mg/dl. As previously mentioned, there may be a small amount of time adaptation for changes in vascular tone, and it is important to understand that if our volunteers were intubated and ventilated to etCO2 = 40 mmHg, the cerebral blood flow would be 24.4% higher compared to their sober status. If patients present with increased intracranial pressure, alcohol related increases in CBF could be one of the causative factors of such an increase. As a treatment strategy, it is essential to avoid hyperventilation; and if ICP needs to be targeted, mild hyperventilation to etCO2 = 3436 mmHg can be used. Hypocapnia decreases CBF by approximately 13.6–20.4% and compensates for the vasodilatative effect of alcohol. Further data are needed to better determine the time adjustment of the cerebral vasculature to changes in CO2 and to identify changes in CBF relative to blood alcohol level.

Autoregulation

Dynamic cerebral autoregulation was assessed with the method developed by Aaslid et al. using a rapid-step decrease in arterial blood pressure after the release of large blood pressure cuffs placed around the thighs of the subjects. The drop and consequent return of blood pressure back to baseline is compared with velocities in middle cerebral arteries, and the ability of the cerebral vasculature to compensate for blood pressure fluctuations is calculated as an ARI. It was previously demonstrated that volatile anesthetic agents such as isoflurane or desflurane disturbed autoregulatory responses. Studies on patients with severe head trauma [Glasgow Coma Scale (GCS) ≤ 8] showed significant impairment of autoregulation as a result of decreased vascular tone. In a group of patients with minor head injury (GCS 13–15) there was a subgroup of patients with impaired autoregulatory response. The statistically significant cutoff between “intact” and impaired autoregulation was found to be 2.5. The mean ARI before ingestion of alcohol was, in our study, 4.5 ± 1.1 and decreased to 3.6 ± 1.2 when the BAL reached 90.3 mg/dl. Because of unequal etCO2 39 and 37.2 mmHg, respectively, we corrected the original values to etCO2 equal to 40 mmHg. For this correction we used our data from testing dynamic cerebral autoregulation during CO2 challenge, which showed an 8.24% decrease in ARI per 1 mmHg of CO2 increase. We are aware that the index for this correction is based on a small number of subjects and gave us only a rough estimation for correction. Our target was to find whether this correction brought any significant difference compared to uncorrected values. The paired Student’s t test was performed and did not show statistical significance between baseline and alcohol values, for either uncorrected or corrected ARI (p = 0.136 and 0.078). On the other side, dynamic cerebral autoregulation tests with CO2 challenge showed significant impairment under hypocapnic conditions as previously described by Aaslid et al. The ARI decreased from baseline values of 4 ± 0.8 to 0.9 ± 0.9 as a result of decreased vascular tone in the cerebral peripheral vasculature.

Our results showed only mild, statistically not significant, decreases in the dynamic autoregulation response based on mild alcohol-related vasodilatation. As the most important regulator of this physiological principle, the etCO2 (PaCO2) was identified. During hyperventilation-related vasodilatation, the cerebral vasculature does not have an adequate mechanism to compensate for a sudden drop in blood pressure, which results in severe autoregulation impairment. Conversely, hyperventilation can temporarily improve the autoregulatory response as a result of an increase in vascular tone. Severe head-injured patients and approximately one-third of patients following minor head injury demonstrate impairment of their autoregulation due to trauma-induced decreases in cerebral vascular tone. The most efficient treatment strategy is to protect our patients from hypoventilation, which causes rising PaCO2 and further impairment of the autoregulatory response.

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REFERENCES


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