High Ethanol Consumption as Risk Factor for Intracerebral Hemorrhage in Young and Middle-Aged People

R. Monforte, MD, R. Estruch, MD, F. Graus, MD, J.M. Nicolas, MD, and A. Urbano-Marquez, MD

We examined the prevalence of high ethanol intake, hypertension, and other risk factors for intracerebral hemorrhage in a case-control study of 24 young and middle-aged patients with intracerebral hemorrhage. We recorded ethanol consumption, history of hypertension, liver disease, cigarette smoking, and mild or severe coagulation disorder in each case of intracerebral hemorrhage and in 48 control patients matched by sex and age. In univariate matched analyses, the frequencies of high ethanol intake ($p=0.009$), hypertension ($p=0.05$), and coagulation disorder ($p=0.05$) were higher in the cases than in the controls. After controlling for possible confounding factors, we found that high ethanol intake and hypertension were the only independent risk factors for intracerebral hemorrhage ($p=0.02$ and $p=0.05$, respectively). The hemorrhagic lesion found in cases with a high ethanol intake tended to be located in the cerebral lobes ($p=0.01$), contrasting with the typical basal ganglia location of hypertensive hematomas ($p=0.009$). We conclude that chronic, high ethanol intake should be considered as an important risk factor for lobar hematomas in young and middle-aged people. (Stroke 1990;21:1529-1532)

Subjects and Methods

As cases, we considered the 85 patients admitted to the Department of Internal Medicine of the Hospital Clinic of Barcelona between March 1987 and June 1989 who had a diagnosis of intracerebral hemorrhage supported by computed tomography (CT) performed on admission. We excluded patients with hemorrhage in cerebral tumors or arteriovenous malformations as suggested by the clinical features, CT, or angiography. We also excluded patients >65 years of age to reduce the influence of confounding factors associated with aging such as amyloid angiopathy. Only 24 patients with an intracerebral hemorrhage (20 men and four women) met the inclusion criteria. They had a mean±SD age of 51.4±10.6 (range 33–63) years. The controls included patients with a diagnosis of chronic respiratory disease (seven), neoplasia (six), infectious diseases (16), cardiac disorders (four), decompensated liver disease (three), pancreatitis (two), connective tissue diseases (three), hematologic disorders (two), diabetes (two), gastrointestinal bleeding (two), or pulmonary embolism (one). Ne-
TABLE 1. Matched Logistic Regression Analysis of Risk Factors for Intracerebral Hemorrhage

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Cases (n=24)</th>
<th>Controls (n=48)</th>
<th>Univariate analysis</th>
<th>Multivariate analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>High ethanol intake</td>
<td>16</td>
<td>14</td>
<td>15.82</td>
<td>2.01-124.08</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.009</td>
<td>10.31</td>
</tr>
<tr>
<td>Hypertension</td>
<td>12</td>
<td>12</td>
<td>2.6</td>
<td>1.01-6.86</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.05</td>
<td>3.37</td>
</tr>
<tr>
<td>Coagulation disorder</td>
<td>5</td>
<td>3</td>
<td>8.58</td>
<td>1.02-74.87</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.05</td>
<td>4.82</td>
</tr>
<tr>
<td>Severe</td>
<td>2</td>
<td>2</td>
<td>4.6</td>
<td>0.46-46.84</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.19</td>
<td>0.05</td>
</tr>
<tr>
<td>Liver dysfunction</td>
<td>4</td>
<td>6</td>
<td>1.38</td>
<td>0.35-5.28</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.63</td>
<td>...</td>
</tr>
<tr>
<td>Cigarette smoking</td>
<td>16</td>
<td>29</td>
<td>1.52</td>
<td>0.41-5.57</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.52</td>
<td>...</td>
</tr>
</tbody>
</table>

OR, odds ratio; CI, confidence interval.

*Includes severe and mild coagulation disorders. Severe coagulation disorder was defined as prothrombin time of >14.9 (control value 12) seconds and/or platelet count of <30×10^9/l. Mild coagulation disorder was defined as prothrombin time of 13.1–14.9 seconds and/or platelet count of 30–50×10^9/l.

Results

In most cases clinical manifestations of intracerebral hemorrhage included focal neurologic deficits, headache, and alteration of consciousness. Seizures were seen in eight cases, three upon clinical alcohol withdrawal and delirium tremens prior to admission. No evidence of head trauma was seen in any case.

Of the 24 cases, 16 had a high ethanol intake. Five of these 16 patients also had a history of hypertension, one had a severe coagulation disorder (prothrombin time of 16.5 seconds), three had a mild coagulation disorder, and four showed increased concentrations of hepatic enzymes. Two of the latter had been diagnosed as having cirrhosis of the liver. A history of hypertension was recorded in 12 cases, five of whom also had a high ethanol intake. Sixteen cases had smoked 1–3 packs/day since the second decade of their lives, while the remainder did not smoke. Finally, the last case had a thrombocytopenia (10^9 platelets/l) due to infection with the human immunodeficiency virus (HIV). This patient was addicted to heroin, but the remainder were not users of street drugs. No significant differences in the other laboratory findings were seen between the cases and controls except for erythrocyte mean corpuscular volume and the serum concentration of γ-glutamyl transpeptidase (p<0.05 for both).

In univariate matched analyses, the prevalences of high ethanol intake, hypertension, and mild or severe coagulation disorder differed significantly between cases and controls (Table 1). After adjusting for the variables high ethanol intake, hypertension, and coagulation disorder by the multiple logistic regression technique, only high ethanol intake and hypertension were independent risk factors for intracerebral hemorrhage (Table 1). By contrast, no significant relation between high ethanol intake and hypertension was observed in the matched analysis (p=0.3).
Depending on the location of the hematoma in the CT scan, cases were classified as having lobar (11) or other (13; 11 in the basal ganglia, one in the thalamus, and one in the pons) hematomas. Nine of the 11 cases with lobar hematomas had a high ethanol intake, one had a history of hypertension, and the remaining case had a severe coagulation disorder related to an HIV infection. On the other hand, the associated risk factors for the 13 cases with hematomas located in other areas were hypertension and high ethanol intake in five, hypertension alone in six, and high ethanol intake alone in only two. Thus, alcohol drinkers without hypertension tended to have lobar hematomas, whereas patients with hypertension alone tended to have hematomas in other central areas.

After considering the variable location of the hematoma in the multivariate analysis, we obtained a significant association between high ethanol intake and lobar hematoma (odds ratio 6.9, 95% confidence interval [CI] 1.45–32.78; \( p = 0.01 \)). Moreover, we observed a significant relation between hypertension and basal ganglia hematoma (odds ratio 7.8, 95% CI 1.67–36.75; \( p = 0.009 \)), confirming that both variables were independent risk factors for the development of intracerebral hemorrhage.

Discussion

Alcohol intake has been recognized as a risk factor for stroke only during the last decade. However, the pathogenetic role of high ethanol intake in the development of ischemic and hemorrhagic stroke continues to be unclear. Whether the effect of ethanol is mediated by hypertension or other indirect mechanisms, or whether ethanol is toxic to the cerebral vessels, is a point of controversy.

Recent controlled epidemiologic studies suggest that high ethanol intake is not an independent risk factor for ischemic cerebral infarction when hypertension and smoking are taken into account. By contrast, in some series of spontaneous intracerebral hematomas high alcohol consumption has been considered to be one of the most important risk factors for hemorrhagic stroke. Thus, Donahue et al reported a high prevalence of moderate and heavy drinkers among patients with hemorrhagic strokes, especially strokes of subarachnoid origin. Calandre et al found that chronic alcoholism was the strongest risk factor for intracerebral hemorrhage in a retrospective case–control study in Spain. Finally, in their prospective series Niizuma et al explored the influence of liver dysfunction in the pathogenesis of intracerebral hemorrhage and found an ethanol intake of \( > 50 \, \text{g/day} \) in 37% of their patients. Although the selection criteria for the cases in those three studies differed, the concurrence of their results provides strong evidence of a pathogenetic link between chronic high ethanol intake and hemorrhagic stroke. Thus, our results seem to confirm the link between chronic high ethanol intake and hemorrhagic stroke in young and middle-aged people. On the other hand, the higher frequency in alcoholic patients of lobar hematomas rather than basal ganglia hematomas (which our hypertensive cases exhibited) suggests that the pathogenetic mechanisms of hematomas in these locations differ. The fact that Calandre et al found no differences in the risk factors for lobar and basal ganglia hematomas could be attributed to the effect of other confounding factors, mainly age, since elderly people were included in that series.

Although studies of large series of alcoholic patients have demonstrated a correlation between high ethanol intake and hypertension, we observed no such relation. Thus, we consider both variables to be independent risk factors. Based on previous studies and on our results, it seems unlikely that the chronic effect of hypertension is the main mechanism by which high ethanol intake increases the risk of intracerebral hemorrhage. The cerebral damage produced by sudden, transient elevations in blood pressure secondary to increases in the concentrations of circulating catecholamines in ethanol withdrawal, minor trauma, coagulation disturbances (related to an underlying liver disease or not), changes in regional cerebral blood flow, or direct endothelial damage in the cerebral vasculature may contribute to the increased risk in such persons.

In our series, three cases presented with ethanol withdrawal and seizures; thus, the possibility of minor trauma as a mechanism contributing to intracerebral hemorrhage could not be excluded although no evidence of head trauma was observed in any case. Among the remaining alcoholic cases, only one had a known risk factor for intracerebral hemorrhage (a prothrombin time of 16.5 seconds) associated with an alcoholic liver disease. Cases with a high ethanol intake without hypertension tended to have lobar hematomas, in contrast to those with hypertension, who were predisposed to bleed in the region of the basal ganglia. This finding suggests that the pathogenetic mechanisms of hematomas in these locations may differ and that high ethanol consumption could be one of the major causes of unexplained lobar hematomas.

In conclusion, we support the hypothesis that chronic high ethanol intake should be considered as one of the most important risk factors for hemorrhagic stroke in young and middle-aged people, especially those with lobar hematomas. Like other authors, we found that the effect of high ethanol intake is independent of that of chronic hypertension; however, further investigations are necessary to elucidate the relevancy of the different possible mechanisms by which ethanol may damage the cerebral vessels.

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References


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