Alcohol Use and Subsequent Cerebrovascular Disease Hospitalizations

Arthur L. Klatsky, MD, Mary Anne Armstrong, MA, and Gary D. Friedman, MD

We studied the relations between reported alcohol use and the incidence of hospitalization for several types of cerebrovascular disease. Daily consumption of three or more drinks, but not lighter drinking, was related to higher hospitalization rates for hemorrhagic cerebrovascular disease, especially intracerebral hemorrhage. Age, blood pressure, and black race were other independent predictors of hemorrhagic events; higher blood pressure appeared to be a partial mediator of the relation between alcohol use and hemorrhagic events. Alcohol use was associated with lower hospitalization rates for occlusive cerebrovascular disease; an inverse relation was present in both sexes, whites and blacks, and for extracranial and intracerebral occlusive lesions. Other predictors of hospitalization for occlusive disease included age, blood pressure, smoking, blood glucose and total cholesterol concentrations, and baseline disease. Our data suggest that heavier drinking increases the risk of hemorrhagic cerebrovascular events, but that alcohol use may lessen the risk of occlusive lesions. (Stroke 1989;20:741–746)

Most relevant investigations suggest that alcoholic beverage use, especially heavier drinking, is associated with a higher risk of stroke.1–9 Some studies5,8 did not differentiate hemorrhagic from occlusive strokes; others retrospectively examined the role of drinking sprees in both occlusive1,2 and hemorrhagic3,4 stroke in young persons. One study7 suggested that alcohol was involved in both types of stroke and another10 that alcohol was associated only with hemorrhagic stroke. The study of a large cohort of women10 showed drinkers to be at a higher risk of subarachnoid hemorrhage but at a lower risk of occlusive stroke. Other studies found no alcohol–stroke association when blood pressure11 or cigarette use12 were taken into account. In view of the need for further data, we present a new prospective study of hospitalization for hemorrhagic and occlusive cerebrovascular disease in a large population.

Subjects and Methods

The study population consisted of 107,137 persons (74,696 white; 33,041 black) who received health examinations in a prepaid health plan from January 1978 through December 1984. The examination was, for most persons, a routine health appraisal. The procedure included questionnaires, a panel of health measurements, and laboratory tests. For individuals who had one or more examinations, we used data from only the first examination as baseline data.

An alcohol questionnaire initially classified persons by their use of alcoholic beverages in the past year. We defined lifelong abstainers as nonusers who answered that they drank alcohol in the past never or almost never. Drinkers were asked how many drinks they usually had during the past year: >9/day, 6–8/day, 3–5/day, 1–2/day, <1/day but >1/month, and <1/month (special occasions only). Drinkers also indicated the number of days per week they consumed wine, beer, and hard liquor (whiskey, gin, rum, cocktails, brandy, vodka, etc.). Among persons who drank ≥1 drink/month, we defined preferers of a beverage as those who drank a beverage type exclusively or at least 1 day/week more often than either of the other two beverage types.

All subjects were followed until they left the health plan or until December 1984, whichever occurred first. Hospitalization for cerebrovascular disease (674 hospitalizations for 581 patients) was detected by a search of computerized hospital records for discharge diagnostic codes 430–438 of the International Classification of Diseases, Adapted for Use in the United States: Eighth Revision (ICDA).13 These codes included subarachnoid hem-
Table 1. Characteristics of Persons Hospitalized for Hemorrhagic or Oclusive Stroke and Noncases

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Hemorrhagic stroke cases (n=69)</th>
<th>Oclusive stroke cases (n=292)</th>
<th>Noncases (n=10,390)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol use</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abstainers</td>
<td>11</td>
<td>58</td>
<td>958</td>
</tr>
<tr>
<td>Former drinkers</td>
<td>3</td>
<td>24</td>
<td>337</td>
</tr>
<tr>
<td>&lt;1 drink/day</td>
<td>33</td>
<td>133</td>
<td>6,154</td>
</tr>
<tr>
<td>1-2 drinks/day</td>
<td>11</td>
<td>56</td>
<td>2,030</td>
</tr>
<tr>
<td>≥3 drinks/day</td>
<td>11</td>
<td>21</td>
<td>911</td>
</tr>
<tr>
<td>Age (&lt;50 years)</td>
<td>17</td>
<td>15</td>
<td>7,313</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>33</td>
<td>162</td>
<td>4,613</td>
</tr>
<tr>
<td>Female</td>
<td>36</td>
<td>130</td>
<td>5,777</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>31</td>
<td>220</td>
<td>7,265</td>
</tr>
<tr>
<td>Black</td>
<td>38</td>
<td>72</td>
<td>3,125</td>
</tr>
<tr>
<td>Coffee (≥4 cups/day)</td>
<td>13</td>
<td>56</td>
<td>1,812</td>
</tr>
<tr>
<td>Smoking (≥1 pack/day)</td>
<td>26</td>
<td>98</td>
<td>2,964</td>
</tr>
<tr>
<td>Quetelet index (≥4.0)</td>
<td>17</td>
<td>77</td>
<td>2,042</td>
</tr>
<tr>
<td>Systolic blood pressure (≥160 mm Hg)</td>
<td>18</td>
<td>84</td>
<td>554</td>
</tr>
</tbody>
</table>

Hemorrhagic stroke, International Classification of Diseases, Adapted, 8th revision codes 430 and 431; oclusive stroke, codes 432, 433, 434, and 435. Noncases in hemorrhagic stroke analyses. Numbers for other types of stroke differ slightly (range 10,389-10,394), but percentages in each category of each characteristic are the same.

Results

Former drinkers, persons drinking <1 drink/day, and persons drinking 1-2 drinks/day had a risk of hemorrhagic cerebrovascular disease similar to that of the reference group, lifelong abstainers (Table 2). The relative risk (RR) for persons who reported a
usual daily intake of ≥3 drinks/day (n=11) was slightly, but not significantly, increased. The risk of hemorrhagic events among ≥3 drinks/day drinkers was higher in the subset free of baseline disease (RR=3.64, 95% confidence interval [CI]=1.11-11.92) and became slightly higher in this subset when blood pressure was excluded from the analysis (Table 3). Even in this subset, lighter drinking showed little relation to hemorrhagic events.

With respect to hemorrhagic events, the RR and 95% CI comparing ≥3 drinks/day drinkers to abstainers for some subset analyses are men (n=15), RR=2.64 and 95% CI=0.29-24.18; women (n=28), RR=4.43 and 95% CI=0.88-22.28; blacks (n=18), RR=2.16 and 95% CI=0.24-19.39; whites (n=25), RR=4.60 and 95% CI=1.11-19.05; subarachnoid hemorrhage (n=15), RR=1.62 and 95% CI=0.22-11.82; and cerebral hemorrhage (n=28), RR=6.82 and 95% CI=1.48-31.44. These RRs were calculated for the subset free of baseline disease and were not controlled for blood pressure.

Former drinkers were at a risk similar to abstainers for occlusive disease, but all drinkers were at lower risk (Table 2). This inverse alcohol–occlusive disease relation was weaker in persons with no baseline illness and was weakened further by excluding blood pressure from the analysis (Table 3). We found no major sex differences, but the inverse relation was stronger in blacks than whites (Table 4). There were no major differences with respect to the alcohol–cerebrovascular disease relation between occlusion of precerebral arteries, cerebral thrombosis, or transient ischemic attacks (Table 5).

Among the few persons (n=6) who drank ≥6 drinks/day, the RR of occlusive disease was 0.60 (95% CI=0.25-1.49), whereas the RR was 0.39 (95% CI=0.21-0.72) for persons drinking 3–5 drinks/day (n=15). Thus, the inverse alcohol–occlusive disease relation was not progressive at the heaviest levels of drinking.

Controlling for all other traits (including the total number of usual daily drinks), use of specific beverage types had no significant independent relation to the risk of hemorrhagic cerebrovascular disease. The use of wine had a weaker inverse relation to occlusive cerebrovascular disease than use of hard liquor or beer. For all persons reporting drinking specific beverage types at least 2 days/week compared with lifelong abstainers, the RR and 95% CI for occlusive disease was for wine, 0.66 and 0.41-1.06; for hard liquor, 0.38 and 0.24-0.60; and for beer, 0.42 and 0.24-0.73.

Alcohol was not related to ill-defined or nonspecific cerebrovascular disease (ICDA codes 436-438) diagnosed in a large group (n=274) of persons. Compared with abstainers, the RR and 95% CI for <1/day, 1–2/day, and ≥3/day drinkers with these diagnoses were 0.83 and 0.59-1.16, 0.68 and 0.44-1.07, and 0.95 and 0.53-1.60, respectively. Combining all cerebrovascular disease categories (ICDA codes 430-438), the alcohol-associated risk was...
Table 4. Relative Risk of Hospitalization for All Occlusive Cerebrovascular Disease by Sex and Race According to Alcohol Use

<table>
<thead>
<tr>
<th>Alcohol use</th>
<th>Sex</th>
<th>Race</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Men (n=162)</td>
<td>Women (n=130)</td>
</tr>
<tr>
<td>Abstainers</td>
<td>RR 95% CI</td>
<td>RR 95% CI</td>
</tr>
<tr>
<td>Former drinkers</td>
<td>0.97 0.49-1.91</td>
<td>0.87 0.37-2.03</td>
</tr>
<tr>
<td>&lt;1/day</td>
<td>0.58 0.34-0.98</td>
<td>0.63 0.40-0.98</td>
</tr>
<tr>
<td>1-2/day</td>
<td>0.48 0.27-0.87</td>
<td>0.66 0.36-1.22</td>
</tr>
<tr>
<td>≥3/day</td>
<td>0.50 0.25-0.98</td>
<td>0.11 0.02-0.84</td>
</tr>
</tbody>
</table>

RR, relative risk computed from coefficients estimated by Cox proportional hazards model controlled for age, sex, race, coffee, smoking, Quetelet index, systolic blood pressure, and history of baseline disease; CI, confidence interval.

Discussion

Incorrect diagnosis is one of the major inherent difficulties encountered in epidemiologic studies of cerebrovascular disease, although the likelihood of error presumably has lessened substantially with the widespread use of diagnostic imaging techniques. Computed tomography was used in almost all the cases we reviewed. Assuming some incorrect diagnoses, it is possible that alcohol-associated head injury might spuriously increase the apparent incidence of cerebrovascular disease among heavier drinkers. However, such an artifact could not explain the reduced incidence of occlusive disease observed among drinkers.

Incorrect classification of the type of cerebrovascular disease is another potential problem. The differences we found between hemorrhagic and occlusive disease with respect to the associations of alcohol, race, and other characteristics suggest that we were studying different clinical entities. Since most of our subjects with extracranial occlusions were admitted for carotid arteriography or endarterectomy, we use the term "cerebrovascular disease" rather than stroke.

Incorrect assessment of alcohol consumption is frequently, but erroneously, cited as an indirect

Table 5. Relative Risk of Hospitalization for Selected Subsets of Occlusive Cerebrovascular Disease According to Alcohol Use

<table>
<thead>
<tr>
<th>Alcohol use</th>
<th>Precerebral occlusion (ICDA 432, n=124)</th>
<th>Cerebral thrombosis (ICDA 433, n=104)</th>
<th>Transient ischemic attack (ICDA 435, n=63)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abstainers</td>
<td>RR 95% CI</td>
<td>RR 95% CI</td>
<td>RR 95% CI</td>
</tr>
<tr>
<td>Former drinkers</td>
<td>0.94 0.41-2.14</td>
<td>0.96 0.44-2.10</td>
<td>1.00 0.32-3.45</td>
</tr>
<tr>
<td>&lt;1/day</td>
<td>0.55 0.31-0.97</td>
<td>0.47 0.27-0.81</td>
<td>0.89 0.43-1.81</td>
</tr>
<tr>
<td>1-2/day</td>
<td>0.37 0.19-0.74</td>
<td>0.59 0.31-1.12</td>
<td>0.62 0.25-1.56</td>
</tr>
<tr>
<td>≥3/day</td>
<td>0.46 0.21-1.01</td>
<td>0.28 0.10-0.79</td>
<td>0.47 0.12-1.80</td>
</tr>
</tbody>
</table>

ICDA: International Classification of Diseases, Adapted, 8th revision; RR, relative risk computed from coefficients estimated by Cox proportional hazards model controlled for age, sex, race, coffee, smoking, Quetelet index, systolic blood pressure, and history of baseline disease; CI, confidence interval.
explanation for the associations found in population studies. Underestimation of alcohol intake could weaken a true relation (positive or inverse), but unless underestimation is systematically related to subsequent disease, this problem would not create an apparent association that did not exist.

The higher risk of hemorrhagic cerebrovascular disease we found among heavier drinkers is compatible with the results of other reports. However, in contrast to one study, we found no relation to lighter alcohol intake, and we found the alcohol relation to be stronger for intracerebral hemorrhage than for subarachnoid bleeding. Heavier drinking has consistently been found to be associated with hypertension, and this may partly explain the higher risk of hemorrhagic cerebrovascular disease. If alcohol-induced hypertension is a link in a causal chain leading from alcohol use to cerebrovascular disease, a thorough analysis should exclude the effects of hypertension.

Another suggested mechanism is an alcohol-induced bleeding tendency. Head trauma related to heavier drinking could also precipitate intracranial hemorrhage. Thus, a direct causal relation between alcohol use and hemorrhagic cerebrovascular disease remains unproven.

To our knowledge, our study is the first to report a significant inverse relation in both sexes between alcohol intake and occlusive cerebrovascular disease. In a study of Japanese men that distinguished hemorrhagic from occlusive disease, no significant relation between alcohol use and occlusive disease was seen. In a case-control study that did not subdivide cerebrovascular disease, lighter drinkers were at slightly lower risk than abstainers, possibly due to an inverse relation between alcohol use and occlusive disease. Our findings among women are similar to prospective data among female nurses, which showed a lower risk of occlusive stroke among drinkers.

Relations between alcohol use and various cerebrovascular diseases are complex. Mechanisms have been postulated by which heavier drinking might produce the opposite of our finding—an increased risk of occlusive cerebrovascular disease. These include 1) emboli secondary to cardiomyopathy, 2) emboli secondary to supraventricular arrhythmias, 3) a thrombotic tendency in some drinkers, and 4) possible cerebrovascular spasm. Judging from our large study group, these potential causes of occlusive disease among heavier drinkers must be relatively uncommon. A relation between spree drinking and stroke in young persons has been attributed possibly to hypercoagulability, hemoconcentration, or prolonged neck posturing during drunken stupor in spree drinkers. Spree drinkers may be underrepresented in population studies of cooperative patients. It is probable that spree drinking has health effects different from those of steady drinking.

Since blood pressure is directly related to both occlusive cerebrovascular disease and alcohol consumption, the weakening of the inverse alcohol–occlusive disease association with exclusion of blood pressure from the analysis was expected. Without analytic control for blood pressure, its cerebrovascular disease–inducing effects would tend to counteract any possible protective effects of alcohol and to reduce the apparent inverse association.

Biologically plausible explanations for a lower incidence of occlusive cerebrovascular disease in drinkers include 1) less coronary artery disease and resulting cerebral emboli, 2) reduced extracranial and intracerebral atherosclerosis due to a possible protective effect of increased high density lipoprotein (HDL) cholesterol concentration, 3) a similar favorable effect on serum apolipoproteins, and 4) the cited hypothetical antithrombotic action of alcohol. The evidence is good that the concentration of HDL cholesterol, believed to protect against coronary artery disease, is raised by consumption of alcohol. So far, data with respect to HDL cholesterol and apolipoprotein concentrations and cerebrovascular disease are not available. The possible effects of alcohol upon lipoproteins and thrombosis might coexist as protective mechanisms against occlusive cerebrovascular disease; such coexistence is supported by some data pertinent to coronary disease.

A single study cannot establish an inverse relation between alcohol use and occlusive cerebrovascular disease. Features of our study that favor a true inverse relation are 1) the strength of the association, 2) apparent substantial independence from potential risk factors, 3) general similarity among several subsets of occlusive disease, 4) substantial independence from beverage type, and 5) biologic plausibility. However, the association of alcohol drinking with a lesser risk of occlusive cerebrovascular disease could be indirect. We have no data, for example, about aspirin use or food habits among alcohol drinkers and abstainers. Despite these disclaimers, a causal protective effect of alcohol against occlusive cerebrovascular disease is a real possibility; it is probably the most plausible explanation for our findings.

Public health considerations with respect to alcohol use must always be dominated by the established risks of uncontrolled drinking. The increased risk of hemorrhagic cerebrovascular disease should be added to the already compelling list of the hazards of heavier drinking, but there is nothing in our findings to suggest that lighter drinking increases hemorrhagic cerebrovascular disease risk. The apparent inverse relation between alcohol use and occlusive cerebrovascular disease needs confirmation and is not yet sufficiently established to advise persons to use alcohol to reduce cerebrovascular disease risk. However, it is also not appropriate to advise lighter drinkers at risk of cerebrovascular disease to abstain if such persons do not exhibit.
uncontrolled alcohol use or idiosyncratic reactions to alcohol. There is nothing in our data to justify heavier drinking since the apparent possible benefit for occlusive cerebrovascular disease is similar for lighter and heavier drinking.

Acknowledgments

The authors thank Harald Kipp for computer programming, Cynthia Landy and Rita J. Coston for data collection, and Lyn Wender for assistance in preparation of the manuscript.

References


Key Words: alcohol drinking • cerebrovascular disorders • epidemiology • ethanol
Alcohol use and subsequent cerebrovascular disease hospitalizations.
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*Stroke*. 1989;20:741-746
doi: 10.1161/01.STR.20.6.741

*Stroke* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0039-2499. Online ISSN: 1524-4628

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