Ethanol Intoxication: A Risk Factor for Ischemic Brain Infarction

MATTI HILLBOM, M.D., AND MARKKU KASTE, M.D.

SUMMARY One hundred consecutive patients (67 men, 33 women) aged from 15–55 with acute ischemic brain infarction verified by computed tomography and/or angiography and/or brain scanning were studied.

In 40 cases the onset of symptoms was preceded within 24 hours by ethanol intoxication. Ethanol intoxication preceding brain infarction was 4–7 times as common in men and 6–15 times as common in women as ethanol intoxication in the general Finnish population of the same age and sex. Nineteen of the patients were heavy drinkers. Heavy drinking was twice as common in men and 5 times as common in women as heavy drinking in the general Finnish population of the same age and sex.

Both occasional ethanol intoxication and regular heavy drinking seem to carry an increased risk of ischemic brain infarction. The ethanol-induced risk was highest in middle-aged women and young men.

OCCASIONAL ETHANOL INTOXICATION and heavy drinking have recently been recognized as risk factors for ischemic brain infarction in young adults.1-5 Some studies suggest a relationship between ethanol abuse and stroke in older age groups.6,7 These studies do not differentiate between ischemic and hemorrhagic stroke.

To clarify the possible role of occasional ethanol intoxication and regular heavy drinking as risk factors for ischemic brain infarction, and their relationship to other risk factors, an interview study was undertaken.

Patients and Methods

One hundred consecutive patients aged 15–55 years who were admitted to the Department of Neurology, University of Helsinki, since the beginning of January, 1978 for an ischemic brain infarction verified by computed tomography and/or serial brain scanning and/or cerebral angiography were included. Patients with cerebral arteritis or transient ischemic attacks, i.e., with symptoms and signs lasting less than 24 hours, were excluded. All patients had clinical localizing signs, such as unilateral motor and/or sensory disturbances, visual-field defects or aphasia.

Computed tomography was performed in 61 cases, serial brain scanning in 57 cases and aortic arch or carotid angiography in 44 cases. The ischemic area was situated in the vertebral-basilar territory in 11 cases and in the territory of the carotid arteries in 89 cases. Total occlusion of one internal carotid artery was detected in 10 patients. In all cases the neuroradiological findings correlated with the localizing signs and symptoms and confirmed the clinical diagnosis.

We examined all patients ourselves and asked them about their drinking and smoking habits, use of oral contraceptives, pregnancy and puerperium, recent head trauma, surgical operations, and infections. Previous diseases such as cerebrovascular disorders, heart disease, recent episodes of cardiac arrhythmia, arterial hypertension, diabetes, or migraine were also noted. Detailed information about alcohol consumption preceding the ischemic brain infarction was obtained from the patients themselves and/or from their relatives or friends. Five patients could not be interviewed because they were aphasic or moribund, but reliable data could be obtained from their relatives and friends.

The clinical examination included careful auscultation over the heart and vessels at cranial and cervical sites. A chest x-ray and electrocardiogram were performed in all cases, but cardiologic consultation and echocardiogram were performed only if clinically important murmurs or a midsystolic click was detected suggesting mitral valve prolapse. Laboratory examinations included hemoglobin, hematocrit, mean corpuscular volume, total and differential white cell count, platelet count, erythrocyte-sedimentation rate, serum electrolytes, cholesterol and triglycerides, fasting blood sugar, creatinine, transaminases and gammaglutamyl transpeptidase.

The term “ethanol-related infarction” is reserved here for cases in which the first symptoms of ischemic brain infarction were preceded within 24 hours by ethanol intoxication. All patients considered as having been intoxicated had consumed at least 80 g of absolute ethanol within a few hours. By a heavy drinker we mean a person who consumes more than 5 drinks per day almost daily.

The results were compared with the findings of Finnish population studies.8-11 The chi-square test with Yates’ correction was used in statistical comparisons if not otherwise stated.

Results

Ethanol intoxication preceded symptoms of ischemic brain infarction in 40 of the 100 patients studied. Twenty patients were still intoxicated at the time of admission. The highest breath ethanol concentration measured by Alcolmeter was 2.4 o/oo. The age and sex distribution of patients is shown in figure 1. The percentage of ethanol-related cases in different age and sex groups and the daily ethanol intoxication rate of the general Finnish population of the same age and sex8 is shown in table 1. Accordingly, ethanol intoxication preceding brain infarction was 4–7 times as common in males and 6–15 times as common in female patients as...
ethanol intoxication in the general Finnish population of the same age and sex.

The percentage distribution of onset of brain infarction on different days was compared with the weekly rhythm of ethanol consumption in Finland. Alcohol consumption on Fridays is almost double and on Saturdays treble that on any other day of the week. Consumption of alcohol on Friday is concentrated during the evening hours, but on Saturday, alcohol consumption is more evenly distributed throughout the day. We hypothesized that if ethanol intoxication provokes ischemic brain infarction, then a greater number of infarctions would occur on Saturday and Sunday.

Chi-square analysis was used in the evaluation of day of admission based on the assumption that admissions from Saturday to Sunday should have been only 2/7 of the total. Twenty-one of the 40 patients with ethanol-related infarctions were admitted on Saturday and Sunday ($X^2 = 10.08$, df = 1, $p < 0.01$). These cases clearly caused the peak occurrence of brain infarctions on Saturdays and Sundays, since the admission of the ethanol-unrelated cases took place rather evenly throughout the week (22 of 60 were admitted on Saturdays and Sundays $X^2 = 1.55$, df = 1, N.S., fig. 2). The effect was more clearly seen, if all the patients having consumed alcoholic beverages during the 24 hours before they were stricken were included into the ethanol-related group. Since 18 patients reported less than six drinks, this group now comprised 58 patients. As a matter of fact, we do not know how small doses of ethanol may provoke brain infarction in susceptible individuals and some of the patients may also have underestimated their ethanol consumption. The fluctuation of these 58 ethanol-related cases across the week is shown in figure 3 and their seasonal fluctuation in figure 4. Unfortunately, we do not have any reliable data to show the seasonal periods of heavy drinking and intoxication in Finland. But they may very well be the months showing the peak occurrence of brain infarction.

The incidence of various risk factors for ischemic brain infarction among the patients studied is shown in table 2. Transient cardiac arrhythmias were not observed on admission in any of the patients, but heart disease was frequent among older patients. There were no cases with a mitral valve prolapse. Acute migraine attacks immediately preceded the onset of symptoms of brain infarction in 9 of the 24 patients who revealed migraine in their past history. Nineteen of our 100 patients with brain infarction were heavy drinkers, while the proportion of heavy drinkers in the general Finnish population of the same age and sex is 7%.

Heavy drinking was twice as common in men and 5 times as common in women as heavy drinking in the general Finnish population of the same age and sex (table 3). Heavy drinking was more common ($X^2 = 21.45$, df = 1, $p < 0.001$) among the ethanol-related cases (17 of 40) than among patients whose brain infarction was not preceded by ethanol intoxication (2 of 60).

Cigarette smoking was about as common in men and 3 times as common in women as smoking in the general population.
al Finnish population of the same age and sex. Smoking was more common ($X^2 = 4.34$, df = 1, $p < 0.05$) among ethanol-related cases (31 of 40) than among the ethanol-unrelated cases (33 of 60). There were no significant differences between the smoking habits of heavy drinkers (15 of 19) and the smoking habits of other patients (49 of 81).

Arterial hypertension was revealed in the past history of 37 patients. Arterial hypertension was as common in women and one and a half times as common in men as arterial hypertension in the general Finnish population of the same age and sex. There were no significant differences in the incidence of hypertension among ethanol-related (18 of 40) and ethanol-unrelated cases (19 of 60) or among heavy drinkers (9 of 19) and the other patients (28 of 81).

Migraine was revealed in the past history of 17 female and 7 male patients. Migraine was as common in men and one and a half times as common in women as migraine in the general Finnish population of the same age and sex. Migraine was more common ($X^2 = 3.84$, df = 1, $p < 0.05$) among ethanol-unrelated cases (19 of 60) than among ethanol-related cases (5 of 40).

The frequencies of other risk factors listed in table 2 were not significantly different between the ethanol-related and ethanol-unrelated cases. However, a difference in risk factors was observed when young adults were compared with middle-aged adults (table 4). Hypertension, transient ischemic attacks, diabetes, heart disease, transient cardiac arrhythmias, intermittent claudication, and heavy drinking were more frequent risk factors in middle-aged patients while migraine and the use of oral contraceptives were more common risk factors in young adults.

The proportion of men to women was equal in the age group 15–40 (table 4), but in the age group 41–55 there was four times more men than women ($X^2 = 10.12$, df = 1, $p < 0.01$). These two age groups and sex were used as confounding variables in another analysis. Of the major risk factors (table 2) migraine was frequent among women and arterial hypertension among middle-aged men. Eleven and 6 women versus 1 and 6 men had migraine in the age groups 15–40 and

### Table 2: The Frequencies of Known or Possible Risk Factors in the 100 Patients with Ischemic Brain Infarction

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoking</td>
<td>64</td>
</tr>
<tr>
<td>Ethanol intoxication</td>
<td>40</td>
</tr>
<tr>
<td>Arterial hypertension</td>
<td>37</td>
</tr>
<tr>
<td>Transient cardiac arrhythmia</td>
<td>26</td>
</tr>
<tr>
<td>Migraine</td>
<td>24</td>
</tr>
<tr>
<td>Heavy drinking</td>
<td>19</td>
</tr>
<tr>
<td>Transient ischemic attack</td>
<td>18</td>
</tr>
<tr>
<td>Cardiac disease</td>
<td>17</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>15</td>
</tr>
<tr>
<td>Recent respiratory infection</td>
<td>15</td>
</tr>
<tr>
<td>Oral contraceptive medication</td>
<td>7</td>
</tr>
<tr>
<td>Intermittent claudication</td>
<td>7</td>
</tr>
<tr>
<td>Recent head trauma</td>
<td>3</td>
</tr>
<tr>
<td>Anemia (Hb &lt; 10.0 gr%)</td>
<td>3</td>
</tr>
<tr>
<td>Hyperlipemia</td>
<td>2</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>1</td>
</tr>
<tr>
<td>Recent surgery</td>
<td>1</td>
</tr>
<tr>
<td>Pheochromocytoma</td>
<td>1</td>
</tr>
</tbody>
</table>

### Table 3: The Frequencies of Smoking, Arterial Hypertension, Heavy Drinking, and Migraine in the 100 Patients with Ischemic Brain Infarction and in the General Finnish Population of the Same Age and Sex

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Patients</th>
<th>General population</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Men</td>
<td>Women</td>
</tr>
<tr>
<td>Smoking</td>
<td>67% (45/67)</td>
<td>50% (19/33)</td>
</tr>
<tr>
<td>Arterial hypertension</td>
<td>45% (30/67)</td>
<td>21% (7/33)</td>
</tr>
<tr>
<td>Heavy drinking</td>
<td>24% (16/67)</td>
<td>9% (3/33)</td>
</tr>
<tr>
<td>Migraine</td>
<td>11% (7/67)</td>
<td>52% (17/33)</td>
</tr>
</tbody>
</table>

### Table 4: The Frequencies of Known or Possible Risk Factors in Young and Middle-aged Adults with Ischemic Brain Infarction

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoking</td>
<td>Age group 15-40</td>
</tr>
<tr>
<td></td>
<td>(20 men, 21 women)</td>
</tr>
<tr>
<td>Ethanol intoxication</td>
<td>(44%) 22 (37%)</td>
</tr>
<tr>
<td>Migraine</td>
<td>(29%) 12 (20%)</td>
</tr>
<tr>
<td>Transient cardiac arrhythmia</td>
<td>(20%) 18 (31%)</td>
</tr>
<tr>
<td>Arterial hypertension</td>
<td>(17%) 30 (51%)</td>
</tr>
<tr>
<td>Recent respiratory infection</td>
<td>(17%) 8 (14%)</td>
</tr>
<tr>
<td>Oral contraceptive medication</td>
<td>(12%) 2 (3%)</td>
</tr>
<tr>
<td>Transient ischemic attack</td>
<td>(10%) 14 (24%)</td>
</tr>
<tr>
<td>Cardiac disease</td>
<td>(10%) 13 (22%)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>(7%) 16 (27%)</td>
</tr>
<tr>
<td>Heavy drinking</td>
<td>(7%) 12 (20%)</td>
</tr>
<tr>
<td>Intermittent claudication</td>
<td>(2%) 6 (10%)</td>
</tr>
</tbody>
</table>
41–55, respectively (X^2 = 20.93, df = 3, p < 0.01). Twenty-six men but only 4 women had arterial hypertension in the age group 41–55. The corresponding figures for young adults were 4 and 3 (X^2 = 13.96, df = 3, p < 0.001). On the other hand, significant differences were not found in smoking, ethanol intoxication, cardiac arrhythmia and heavy drinking.

Four of the patients died in the acute stage of brain infarction and 1 patient died of a recurrent brain infarction several months after the first stroke. Four of the 5 patients were autopsied. Massive brain infarctions and atherosclerotic changes in the arteries supplying the infarcted brain areas were observed in all 4 patients. One of them demonstrated signs of earlier myocardial infarction and his brain infarction was complicated by pulmonary embolism. Another patient had arterial hypertension and pheochromocytoma. He died of recurrent brainstem infarction. The fourth patient, a 46-year old man, had diabetes as a consequence of alcoholic pancreatitis. He also had had transient cardiac arrhythmias on several occasions. He was stricken while having been intoxicated for 3 days. Autopsy revealed total occlusion of the left internal carotid artery with the thrombus extending intracranially both into the left middle and anterior cerebral arteries. Severe brain edema caused tentorial herniation and death in his case.

**Discussion**

In 40% of our patients with ischemic brain infarction the onset of symptoms was preceded by ethanol intoxication. These results confirm our earlier observations that occasional ethanol intoxication is a risk factor for ischemic brain infarction in young adults.\(^1,2\) Furthermore, the results also demonstrate that ethanol intoxication increases the risk of brain infarction not only in young adults but also in middle-aged people. In 46% of the men and 27% of the women, the infarction was preceded by alcohol intoxication. These results suggest that ethanol intoxication increases the risk of ischemic brain infarction 4–7 times for men and 6–15 times for women.

Not only occasional ethanol intoxication but also regular heavy drinking increased the risk of ischemic brain infarction as suggested by other authors.\(^3,6,7,13\) Our results suggest that heavy drinking increases the risk of brain infarction 2 times for men and 5 times for women.

Men were over-represented among the ethanol-related cases (78% of them); probably because they consume 4/5 of all alcoholic beverages in Finland.\(^8\) If occasional ethanol intoxication is a risk factor for ischemic brain infarction, Finnish male drinking habits could be one explanation why we have more men than women in our series.

We compared the percentage distribution of brain infarctions by days of the week with the weekly cycle of ethanol consumption in Finland.\(^9\) Drinking to intoxication in Finland occurs in 65% of men and 39% of women for all drinking occasions. Drinking to intoxication refers only to a situation in which ethanol has been consumed to the point that estimated blood ethanol concentration exceeds one part per thousand.\(^0\) Occasional heavy drinking in Finland is concentrated during the weekend.\(^8,9\) Drinking to intoxication and ischemic brain infarction both concentrated on weekends.

The facts that ischemic brain infarction is preceded more often by ethanol intoxication than would be expected from the data obtained from Finnish population studies,\(^8,9\) the male preponderance and the weekly distributions of the ethanol-related and ethanol-unrelated infarctions all implicate the role of ethanol intoxication.

Smoking is associated with heavy drinking,\(^14,15\) but it is not generally regarded as a risk factor for brain infarction. Accordingly we found that smoking was more common among patients having ethanol-related brain infarction than among those whose brain infarction was not preceded by ethanol intoxication. It is interesting to note that both cigarette smoking and ethanol have been reported to increase blood viscosity.\(^16,17\)

In at least half of the cases, the first symptoms of brain infarction occurred while the patient was still intoxicated. This finding suggests that both ethanol intoxication itself, and the resultant hangover, may be precipitating factors in the onset of ethanol-related infarction.

There is evidence to suggest that the consumption of alcoholic beverages increases blood pressure.\(^18\) No significant difference was found between the incidence of hypertension in the heavy drinkers and in the other patients, nor between ethanol-related cases and those whose brain infarction was not preceded by a bout of ethanol drinking. The results cannot, however, exclude the possibility that increased blood pressure induced by ethanol consumption may contribute to the onset of brain infarction.\(^19\) We think, however, that ethanol-induced disturbances in the regulation of cerebral blood flow\(^20\) and cardiac rhythm,\(^21\) together with effects of ethanol on haemoagulation,\(^22\) platelet thromboxane formation\(^23\) and blood viscosity\(^17\) may play a more important role.

The interesting finding of a relatively low proportion of middle-aged women compared to middle-aged men, a fact already revealed in Finnish stroke registers,\(^24\) may have many explanations. Finnish middle-aged men also have other signs of early atherosclerosis as demonstrated by the high mortality of coronary heart disease.\(^25\) Also, female-associated risk factors such as migraine, use of oral contraceptives, pregnancy and puérperium, which may in younger age groups balance the ethanol-induced risk in males, become less frequent in middle-aged women. In addition, the daily ethanol intoxication rate is lowest among middle-aged women. Thus, the overall significance of ethanol intoxication as a risk factor in middle-aged women is decreased. However, when ethanol intoxication does occur in middle-aged women, it seems to be the highest risk factor for ischemic brain infarction in the present series. Young men and middle-aged women share the common feature of a limited number of other risk factors.
factors for ischemic brain infarction as compared to other age and sex groups.

One may ask why ethanol intoxication as a possible risk factor for ischemic brain infarction has not been revealed earlier. Most countries lack detailed information on the daily ethanol intoxication rates of different age and sex groups as Finland also did earlier. Without this data it is not possible to evaluate the role of ethanol intoxication as a risk factor. Moderate daily ethanol consumption is quite common in many industrialized countries and may be less risky, whereas in Finland occasional drinking for intoxication is quite common. Furthermore, Finns may have other factors that contribute to early atherosclerosis as suggested by high morbidity and mortality from coronary heart disease in men of working age. These factors may predispose Finns to the provoking effect of ethanol intoxication.

One may also ask the comparability of our patient and control data. Originally, we planned our study to be a case-control one. However, it was not possible to find proper controls among hospitalized patients because we did not know which emergent illnesses are a priori related (either positively or negatively) to occasional ethanol intoxication or regular heavy drinking. Furthermore, hospital inpatients seem to comprise a larger proportion of alcoholics than the general population which also decreases the validity of case-controls from hospital inpatients.

We think that the Finnish population studies offer adequate reference data especially because Finland has a homogenous population of four and a half million people and the evidence points that drinking to intoxication is not much dependent on where people live in Finland. Furthermore, both in our study and in the population studies the same criteria for acute ethanol intoxication and heavy drinking were used.

Finland is divided in central hospital districts which are responsible for the treatment of all patients living in the area. Accordingly, our department as a part of the University Central Hospital of Helsinki is responsible for the treatment of all neurological patients in our area which covers about one sixth of the whole population of Finland. Accordingly, there is no reason to believe that our stroke patients are not comparable to those of the whole country.

We also would like to stress that all patients with ethanol ingestion of unknown quantity (patients with aphasia, confusion, poor co-operation etc.) were considered to be ethanol-unrelated cases so that the weight of ethanol as a risk factor for ischemic brain infarction would not be overestimated under any circumstances. We do not know the amount of ethanol that may provoke brain infarction. Some data suggest that even a few drinks may be dangerous to susceptible individuals and our observations support this concept. Figure 3, for example, underlines the important role that any amount of ethanol may play. However, we included, as stated above, only those patients in the ethanol-related infarctions who had consumed at least 80 g of absolute ethanol within a few hours before the onset of symptoms of the brain infarction.

Interestingly, the observations that ethanol abuse is related to brain infarction was recently also suggested by data from Yugoslavia and an autopsy study from the United States. Accordingly, we think that the ethanol-related brain infarction is not restricted to Finns. Furthermore, ethanol intoxication may not only precipitate ischemic brain infarction but also subarachnoid hemorrhage.

In conclusion, both occasional ethanol intoxication and regular heavy drinking are associated with increased risk of ischemic brain infarction. It is unclear why ethanol increases the risk. In our patients the risk caused by ethanol was higher than that caused by arterial hypertension or other classical risk factors. The increased risk exists in all the age groups studied, although the significance of the risk factor varies between different age and sex groups. The ethanol-induced risk was highest in middle-aged women and young men.

Acknowledgement

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The Changing Pattern of Survival Following Stroke
W. MICHAEL GARRAWAY, M.D., JACK P. WHISNANT, M.D., AND IVO DRURY, M.R.C.P.

SUMMARY This study, compared survivorship for first episodes of cerebral infarction, intracerebral hemorrhage and subarachnoid hemorrhage which occurred in residents of Rochester, Minnesota during 5-year periods from 1945-49 through 1975-79. The progressive improvement in long-term survival following cerebral infarction which occurred between 1945-49 and 1970-74 was such that a higher proportion of patients survived for six years in 1970-74 (45%) than survived for three years in 1945-49 (42%). A modest improvement in short-term survival following cerebral infarction occurred up to 1975-79 but a marked improvement in 30-day survival following intracerebral hemorrhage was noted. The reasons for the improvement in survival have not been established, but possible changes in the diagnosis and management of stroke which might have been contributory factors are discussed.

STROKE IS A MAJOR CAUSE of mortality throughout the world and several studies have reported survival of stroke hospitalization and subarachnoid hemorrhage in different populations. What has not been reported is how survival following stroke has changed over time. The recent collation of data from several epidemiological studies of stroke in Rochester, Minnesota has enabled a comparison of survival experience following stroke to be carried out during different time periods using the same definition, uniform diagnostic criteria and the same method of case ascertainment in a stable, well-defined population.

Methods
Medical practice in Rochester and the surrounding area of Olmsted County has been centered on the Mayo Clinic since the beginning of this century. Diagnoses made by Mayo Clinic physicians for all patients, whether they are seen in hospitals, as outpatients, on home visits or at autopsy are all indexed in the patient’s medical record and are retrievable, by diagnosis, for the study of a variety of medical problems. A medical record indexing and retrieval system similar to that used at the Mayo Clinic has been established for local residents seen in all of the other medical institutions in and around Rochester. Thus, virtually complete case ascertainment is assured for all residents of Rochester who have a diagnosis of stroke made in any medical facility in the community. Only patients who had been living in Rochester for a continuous period of one year before their stroke were considered to be bonafide residents. This rule was designed to exclude those patients who might have migrated into the community to obtain medical care.

Records were retrieved for all diagnostic categories in which the diagnosis might have been stroke for the period January 1, 1945 to December 31, 1979 using the following definition: — the onset of a focal neuro­logical deficit lasting for more than 24 hours and due to a presumed local disturbance in blood supply to the
Ethanol intoxication: a risk factor for ischemic brain infarction.
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