Alcohol and Stroke

Philip B. Gorelick

The acute and chronic effects of alcohol abuse on the brain are well known and generally accepted. Stroke has recently been mentioned as another risk for alcohol users. This paper will review the evidence linking alcohol and cerebrovascular disease.

Cardiovascular Effects

Alcohol has various cardiovascular effects. Acute ingestion may be associated with increased cardiac rate and output, depression of left ventricular contractile function, increased systolic blood pressure and pulse pressures, diminished preload and systemic vascular resistance, cutaneous vasodilation at the expense of splanchnic constriction, and increased coronary blood flow in response to an alcohol-induced increase in myocardial oxygen consumption. When used in moderation, alcohol may reduce the incidence of death caused by coronary heart disease. Heavy alcohol ingestion, however, is associated with several cardiovascular complications that place the patient at risk for ischemic brain infarction.

One such complication is the “holiday heart” syndrome. Ettinger and colleagues described cardiac rhythm disturbances, including 12 examples of atrial fibrillation, among 24 patients aged 25–62 years with recent heavy alcohol ingestion and known past prolonged excessive ethanol use. Episodes usually followed heavy weekend or holiday drinking sprees. After resolution of the arrhythmias, most patients were allowed heavy weekend or holiday drinking sprees.

Coagulation and Platelet Disorders

In healthy volunteers with acute alcohol intoxication, the coagulation cascade may be activated. Hillbom et al. reported decreased fibrinolytic activity; increased factor VIII coagulant activity, factor VIII-related antigen, and factor VIII ristocetin cofactor; and shortened bleeding times. There were no effects on platelet count, β-thromboglobulin, antithrombin III, or fibrin/fibrinogen degradation products. In a sequel study Hillbom and colleagues showed that acute ingestion of substantial amounts of alcohol increased platelet reactivity to ADP and associated thromboxane B2 formation.

Chronic use of alcohol is also associated with a variety of blood clotting and platelet abnormalities. In alcoholics with cirrhosis, there are decreased circulating levels of clotting factors produced in the liver, excessive fibrinolysis, laboratory evidence of dissemi-
nated intravascular coagulation, and qualitatively abnormal fibrinogens. In the noncirrhotic alcoholic coagulation abnormalities have not been found.

Several platelet disorders that might trigger or potentiate cerebral ischemia have been described after alcohol withdrawal. Haselager and Vreeken reported "rebound thrombocytosis" in 5 alcoholic patients 10-15 days after hospital admission. Platelet counts at admission varied from 80,000 to 180,000/mm³ and reached a maximum of 525,000-745,000/mm³. Increases were not always preceded by thrombocytopenia. Two patients had a history of unexplained recurrent venous thrombosis and pulmonary embolism. None had clinical evidence of underlying malignancy or familial thrombotic tendencies. An increased incidence of thromboembolic disease might be expected when other factors provoking thrombosis were operative during episodes of rebound thrombocytosis. Hutton and colleagues assessed platelet function in 18 male alcoholics before and 1 week after acute alcohol withdrawal. Compared with those of normal male controls, the platelets of the alcoholics were slightly hypoaggregable on admission but became hyperaggregable 1 week after alcohol withdrawal. In all patients symptoms of acute alcohol withdrawal had abated before platelet hyperaggregability was demonstrated. None had clinical evidence of acute thromboembolic disease.

While heavy ethanol ingestion may promote cerebral infarction by the above mechanisms, in vitro study suggests that "moderate" concentrations of ethyl alcohol augment the fibrinolytic system by enhancing vascular plasminogen activator secretion. This beneficial effect may be responsible in part for the lower risk of death from coronary heart disease in persons consuming moderate amounts of ethanol.

Cerebral Blood Flow

Habitual alcohol consumption is associated with reduction in regional cerebral blood flow (rCBF). Rogers et al studied rCBF using the ¹³³Xe inhalation method in 136 healthy subjects, 82 subjects with well-established risk factors for stroke, and 4 with chronic alcoholic dementia of the Wernicke-Korsakoff type. Estimates of frequency and amounts of alcohol consumed were correlated with measurements of gray matter blood flow. The rCBF correlated inversely with the amount of alcohol consumed and the presence of alcohol consumption. When stroke risk factors were also present, cerebral blood flow was further reduced. Patients with chronic Wernicke-Korsakoff syndrome had the most substantial reduction in blood flow. Similar findings have been reported in acute Wernicke's encephalopathy.

Decreased rCBF associated with chronic and excessive alcohol consumption is usually explained by the toxic effects of alcohol on cerebral metabolism rather than by enhanced atherogenesis. Acute alcohol ingestion, however, can cause reduced rCBF by a direct effect on blood vessels. Recent experiments show that alcohol has a direct action on cerebral vascular smooth muscle, causing vasospasm. This effect is noted both in the pial microvasculature and the large cerebral arteries. With the administration of specific calcium ion channel blockers, vasospasm can be prevented or inhibited. Hemoconcentration associated with alcohol consumption may be an additional factor that further reduces cerebral blood flow.

Epidemiological Perspectives

Several clinical studies have suggested that alcohol consumption is related to stroke. In an autopsy study Walbran and colleagues noted cerebral infarction more commonly at an earlier age in alcoholics than in nonalcoholics. In a controlled retrospective study examining the association between alcoholism and thrombosis in normotensive patients under 50 years of age, Lee found that a history of excessive alcohol intake was significantly more frequent in index cases than in controls. The Honolulu Heart Study showed that alcohol consumption was associated with fatal and nonfatal intracranial hemorrhage but not thromboembolic strokes. These relationships remained significant after controlling for the effects of hypertension. The Framingham study also suggested an association between alcohol intake and the incidence of stroke and brain infarction but only in men. In the Yugoslavia Cardiovascular Disease Study those consuming alcoholic beverages most frequently were at increased risk of death from stroke.

In Finland an increased risk of ischemic brain infarction in young adults and adolescents with occasional ethanol intoxication and in middle-aged women and young men with both occasional alcohol intoxication and regular heavy drinking has been reported. Alcohol intoxication was also linked to subarachnoid hemorrhage.

These reports have stimulated interest and criticism. Select populations of patients with ischemic or hemorrhagic stroke are compared to the general Finnish population from a different time period, and ascertainment of data on alcohol consumption is different in cases and controls. Better controlled studies and more rigorous application of statistical methodology are needed to clarify the relationship between alcohol and stroke. In one such study Taylor and Coombs-Orme reported that drinking within 24 hours of hospitalization was significantly more common in stroke patients 50 years of age or younger than in hospitalized general medical patients matched by age, race, sex, and day of hospital admission.

Our own research group is in the process of completing a case-control study to assess the role of acute alcohol ingestion as a risk factor for stroke. We have targeted middle-aged and elderly acute ischemic stroke patients selected from hospital-based populations and outpatient controls matched by age, sex, race, and method of hospital payment. Over 200 cases and 400 controls will be interviewed. Comparisons in the two groups will be made to determine differences in the frequency, quantity, and type of alcohol consumed during the past year and within 24 hours of stroke.
onset. The distribution of known or potential risk factors for stroke will also be examined in the two populations, and confounding factors will be controlled.

Summary

Alcohol might contribute to stroke in several ways: 1) induction of cardiac arrhythmias and cardiac wall motion abnormalities which predispose to cerebral embolism,13-14,18,19 2) induction of hypertension,20,22 3) enhancement of platelet aggregation and activation of the clotting cascade,26-30 and 4) reduction of cerebral blood flow by stimulation of cerebral vascular smooth muscle contraction35 or by altering cerebral metabolism.32-34 While these pathophysiological mechanisms have gained enthusiastic experimental and theoretical support, the findings are preliminary and will require further large-scale clinical and epidemiological analyses to substantiate their roles as causal factors or potentiators of stroke. Documentation of measurable platelet and coagulation cascade abnormalities reported in healthy volunteers who have ingested alcohol26,27 will need to be confirmed on a broader scale in stroke patients with recent ethanol consumption. The risk of stroke in those with alcohol-induced atrial fibrillation and cardiomyopathy must be ascertained for the general population.

While the experimental evidence is exciting and provocative, epidemiological evidence also suggests a link between alcohol consumption and stroke. Regular alcohol ingestion is associated with hypertension,21,22 fatal and nonfatal intracranial hemorrhage,12-38 cerebral infarction,36-37,39 and increased risk of death from stroke.40 Recent, less stringently controlled studies5-7 suggest that alcohol consumption is a risk factor for cerebral infarction in young adults with occasional ethanol intoxication and middle-aged women and young men with occasional alcohol intoxication and regular heavy drinking. Alcohol may also be a risk factor for subarachnoid hemorrhage.9

Acknowledgment

The author wishes to thank Juan Chediak, MD, Director, Coagulation Laboratory, Michael Reese Hospital and Medical Center, for reviewing the manuscript.

References

31. Lang WE: Ethyl alcohol enhances plasminogen activator secretion by endothelial cells. JAMA 1983;250:772-776
35. Alturas BM, Alturas BT, Gebrewold A: Alcohol-induced spasms


42. Gorelick PB, Rudin M, Langenberg P, Hier DB, Costigan J, Gomez I, Spontak S: Case–control study of alcohol consumption prior to stroke. Funded by a Student Scholarship in Stroke, American Heart Association (to be published)
Alcohol and stroke.
P B Gorelick

Stroke. 1987;18:268-271
doi: 10.1161/01.STR.18.1.268

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/18/1/268

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Stroke can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at: http://www.lww.com/reprints

Subscriptions: Information about subscribing to Stroke is online at: http://stroke.ahajournals.org//subscriptions/