Retinal Infarction During Sleep and Wakefulness

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Brain and retinal infarctions during sleep have been attributed to focal hypoperfusion caused by systemic hypotension combined with underlying arterial stenosis, rather than to embolism. Because some retinal emboli may be visualized on ophthalmoscopy, we studied 24 consecutive patients (18 men and six women) aged 26–78 (mean 58) years with recent retinal infarction and determined whether the infarction had occurred during sleep or wakefulness. All patients underwent dilated ophthalmoscopy and a carotid artery study (angiography in 20, duplex ultrasound in the remaining four), and 12 had echocardiography. Retinal infarction occurred during sleep at an unexpectedly high rate (14 of 24 observed compared with eight of 24 expected, \( p=0.02 \)). Retinal cholesterol emboli were seen in one half of the patients regardless of whether the retinal infarction had occurred during sleep or wakefulness. Carotid artery disease was found in seven of the 14 patients in whom infarction had occurred during sleep and in eight of the 10 patients in whom infarction had occurred during wakefulness (\( p=0.21 \)). Cerebrovascular occlusive disease was not found in the five patients aged <50 years. Our findings suggest that embolism is a common mechanism of retinal infarction during sleep or wakefulness, that in patients aged >50 years extracranial carotid artery disease is a common source of retinal emboli, and that the retina may be especially susceptible to infarction during sleep. (Stroke 1990;21:1494–1496)

A n embolic, thrombotic, or hemodynamic mechanism is usually postulated to explain retinal infarction. Better understanding of the mechanisms of retinal infarction may lead to a more effective therapy. Because of circadian fluctuations in blood pressure\(^1\) and certain hematologic factors,\(^2\) the incidence and mechanism of retinal infarction may vary during the day–night cycle. To investigate these possibilities, we took advantage of the opportunity to visualize emboli directly on ophthalmoscopy and studied 24 consecutive patients with recent retinal infarction.

Subjects and Methods

Between August of 1986 and June of 1988, we studied 24 consecutive patients (18 men and six women) aged 26–78 (mean 58) years referred for evaluation of retinal infarction to the University of Iowa Hospitals and Clinics or the Iowa City Veterans Administration Medical Center. All patients had sudden persistent monocular visual loss within 21 days of evaluation (18 within 7 days, four within 8–14 days, and the remaining two within 15–21 days). Infarction was considered to have occurred during wakefulness if the patient first noted the visual deficit while awake and to have occurred during sleep if the patient first noted the deficit upon awakening. All patients slept during the night and awoke in the morning. The time of awakening in the morning and the exact time of onset of symptoms during wakefulness were not determined. All patients had a complete blood cell count; prothrombin time, partial thromboplastin time, and erythrocyte sedimentation rate determinations; an ophthalmologic evaluation; and a carotid artery study (angiography in 20 and duplex ultrasound in the other four). Twelve patients had echocardiography. Carotid artery stenosis was classified as mild (16–49%), moderate (50–79%), severe (80–99%), or occlusion (100%) depending on the reduction of luminal diameter. Carotid artery ulceration was diagnosed when arteriography showed a well-defined concavity on the surface of an atherosclerotic plaque.

We used Fisher’s two-sided exact test to compare patient groups, except for a two-sided, two-sample \( t \)
test to compare mean ages and a test of binomial proportions to evaluate the hypothesis that retinal infarction occurs at random times during the day-night cycle. The expected number of infarctions during sleep was based on two assumptions: first, that patients slept 8 hours/night, similar to comparable-age individuals in the general population without sleep disorders,7 and second, that retinal infarction occurred at random times.

Results

Clinical characteristics and findings of the 24 patients with retinal infarcts are shown in Table 1. The group of patients whose infarcts occurred during sleep did not differ significantly from the group of patients whose infarcts occurred during wakefulness when sex ratio, age, vascular risk factors, frequency and severity of carotid stenosis, or frequency of carotid ulceration were compared. Five patients were <50 years old, and all five had normal extracranial carotid arteries. Four of the five had arteriography, and the results for all four were normal. Among the remaining 19 patients, all >50 years old, 14 (74%) had extracranial carotid artery disease. Among the 20 patients who had arteriography, none had intracranial carotid artery stenosis and six (30%) had ophthalmic artery lesions. Three of the six had ophthalmic artery stenosis (one with a normal cervical carotid artery and the other two with mild cervical carotid artery stenosis, one of which was ulcerated), and the other three had ophthalmic artery occlusion (one with a normal cervical carotid artery, one with mild cervical carotid artery stenosis and ulceration, and the other with severe cervical carotid artery stenosis).

The observed rate of retinal infarction during sleep was significantly (p<0.02) greater than expected. Retinal emboli were found in half of the patients in each group. All emboli contained glistening cholesterol crystals and were in arterioles supplying the infarcted retina. Two patients had a potential cardiac source of emboli (apical akinesis in both), but neither had visible retinal emboli.

Discussion

Our study suggests that the rate of retinal infarction is greater during sleep than during wakefulness. Two factors that may predispose to retinal infarction during sleep are the physiologic decrease in blood pressure during sleep1 and the decrease in fibrinolysis during the early morning.2,3 Both factors involve a nonembolic mechanism; hypotension combined with arterial stenosis may result in ocular hypoperfusion, and decreased fibrinolysis may predispose to thrombosis. However, our findings suggest a high rate of embolic retinal infarction during both sleep and wakefulness. The rates of visible retinal emboli, carotid artery disease, and cardiac abnormalities did not differ in the two groups (Table 1). The actual rate of embolic retinal infarction is probably higher than the rate at which retinal emboli are seen (12 of 24, 50% in this study) since retinal cholesterol emboli can disappear rapidly4 and can involve vessels that are not visible on ophthalmoscopy, such as the pre-retinal portion of the central retinal artery or the ophthalmic artery. The overall prevalence of carotid artery disease in our patients (63%) is similar to that found in other studies of retinal infarction5–11 and retinal cholesterol emboli.12

Most studies on the diurnal fluctuation of brain infarction do not report whether the infarction occurred during sleep or wakefulness. In a recent report from the Stroke Data Bank, Marler et al13 found that among 1,075 patients with ischemic stroke for whom it was known whether symptoms were present on awakening, the stroke occurred during sleep in 331 (31%) patients and during wakefulness in the other 744 (69%) patients. This distribution is not significantly different from that expected (33% during sleep and 67% during wakefulness) under the assumptions made in our study. The reasons for this difference between our findings and those of Marler et al13 regarding brain infarction are not apparent. Differences between the brain and retina in vulnerability to ischemia at different times during the day–night cycle may be responsible.

A possible explanation for the overrepresentation of retinal infarction during sleep may be that the retina is, for unknown reason(s), especially susceptible to ischemia during sleep. Retinal blood flow and metabolism normally increase in darkness.14,15 Since less light falls on the retina during sleep than during wakefulness, retinal blood flow and metabolism may
increase during sleep. This would predispose the retina to ischemic injury during sleep when, for example, an embolus partially obstructs a retinal arteriole.

Our findings suggest that embolism is a common mechanism of retinal infarction during sleep or wakefulness and that extracranial carotid artery disease with mild stenosis is an important source of emboli in patients >50 years old. The retina appears to be especially susceptible to infarction during sleep.

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References


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