

# Think Aspirin for Intracranial Arterial Stenosis

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High-dose aspirin is just as effective as warfarin in treating intracranial arterial stenosis, and appears much safer, with significantly lower rates of death, myocardial infarction, and major hemorrhage over 2 years, Marc Chimowitz, M.B., and colleagues have reported.

"The common practice of administer-

ing warfarin rather than aspirin for symptomatic intracranial arterial stenosis is not supported by the results of this trial," said Dr. Chimowitz of Emory University, Atlanta.

Enrollment in the Warfarin-Aspirin Symptomatic Intracranial Disease (WASID) trial ended early because of the high rate of serious adverse events in the warfarin patients.

In addition to being safer for patients, the researchers said, aspirin therapy did

not require constant monitoring of international normalized ratios (INRs) and treatment of warfarin-associated bleeding. Aspirin also is much cheaper, the investigators noted (*N. Engl. J. Med.* 2005;352:1305-16).

Ralph Sacco, M.D., an investigator in the Northern Manhattan Stroke Study, noted in an interview that the WASID trial's findings add to existing data to dispel beliefs about the benefit of warfarin for certain stroke populations.

The conclusion that warfarin provides no survival benefit over aspirin, but confers added risk, is more expensive, and requires intensive monitoring, should reshape its risk/benefit profile for some patients, said Dr. Sacco, professor of neurology and epidemiology at Columbia University, New York.

Dr. Chimowitz and his associates reported on the trial's final analysis that included 569 patients with symptomatic intracranial arterial stenosis who were

## Light Tx May Surpass Melatonin

SAN DIEGO — Melatonin supplements may be popular to shift circadian rhythms, but bright-light therapy is more effective, Milton Erman, M.D., said at a psychopharmacology congress sponsored by the Neuroscience Education Institute.

People with sleep disorders from working night shifts especially may benefit from therapy to shift their circadian rhythms to match the imposed sleep schedule, said Dr. Erman of the University of California, San Diego.

If the patient mainly is bothered by disrupted or insufficient sleep (wakefulness) or by excessive sleepiness while awake, try focusing treatment on one or the other, he suggested. If sleep problems include both wakefulness and sleepiness, it may be best to try to shift the patient's circadian rhythm.

Light therapy is inexpensive and safe for shifting circadian rhythm. Bright light or light plus exercise worked better than exercise alone, melatonin alone, or placebo to treat night-shift workers in a 1999 study.

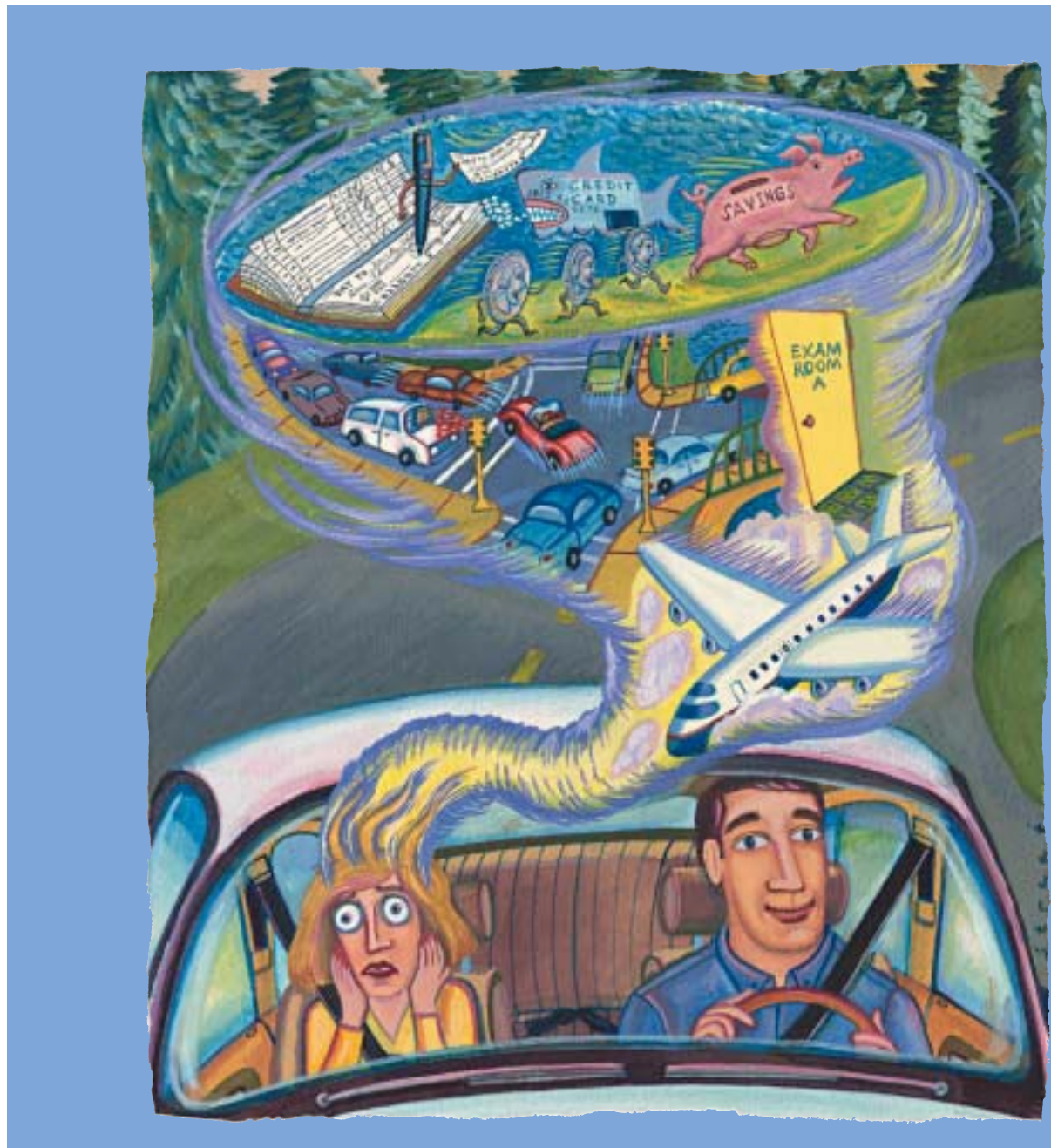
Light therapy or light plus exercise shifted sleep/wake phases by 7-8 hours, compared with approximately 5 hours for melatonin and 3 hours with placebo. Patients achieved close to 7.5 hours of sleep per sleep phase with light therapy or light plus exercise, compared with approximately 6.5 hours of sleep with melatonin or placebo, Dr. Erman said.

To shift the circadian sleep phase, the timing of therapy is critical, whether using light, exercise, or melatonin. Any of these in the morning will advance the circadian rhythm so the patient goes to sleep earlier. To stay up later than usual, delay sleep by exercising or using light or melatonin in the late afternoon or early evening, he said.

For patients complaining mainly of wakefulness, benzodiazepines or nonbenzodiazepine hypnotics such as zolpidem (Ambien) can improve the quantity and quality of sleep, but studies suggest that improvements in job performance are short term. For sleepiness, modafinil (Provigil) is safer than stimulants and is approved to treat chronic shift-work disorder.

Dr. Erman has been a speaker and consultant for, or received honoraria from, the companies that make zolpidem and modafinil.

—Sherry Boschert



NIRAVAM is contraindicated in patients with known sensitivity to this drug or other benzodiazepines, in patients with acute narrow-angle glaucoma, and in patients taking potent CYP3A inhibitors, such as ketoconazole and itraconazole.

At doses greater than 4 mg per day (often required for panic disorder), the risk of dependence may be higher than in those taking smaller doses.

Since NIRAVAM has a CNS depressant effect, patients should be cautioned about mental alertness, impaired performance and taking alcohol or other CNS depressant drugs during treatment with alprazolam. If alprazolam is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to the fetus.

Adverse events ( $\geq 5\%$  and at least 50% greater than placebo) in clinical trials include drowsiness, impaired coordination, memory impairment, dysarthria, increased or decreased libido, and constipation.

Certain adverse clinical events are a direct consequence of physical dependence to alprazolam. These include a spectrum of withdrawal symptoms, the most important being seizure.

Please see brief summary of the complete Prescribing Information on the adjacent page.

