Cardiovascular Risks Rising in Native Americans

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ATLANTA — The prevalence of cardiovascular risk factors and cardiovascular disease is alarmingly high and continues to rise in Native Americans, according to several reports at a prevention conference on heart disease and stroke sponsored by the Centers for Disease Control and Prevention.

In one study of adult Native Americans

(defined as American Indians and Alaska Natives) from Montana who took part in an annual telephone survey, significant increases were seen between 1999 and 2003 in the proportion reporting diabetes (12% $\,$ vs. 16%), hypertension (26% vs. 34%), high cholesterol (23% vs. 30%), and obesity (34% vs. 39%).

About 1,000 adults completed the survey in each of the four study years, Carrie S. Oser reported in a poster presented

After adjustment for age, sex, and survey year, the increases in the proportion reporting hypertension, high cholesterol, and obesity remained significant, said Ms. Oser of the Montana Department of Public Health and Human Services in Helena.

The prevalence of cardiovascular disease increased slightly from 10% to 11% over the course of the study, and smoking rates dropped slightly from 38% to 36%, although they remained high.

In another study of Native Americans in North Carolina, which has the eighthlargest Native American population in the United States, age-adjusted rates of cardiovascular risk factor prevalence were compared with those of North Carolina whites and African Americans.

The 285 Native Americans studied in 2002 and the 230 studied in 2003 had higher rates of hypertension (40% vs. 27%), obesity (33% vs. 21%), and diabetes (14% vs. 7%) than did whites.

They also were less likely than whites to engage in leisure-time physical activity (66% vs. 76%) and to engage in the recommended amount of physical activity for cardiovascular health (29% vs. 40%), and they were less likely to eat five or more

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servings fruits and vegetables daily (19% vs. 25%), Sara L. Huston, Ph.D., reported in a poster.

Smoking and high cholesterol rates in this study were found to be comparable in American Indians and whites. All cardiovascular risk fac-

tors were found to be similar in Native Americans and African Americans, she

Both Ms. Oser and Dr. Huston said that they were struck by the high prevalence of cardiovascular risk factors found in Native Americans; the prevalence in this population had been largely unknown, noted Dr. Huston, who concluded that culturally appropriate intervention and prevention programs are needed to address the problem.

The need for such programs also was highlighted in another poster showing that with the rise in the prevalence of diabetes and hypertension in Native Americans is a likely risk in the prevalence of ischemic heart disease.

Based on 2002 ambulatory care data from the Indian Health Service, the ageadjusted prevalence of ischemic heart disease among Native Americans and Native Alaskans aged 45 years and older was estimated to be nearly three times higher in those with diabetes than in those without diabetes (17% vs. 6%).

Those individuals with hypertension but without diabetes had a higher age-adjusted prevalence of ischemic heart disease than did those with diabetes alone (13% vs. 7%). Those individuals with both diabetes and hypertension were found to have the highest prevalence (20%), reported Nilka Rios Burrows of the CDC, Atlanta.

These rates are likely to rise in tandem with the increasing prevalence of diabetes and other cardiovascular risk factors in Native Americans; interventions to control blood glucose, lipid, and blood pressure levels would benefit this population, she said.

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(zolpidem tartrate)

BRIEF SUMMARY

INDICATIONS AND USAGE

CONTRAINDICATIONS

None known.

WARNINGS

Since skeep disturbances may be the presenting manifestation of a physical and/or psychiatric disorder, symptomatic treatment of insomnia should be initiated only after a careful evaluation of the patient. The failure of insomnia to remit after 7 to 10 days of treatment may indicate the presence of a primary psychiatric and/or medical illness which should be evaluated. Worsening of insomnia or the emergence of new thinking or behavior abnormalities may be the consequence of an unrecognized psychiatric or physical disorder. Such findings have emerged during the course of treatment with sedative/hypnotic drugs, including Ambien. Because some of the important adverse effects of Ambien appear to be dose related (see Precautions and Dosage and Administration), it is important to use the smallest possible effective dose, especially in the elderty.

A variety of abnormal thinking and behavior changes have been reported to occur in association with the use of sedative/hypnotics. Some of these changes may be characterized by decreased inhibition (e.g. aggressiveness and extroversion that seemed out of character), similar to effects produced by alcohol and other CNS depressants. Other reported behavioral changes have included bizarre behavior, agitation, hallucinations, and depersonalization. Amnesia and other neuropsychiatric symptoms may occur unpredictably. In primarily depressed patients, worsening of depression, including suicidal thinking, has been reported in association with the use of sedative/hypnotics.

It can rarely be determined with certainty whether a particular instance of the abnormal behaviors listed above is drug induced, spontaneous in origin, or a result of an underlying psychiatric or physical disorder. Nonetheless, the emergence of any new behavioral sign or symptom of concern requires careful and immediate evaluation.

Following the rapid dose decrease or abrupt discontinuation of sedative/hypnotics, there have been reports of signs and symptoms similar to

own withdrawal from other UNS-depressant drugs (see Drug Abuse and pendence).
Imbien, like other sedative/hypnotic drugs, has CNS-depressant effects. Due he rapid onset of action, Ambien should only be ingested immediately prior joing to bed. Patients should be cautioned against engaging in hazardous upations requiring complete mental alertness or motor coordination such as rating machinery or driving a motor vehicle after ingesting the drug, includ-potential impairment of the performance of such activities that may occur the following ingestion of Ambien. Ambien showed additive effects when comed with alcohol and should not be taken with alcohol. Patients should also be tioned about possible combined effects with other CNS-depressant drugs, age adjustments may be necessary when Ambien is administered with such nts because of the potentially additive effects.

Intererore, the recommenced Ambien dosage is 5 mg in such patients issee Dosage and Administration) to decrease the possibility of side effects. These patients should be closely monitored.

Use in patients with concomitant illness: Clinical experience with Ambien in patients with concomitant systemic illness is limited. Caution is advisable in using Ambien in patients with diseases or conditions that could affect metabolism or hemodynamic responses. Although studies did not reveal respiratory depressant effects at hypnotic doses of Ambien in normals or in patients with mild to moderate chronic obstructive pulmonary disease (COPD), a reduction in the Total Arousal Index together with a reduction in lowest oxygen saturation and increase in the times of oxygen desaturation below 80% and 90% was observed in patients with mild-to-moderate sleep apnea when treated with Ambien (10 mg) when compared to placebo. However, precautions should be observed if Ambien is prescribed to patients with compromised respiratory function, since sedative/hypnotics have the capacity to depress respiratory drive. Post-marketing reports of respiratory insufficiency, most of which involved patients with pre-existing respiratory insufficiency, most of which involved patients with pre-existing respiratory insufficiency, most of which involved patients with pre-existing respiratory insufficiency, most of which involved patients with pre-existing respiratory insufficiency, and the patient in renally impaired patients is required; however, these patients should be closely monitored (see Pharmacokinetics). A study in subjects with hepatic impairment did reveal prolonged elimination in this group; therefore, treatment should be initiated with 5 mg in patients with hepatic compromise, and they should be closely monitored.

Use in depression: As with other sedative/hypnotic drugs, Ambien should be administered with caution to patients exhibiting signs or symptoms of depression. Suicidal tendencies may be present in such patients and protective

tion for patients: Patient information is printed in the complete prescrib-

Laboratory tests: There are no specific laboratory tests recommended.

Drug/Laboratory test interactions: Zolpidem is not known to interfere with commonly employed clinical laboratory tests. In addition, clinical data indicate that zolpidem does not cross-react with benzodiazepines, opiates, barbiturates, occaine, cannabinoids, or amphetamines in two standard urine drug screens.

cocaine, cannabinoids, or amphetamines in two standard urine drug screens. Carcinogenesis: mutagenesis; impairment of fertility. Carcinogenesis: Zolpidem was administered to rats and mice for 2 years at dietary dosages of 4, 18, and 80 mg/kg/day. In mice, these doses are 26 to 520 times or 2 to 35 times the maximum 10-mg human dose on a mg/kg or mg/m² basis, respectively. In rats these doses are 43 to 876 times or 6 to 115 times the maximum 10-mg human dose on a mg/kg or mg/m² basis, respectively. No evidence of carcinogenic potential was observed in mice. Renal liposarcomas were seen in 4/100 rats (3 males, 1 female) receiving 80 mg/kg/day and a renal lipoma was observed in one male rat at the 18 mg/kg/day dose. Incidence rates of lipoma and liposacoroma for zolpidem were comparable to those seen in historical controls and the tumor findings are thought to be a spontaneous occurrence.

controls and the tumor findings are thought to be a spontaneous occurrence. Mutagenesis: Copidem did not have mutagenic activity in several tests including the Ames test, genotoxicity in mouse lymphoma cells in vitro, chromosomal aberrations in cultured human lymphocytes, unscheduled DNA synthesis in rat hepatocytes in vitro, and the micronucleus test in mice.

Impairment of fertility: In a rat reproduction study, the high dose (100 mg basek(g) of 20pidem resulted in irregular estrus cycles and prolonged precoital intervals, but there was no effect on male or female fertility after daily oral doses of 4 to 100 mg basek(g) of 5 to 130 times the recommended human dose in mg/m². No effects on any other fertility parameters were noted.

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This drug should be used during pregnancy only if clearly needed.

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Monteratogenic effects: Studies to assess the effects on children whose mothers
took zolpidem during pregnancy have not been conducted. However, children
born of mothers taking sedative/hypnotic drugs may be at some risk for withdrawal symptoms from the drug during the postnatal period. In addition, neonatal flaccidity has been reported in infants born of mothers who received seattive/
hypnotic drugs during pregnancy.

Labor and delivery: Ambien has no established use in labor and delivery.

Nursing mothers: Studies in flactating mothers indicate that between 0.004 and
0.019% of the total administered dose is excreted into milk, but the effect of zolpidem on the infant is unknown.

The use of Ambien in nursing mothers is not recommended.

have not been established.

Geriatrie use: A total of 154 patients in U.S. controlled clinical trials and 897 patients in non-U.S. clinical trials who received zolpidem were ≥60 years of age. For a pool of U.S. patients receiving zolpidem at doses of ≤10 mg or placebo, there were three adverse events occurring at an incidence of at least 5% for zolpidem and for which the zolpidem incidence was at least twice the placebo incidence (i.g. they could be considered drug related).

Adverse Event	Zolpidem	Placebo
Dizziness	3%	0%
Drowsiness	5%	2%
Diarrhea	3%	1%

patients were dizziness (5%) and drugged feelings (3%). Treatment-mergent adverse experiences in placebo-controlled clinical trials: The following are treatment-emergent adverse events from U.S. placebo-controlled clinical trials. Data are limited to data from doses up to and induding 10 mg. In short-term trials, events seen in zolpidem patients (in-65%) at an incidence equal to 1% or greater compared to placebo (n-473) were: headache (7% vs 5%), of placebo, (forwaisiness (2% vs 0%), dizirates (1% vs 0%), anaisea (2% vs 5%), diarrhea (1% vs 0%), and myalgia (1% vs 2%). In long-term dinical trials, events seen in zolpidem patients (n-152) at an incidence of 1% or greater compared to placebo (n-161) were: dry mouth (3% vs 1% for placebo), allergy (4% vs 1%),

events, Adverse events are further classified and enumerated in order of decreasing frequency using the following definitions: frequent adverse events are defined as those occurring in greater than 1/100 subjects; infrequent adverse events are those occurring in 1/100 to 1/1,000 patients; rare events are those occurring in 1/100 to 1/1,000 patients;

pagnation, seep discrete, vertigo, vision autorimar, vorniturig.

Infrequent: abnormal hepatic function, agitation, arthritis, bronchitis, cere-brovascular disorder, coughing, cystitis, decreased cognition, detached, difficulty concentrating, dysarthria, dysphagia, dyspense, adema, emotional fability very irritation, eye pain, falling, fever, flatulence, gastroenteritis, hallucination, hyper-glycemia, hypertension, hypoesthesia, illusion, increased SQPT, increased sexetting, leg cramps, malaise, menstrual disorder, migraine, pallor, paresthesia, postural hypotension, pruritus, scleritis, sleeping (after daytime dosing), speech disorder, stuppor, synocope, tachycardia, taste perversion, thirst, tinnitus, trauma, tremor, urinary incontinence, vaginitis.

Controlled substance: Schedule IV.

Abuse and dependence: Studies of abuse potential in former drug abusers found that the effects of single doses of zolpidem tartrate 40 mg were similar, but not identical, to diazepam 20 mg, while zolpidem tartrate 40 mg was difficult to distinguish from placebo.

Sedative/hypnotics have produced withdrawal signs and symptoms following abrupt discontinuation. These reported symptoms range from mild dysphoria and insomnia to a withdrawal syndrome that may include abdominal and music cramps, vomiting, sweating, tremors, and convulsions. The U.S. clinical trial experience from zolpidem does not reveal any clear evidence for withdrawal syndrome. Nevertheless, the following adverse events included in DSM-HI-R criteris for uncomplicated sedative/hypnotic withdrawal were reported at an incidence of <1% during U.S. clinical trials following placebo substitution occurring within 48 hours following last zolpidem treatment: fatigue, nausea, flushing, lightheadedness, uncontrolled crying, emesis, stomach cramps, panic attack, nervousness, and abdominal discomfort. Rare post-marketing reports of abuse, dependence and withdrawal have been received. Individual with a history of addiction to, or abuse of, drugs or alcohol are at increased risk of habituation and dependence; they should be under careful surveillance when receiving any hypnotic.

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