Smokeless Tobacco Deemed Harmful, Addictive

Products could pose increased health risks, American Heart Association warns.

BY LORINDA BULLOCK

FROM CIRCULATION

Smokeless tobacco products are not safer alternatives to cigarette smoking, they do not help smokers quit, and their long-term use can, in fact, increase the risk of fatal heart attack, fatal stroke, and cancer, the American Heart Association warned in a scientific statement.

The researchers, led by Mariann R. Piano, Ph.D., examined several international studies to compare smokeless tobacco use and its health risks.

Meta-analysis data involving male, Swedish smokers for 1976-2002 showed a significant decrease in cigarette smoking that corresponded with an increase in use of smokeless tobacco products, the investigators wrote in the AHA journal, Circulation. Despite the decline in cigarette use, concern is warranted, Dr. Piano, professor of biobehavioral science at the University of Illinois at Chicago, explained: "Smokeless tobacco products are harmful and addictive – that does not translate to a better alternative," Dr. Piano, said in a written statement released by the association.

"Scientists and policy makers need to assess the effect of 'reduced risk' messages related to smokeless tobacco use on public perception, especially among smokers who might be trying to quit," Dr. Piano and her colleagues wrote.

Citing "inadequate evidence of smoking cessation efficacy and safety," the researchers deemed as inappropriate the promotion of smokeless tobacco as a way to reduce smoking-related diseases.

The American Heart Association does recommend nicotine replacement therapy (nicotine gum or a nicotine-releasing patch placed on the skin) as a safer option for cigarette smokers wanting to quit. "Clinical studies have found no increased risk of heart attack or stroke with either type of nicotine replacement therapy," the AHA said in the written statement.

Metaanalysis data in the association's scientific statement http://circ.ahajournals.org/cgi/reprint/CIR.0b013e3181f432c3 indicated that smokeless tobacco use was associated with an increased risk of heart disease (relative risk 1.12, n = 8 studies) (Int. J Epidemiol. 2007;36:789-804).

Additionally, a subanalysis of INTERHEART (a study of 15,152 cases of first myocardial infarction in 52 countries) showed that tobacco chewers had a significantly increased risk of first myocardial infarction (odds ratio 2.23) compared with those who never used tobacco. Two other meta-analyses indicated that smokeless tobacco use was also associated with an increased risk of fatal stroke (RR 1.42, n = 5 studies, and RR 1.40, n = 5 studies).

The researchers explained that, like cigarettes, smokeless tobacco (ST) products still contain nicotine of varying concentrations as well as a number of carcinogens that are just as harmful.

Cigarettes and oral snuff have similar amounts of nicotine (milligrams per gram of tobacco), while chewing tobacco appears to have "somewhat lower" amounts compared with cigarettes, Dr. Piano and her colleagues wrote.

"Even though certain manufacturing techniques are used to reduce the level of these compounds in some products, they remain present in substantial concentrations in ST products, including Swedish snus," they said.

In a comparison of nicotine concentration between three types of smokeless tobacco products (chewing tobacco, dry snuff, and moist snuff) and cigarettes sold in the United States, all of the smokeless tobacco products had nicotine concentrations that were similar to cigarettes with the highest concentrations (see chart).

Dr. Piano and her colleagues found that unlike the aforementioned Swedish cohorts, there was no reduction in smoking rates among people in the United States using smokeless tobacco. (The sale of smokeless tobacco products such as moist snuff or snus is banned in most of the European Union with the exception of Sweden and Norway.)

In the United States about 8.1 million people are users of smokeless tobacco and its use is more prevalent in men than women, and people between the ages of 18-25 are the most likely to use smokeless tobacco, the researchers wrote.

It also appears that although U.S. chewing tobacco use has been on the decline since the 1980s, snuff consumption and production are increasing, the researchers said. ■

VITALS

Major Finding: Several meta-analyses indicate that smokeless tobacco use was associated with an increased risk of heart disease (relative risk 1.12,) and fatal stroke (RR 1.42 and RR 1.40).

Data Source: Nonsystematic review of meta-analyses, randomized clinical trials, cohort or case control, and comparative studies regarding CV risk and ST product use primarily conducted in Sweden and the United States.

Disclosures: None was reported.

Nicotine Concentrations in Smokeless Tobacco Products and Cigarettes Sold in the United States

	Chewing tobacco* (mean range)	Dry snuff* (mean range)	Moist snuff* (mean range)	Cigarettes		
				High	Moderate	Low
Nicotine (mg/g)	9.9 (3.41-39.7)	16.8 (10.5-24.8)	12.6 (4.7-24.3)	9.5-13.4	8.9-11.4	7.2-11.5

*Smokeless products sold in Massachusetts in 2003
Source: Circulation

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Ketamine Infusion Relieves Bipolar Depression Quickly

BY ROBERT FINN

FROM ARCHIVES OF GENERAL PSYCHIATRY

A single infusion of ketamine relieved bipolar depression within 40 minutes in patients with treatment-resistant bipolar disorder, according to a randomized, placebo-controlled, double-blind crossover study involving 18 patients.

The effect lasted at least 3 days, wrote Dr. Nancy Diazgranados and her colleagues from the National Institute of Mental Health. Patients in the study were an average of 48 years old, had suffered from bipolar I or bipolar II depression for an average of 28 years, and had failed an average of seven antidepressant treatments before the ketamine study. Fifty-five percent of the participants had failed to respond to electroconvulsive therapy.

Two-thirds of participants were on psychiatric disability, and all but one were unemployed (Arch. Gen. Psychiatry 2010;67:793-802).

Patients were randomly assigned to receive an infusion of 0.5 mg/kg of ketamine or placebo. Two weeks later, the patients who had been given ketamine were given placebo and vice versa. Of the 17 patients who completed the ketamine phase of the study, 12 (71%) responded to ketamine.

In contrast, of the 16 patients who completed the placebo phase of the study, only 1 (6%) responded to placebo.

Investigators assessed the patients at baseline using several rating scales, including the Montgomery-Åsberg Depression Rating Scale, the Hamilton Scale for Depression, and the Beck Depression Inventory. Patients showed statistically significant improvements in depression with ketamine, compared with placebo on all three scales beginning at 40 minutes after infusion and continuing for at least 3 days. Mean scores on the rating scales did not differ from placebo on days 7, 10, and 14.

Within 40 minutes, 9 of 16 patients receiving ketamine (56%) responded and an additional 2 (13%) experienced complete remission of their depression. One day after the infusion, 44% of the patients had responded and 31% had remitted.

None of the patients experienced serious adverse events during the study. Among the adverse events associated with ketamine and experienced by at least 10% of the patients were disassociation; feeling strange, weird, or bizarre; dry mouth; tachycardia; and increased blood pressure.

Ketamine has been used in human and veterinary medicine since 1962, most commonly for inducing and maintaining general anesthesia, sedation in intensive care, analgesia, and treatment of bronchospasm. In the late 1990s, it increasingly became known as a drug of abuse and a date -rape drug. A previous study showed that a single infusion of ketamine improved suicidal ideation within 40 minutes ("Single Ketamine Injection Reduces Suicidal Ideation," November 2009, p. 13).

When used for general anesthesia, the initial dose of intravenous ketamine is typically 1.5-4.5 mg/kg, substantially higher than the level used in this study. Ketamine is thought to act as a noncompetitive inhibitor of the *N*-methyl-D-aspartate (NMDA) receptor, which is part of the glutaminergic neurotransmitter system. Several lines of evidence have implicated the glutaminergic system in bipolar disorder. ■

VITALS

Major Finding: In patients with treatment-resistant bipolar depression, an infusion of 0.5 mg/kg of ketamine significantly relieved depression within 40 minutes, an effect that lasted at least 3 days.

Data Source: Randomized, placebo-controlled, double-blind, crossover study involving 18 patients.

Disclosures: The study was funded by the National Institute of Mental Health and by the National Alliance for Research on Schizophrenia and Depression. A patent application for the use of ketamine for depression has been submitted, listing two of the investigators among the inventors; they have assigned their rights on the patent to the U.S. government.