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 Chica- go, 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 ‘re- duced risk’ messages related to smokeless tobacco use on public perception, especially among smokers who might be trying to quit,” Dr. Piano and her colleague 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 /print/CIR.0b013e318f1421c3 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)

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

<table>
<thead>
<tr>
<th>Cigarettes</th>
<th>Chewing tobacco (mean range)</th>
<th>Dry snuff (mean range)</th>
<th>Moist snuff (mean range)</th>
<th>Source: Circulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>9.9 (3.41-39.7)</td>
<td>16.8 (10.5-24.8)</td>
<td>12.6 (4.7-24.3)</td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>9.5-13.4 1.40</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>8.9-11.4 7.2-11.5</td>
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</tbody>
</table>

*Smokeless products sold in Massachusetts in 2003

**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 psychotropic 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, an effect that lasted at least 3 days.

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.

VITALS

**Ketamine**

- **Clinical uses:** Anesthetic, analgesia, and treatment of bronchospasm.
- **Initial dose:** Typically 1.5-4.5 mg/kg, substantially higher than the level used in this study.
- **Half-life:** 1-4 hours.
- **Metabolism:** Primarily hepatic.
- **Contraindications:** Pre-existing hypertension, obstructive sleep apnea, and glucose-6-phosphate dehydrogenase deficiency.
- **Adverse effects:** Hypertension, tachycardia, and agitation.

Ketamine is thought to act as a non-competitive 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.