Strong oral carcinogen identified in smokeless tobacco

April 2 2012

The chemical (S)-N'-nitrosonornicotine, or (S)-NNN, which is present in smokeless tobacco products, is a strong oral carcinogen, according to results presented at the AACR Annual Meeting 2012, held here March 31 - April 4.

Although smokeless tobacco products have long been linked with certain cancers, including oral cavity cancers and esophageal cancers, this is the first study to identify a specific chemical present in smokeless tobacco products that induces oral cancer in animals, according to Silvia Balbo, Ph.D., research associate at the Masonic Cancer Center of the University of Minnesota in Minneapolis, Minn.

"(S)-NNN is the only chemical in smokeless tobacco known to cause oral cancer," Balbo said. "This finding provides mechanistic underpinning for the epidemiologic observations that smokeless tobacco products cause oral cancer."

Balbo and colleagues administered two forms of NNN called (S)-NNN and (R)-NNN to four groups of 24 rats. The rats were given either (S)-NNN alone, (R)-NNN alone, a combination of both or tap water. The total dose was approximately equivalent to the amount of (S)-NNN to which a smokeless tobacco user would be exposed from chronic use of these products.

All rats assigned to (S)-NNN alone or the combination began losing weight after one year of exposure and died by 17 months. Rats assigned

to (R)-NNN or tap water were terminated at 20 months.

All rats assigned to (S)-NNN had esophageal tumors and demonstrated 100 percent incidence of oral tumors including tumors of the tongue, buccal mucosa, soft palate and pharynx. In contrast, researchers found oral tumors in only five of 24 rats given (R)-NNN and esophageal tumors in three of 24 rats assigned to (R)-NNN. Twelve rats given the combination of (S)-NNN and (R)-NNN had 153 esophageal tumors and 96 oral tumors.

"Measures should be taken to reduce this chemical in smokeless tobacco," Balbo said. "If it is not possible to stop the use of smokeless tobacco products, we should advocate for a reduction of this chemical in these products."

Because the Food and Drug Administration regulates tobacco products, Balbo said she hoped these results will inform regulatory decisions. Moving forward, she and her colleagues hope to identify other chemicals that may be carcinogens in smokeless tobacco and to understand what level of these chemicals is present in smokeless tobacco products.

"In addition, we have to understand how this research translates to human beings," Balbo added. "We have to understand the uptake of NNN from smokeless tobacco products in humans and develop better biomarkers, such as urinary biomarkers, to have a tool to monitor the levels to which smokeless tobacco users are exposed."

Balbo believes these findings are yet another affirmation that tobacco products should be avoided.

Provided by American Association for Cancer Research