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Brief Report

Increased Pouch Sizes and Resulting Changes in the Amounts of Nicotine and Tobacco-Specifc *N*-Nitrosamines in Single Pouches of Camel Snus and Marlboro Snus

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Abstract

Introduction: Initial analyses of the novel smokeless tobacco products Camel Snus and Marlboro Snus demonstrated that these products contain relatively low amounts of nicotine and the carcinogenic tobacco-specifc nitrosamines *N*'-nitrosonornicotine (NNN) and 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK), as compared with traditional smokeless products. It is unknown whether the modifcations in packaging, favors, and pouch sizes that occurred for both Camel Snus and Marlboro Snus since their frst introduction to the market were accompanied by any changes in nicotine or nitrosamine levels.

Methods: We examined the available data on nicotine and NNN and NNK levels in 60 samples of Camel Snus and 87 samples of Marlboro Snus that were analyzed in our laboratory between 2006 and 2010.

Results: Due to the increase in pouch size, the amounts of total nicotine, unprotonated nicotine, and the sum of NNN and NNK present in the large Camel Snus pouches released in 2010 are 1.9-fold, 2.4-fold, and 3.3-fold higher, respectively, than in the original smaller pouches that entered the market in 2006. Total and unprotonated nicotine content in the current version of Marlboro Snus pouches are 2.1-fold and 1.9-fold higher, respectively, and the sum of NNN and NNK is 1.5-fold lower than in the original version.

Conclusions: We observed an increase in nicotine content in single portions of Camel Snus and Marlboro Snus, and an increase in tobacco-specific *N*-nitrosamine content in single portions of Camel Snus, due to the increases in pouch size that occurred between 2006 and 2010. This fnding stresses the importance of tobacco product regulation and ingredient disclosures.

Introduction

Camel Snus and Marlboro Snus—novel "spitless" smokeless tobacco products promoted as an alternative for smokers to use in situations where they cannot smoke—have been marketed in the United States since 2006 and 2007, respectively. Information on the actual use of these products is limited. Available research demonstrates that 10% of smokers try novel snus products, with the trial being more likely among smokers who are young, male, and have no immediate plans to quit smoking (Biener, McCausland, Curry, & Cullen, 2011). Thus, 29% of the smoking men aged 18–24 years were reported to have tried snus over the past year. It is unknown whether these products will persist in the U.S. market. However, the observed high interest in trying snus among certain population groups, along with the successful transition from test marketing to national marketing for both Camel Snus and Marlboro Snus, suggests that there is a reasonable chance for this type of products to continue and grow in popularity in the future.

The public health impact of tobacco use is substantially infuenced by the addictive and carcinogenic potential of the tobacco products. The addictive potential of tobacco is determined by the levels of its main known addictive constituent nicotine. Moreover, the effect of nicotine content on a user is greatly affected by how much of the total nicotine content is present in unprotonated form, which is rapidly absorbed in the mouth and results in a relatively rapid increase in blood nicotine concentration. Salivary pH can also infuence the amount of nicotine present in unprotonated form; however, the buffering capacity of smokeless tobacco is higher than the buffering capacity of saliva, and the pH of a smokeless tobacco product is a major determinant of the amount of unprotonated nicotine to which a user is exposed (Tomar & Henningfeld, 1997).

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While no tobacco product can be classifed as "safe", there exists a diverse spectrum of products that vary in their toxicity profles, the content of the main known addictive tobacco con - stituent nicotine, mode of use, and associated health risks. For example, cigarette smoking delivers a mix of over 5,000 chemicals directly to the lung and is associated with the risk of developing a wide range of cancers, with lung cancer being the highest risk (International Agency for Research on Cancer, 2004). On the other hand, oral use of some smokeless tobacco products that are free of the many combustion products present in cigarette smoke and also contain relatively lower levels of a major group of tobacco carcinogens, the tobacco-specifc *N*-nitrosamines (TSNAs), was reported to be associated with a much lower risk of developing cancer (Greer, 2011; Luo et al., 2007). The importance of TSNA content is based on the existing strong evidence supporting their role in causation of cancers of the lung, pancreas, oral cavity, and esophagus in smokers and oral cavity and pancreas in smokeless tobacco users (Bartsch & Spiegelhalder, 1996; Hecht, 1998; Hecht & Hoffmann, 1988; Magee, 1996; Preston-Martin & Correa, 1989) and the relationship between amount of exposure to TSNAs and cancer risk (Church et al., 2009; Yuan et al., 2009). Thus, completely switching to the use of lower-TSNA smokeless products instead of smoking is seen by some public health researchers as a potential strategy to reduce harm in those smokers who are unable or unwilling to quit tobacco use (Bates et al., 2003; Levy et al., 2004).

Whereas the actual public health impact of oral products like Camel Snus and Marlboro Snus is yet unknown, the initial analyses revealed that single pouches of these products contain relatively low amounts of TSNA and nicotine, as compared with traditional smokeless products (Stepanov, Jensen, Hatsukami, & Hecht, 2008). However, since their frst introduction to the market, there have been a number of changes in the design of both Camel Snus and Marlboro Snus, including modifcations in packaging, favors, and pouch sizes. It is unknown whether these changes were accompanied by changes in the processing and/or type of tobacco used for the manufacturing of these products. Furthermore, it is unknown how changes in pouch size affected the dose of constituents to which consumers are exposed from the use of a single pouch. To determine whether these alterations were accompanied by any changes in TSNA and nicotine content, we examined the available data on 60 samples of Camel Snus and 87 samples of Marlboro Snus that were either purchased by our group or received from other researchers in the period 2006–2010. Analyses of these products were conducted for different purposes and at different times; however, the standard methods routinely used in our laboratory, as well as the inclusion of positive and negative controls for quality control purposes, ensure comparability of these results. We examined the levels of total nicotine, unprotonated nicotine, and the sum of *N*'-nitrosonornicotine (NNN) and 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK), the only TSNA classifed as carcinogenic to humans (International Agency for Research on Cancer, 2007).

Materials and Methods

Snus Samples

Snus samples were either purchased in Minneapolis and St. Paul, Minnesota area or received from other researchers in different parts of the United States, as a part of various projects. A total of 60 samples of various favors of Camel Snus were obtained in 2006, 2008, 2009, and 2010; and a total of 87 samples of various favors of Marlboro Snus were obtained in 2007, 2008, 2009, and 2010.

Constituent Analyses

Upon arrival in the laboratory, tobacco samples were sealed in plastic sleeves and refrigerated until analysis. Sample preparation for analysis of nicotine, pH, moisture content, and TSNA was always conducted shortly after the samples were obtained in the laboratory. Moisture content and pH were analyzed immediately after opening the new package of tobacco product, and nicotine and TSNAs were generally analyzed within a few weeks after the package was frst opened. All samples were stored sealed and refrigerated between analyses. All analyses were performed by standard validated methods (Stepanov et al., 2008). Nicotine was analyzed by gas chromatography–mass spectrometry–selected ion monitoring. The amount of unprotonated nicotine was calculated using the Henderson–Hasselbalch equation, based on the measured total nicotine, pH values, and a pK_a of 8.02 (Richter & Spierto, 2003). TSNAs were analyzed by gas chromatography interfaced with a thermal energy analyzer. During sample preparation, one blank sample (corresponding extraction solvent without addition of tobacco) and one positive control sample (Copenhagen Snuff for which nicotine and TSNA content were previously established) were included in order to monitor for potential contamination and day-to-day analytical variation.

Statistical Analyses

Kruskal–Wallis and Wilcoxon rank-sum tests were used to compare moisture content, pH, total and unprotonated nicotine, and the sum of NNN and NNK in Camel Snus and Marlboro Snus pouches of different sizes. A signifcance level of .01 was used for each Kruskal–Wallis test: Wilcoxon rank tests were used to determine which pouch sizes differed from each other.

Results

Since their frst introduction to the market, there have been increases in pouch weights for both Camel Snus and Marlboro Snus. Thus, Camel Snus samples obtained and analyzed in our laboratory between 2006 and 2010 can be divided into three groups, according to the pouch weight, and Marlboro Snus samples can be divided into two groups. At any given time, all three pouch sizes of Camel Snus were available for purchase, while Marlboro Snus was available in smaller pouches only prior to 2009 and in larger version since 2009. Table 1 summarizes mean values for moisture content, pH, total and unprotonated nicotine, and the sum of NNN and NNK in Camel Snus and Marlboro Snus pouches of different sizes. There were no detectable differences in the constituent levels among different favors of each product; therefore, we combined various favors for the subsequent analyses.

Moisture content was not different among Camel Snus pouches of various sizes. The larger pouches of Marlboro Snus released in 2009 had higher moisture content, as compared with those available prior to 2009: 16 ± 3% versus 10 ± 1%, respectively ($p < .0001$). No signifcant changes in the product pH occurred for either Camel Snus or Marlboro Snus.

Levels of Constituents per Gram Product Weight

When expressed per gram wet weight of product, the mean levels of total nicotine in Camel Snus were lower in the latest large-pouch version of the product, as compared with the original one: 9.4 ± 0.4 mg/g wet weight versus 13 ± 3.2 mg/g wet weight, respectively (Table 1); however, this difference was not statistically signifcant. The opposite was true for the Marlboro Snus samples: the tobacco of larger pouches released in 2009 contained higher levels of total nicotine than the original ones ($p < .0001$, Table 1). The levels of unprotonated nicotine per gram product were not different among pouches of various sizes within the same product.

The sum of carcinogenic nitrosamines NNN and NNK in the tobacco of the large Camel Snus pouches was not signif - cantly different than in the tobacco of original and medium pouches. The levels of NNN + NNK in the tobacco of large Marlboro Snus pouches were lower than in the tobacco of original pouches: 1.27 ± 0.7 µg/g versus 0.50 ± 0.1 µg/g wet weight, respectively ($p < .0001$; Table 1).

Amounts of Constituents in Single Pouches

Comparison of the amounts of analytes contained in a single pouch shows that the large Camel Snus pouches introduced in 2010 contain higher amount of total and unprotonated nicotine than the original small pouches released in 2006 ($p < .0001$ for both comparisons) and the medium-size pouches introduced in 2008 ($p < .0001$ for total nicotine and $p < .0002$ for unprotonated nicotine; Table 1). In the case of Marlboro Snus, the larger pouches released in 2009 also contained higher amounts of total and unprotonated nicotine than those purchased prior to 2009 ($p < .0001$ for both comparisons).

The amount of NNN + NNK present in large pouches of Camel Snus was 2.3 times higher than in the pouches of medium size ($p < .0001$) and 3.3 times higher than in the original small pouches ($p < .002$). Large Marlboro Snus pouches contained lower amounts of NNN + NNK than the earlier version: 0.21 µg/pouch versus 0.31 µg/pouch, respectively (Table 1); however, the difference was not statistically signifcant.

Discussion

The initial analyses of the new smokeless tobacco products Camel Snus and Marlboro Snus revealed that single pouches of these products contain relatively low amounts of nicotine and the tobacco carcinogens NNN and NNK, as compared with traditional smokeless products. However, modifcations in pack - aging, favors, and pouch sizes occurred for both Camel Snus and Marlboro Snus since their frst introduction to the market. We examined the available data on nicotine and NNN and NNK levels in Camel Snus and Marlboro Snus samples analyzed in our laboratory between the years 2006 and 2010 and report here some notable changes that occurred in the amounts of these constituents present in single pouches of both products.

Table 1. Pouch Weights, pH, Moisture content, Nicotine, and the Sum of NNN and NNK in Camel Snus and Marlboro Snus Purchased and Analyzed Between 2006 and 2010.

		Weight per pouch, mg	% Moisture	pH	Total nicotine, *M* (*SD*)		Unprotonated nicotine, *M* (*SD*)			NNN + NNK, *M* (*SD*)	
Product	Pouch description (no. of samples)	*M* (*SD*)	*M* (*SD*)	*M* (*SD*)	mg/g wet wt	mg/pouch	% of total	mg/g wet wt	mg/pouch	µg/g wet wt	µg/pouch
Camel Snus	Original, introduced in 2006 (11)	370 (23)	31 (4)	7.50 (0.2)	13.0 (3.2)	4.75 (0.9)	24.2 (6.9)	3.20 (1.4)	1.17 (0.5)	0.98 (0.2)	0.36 (0.1)
	Medium, introduced in 2008 (43)	531 (51)	31 (3)	7.47 (0.2)	11.4 (1.9)	6.04 (1.0)	23.2 (8.2)	2.60 (0.8)	1.39 (0.5)	0.98 (0.2)	0.52 (0.1)
	Large, introduced in 2010 (6)	970 (90)	34 (1)	7.67 (0.1)	9.4 (0.4)	9.14 (0.9)	30.8 (3.4)	2.89 (0.3)	2.82 (0.5)	1.23 (0.1)	1.19 (0.1)
Marlboro Snus	Original, introduced in 2007 (12)	240 (11)	10 (1)	6.74 (0.2)	14.1 (1.9)	3.39 (0.5)	7.0 (3.0)	0.79 (0.4)	0.19 (0.1)	1.27 (0.7)	0.31 (0.2)
	Large, introduced in 2009 (75)	410 (26)	16 (3)	6.75 (0.1)	17.3 (2.9)	7.09 (1.4)	5.2 (1.3)	0.89 (0.2)	0.36 (0.1)	0.50 (0.1)	0.21 (0.1)

Note. NNK = 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone; NNN = *N'*-nitrosonornicotine.

An increase in pouch size is the common change that occurred for both Camel Snus and Marlboro Snus since their frst release. If constituent levels per gram tobacco remain constant, larger pouch size means more tobacco per pouch and subsequently higher levels of various constituents to which consumers are exposed from a single portion of the product. However, we observed some variations in the constituent levels per gram of product weight over time, which affected the amounts of these constituents present in single pouches in a less straightforward manner. Thus, while not reaching statistical signifcance, total nicotine levels in tobacco of Camel Snus were lower in tobacco of large pouches, as compared with the original ones (Table 1); however, due to the signifcant increase in pouch size, the currently marketed large pouches contain higher amounts of this important constituent, as compared with the original smaller pouches. In the case of Marlboro Snus, the modest increase in the levels of total nicotine per gram product weight, combined with the increase in the pouch size, led to nearly doubling of the amount of total nicotine present in a single pouch of the currently sold version of this product, as compared with the original version (Table 1). With the pH of both products remaining relatively stable over time, the increase in total nicotine content per single pouch resulted in the corresponding increase of the amount of unprotonated nicotine. This increase could be perceived as having both positive and negative effects. As a less harmful alternative to smoking, smokeless tobacco has been proposed by some as a smoking cessation aid (Rodu & Phillips, 2008), and in this context, smokeless products with higher nicotine content could be more effective at completely substituting for cigarettes than those with less nicotine (Hatsukami et al., 2011; Kotlyar et al., 2011). On the other hand, the levels of unprotonated nicotine in large pouches of Camel Snus released in 2010 are similar to, or even higher than, those in some conventional smokeless tobacco products that are capable of inducing and sustaining nicotine addiction (Hatsukami & Severson, 1999; Stepanov et al., 2008).

While the increase in the levels of NNN + NNK per gram wet weight of tobacco used for the manufacturing of Camel Snus was not signifcant between 2006 and 2010 (Table 1), the amount of these carcinogens in the pouches of Camel Snus released in 2010 was more than threefold higher than in the original smaller pouches (Table 1). This increase in exposure to the carcinogenic TSNA, although not reaching the levels found in conventional smokeless tobacco products (Stepanov et al., 2008), is clearly a negative change. In the case of Marlboro Snus, the levels of NNN and NNK in tobacco of the latest product version are among the lowest observed in new smokeless products and are comparable to those found in dissolvable lozenges Ariva and Stonewall (Stepanov, Jensen, Hatsukami, & Hecht, 2006). This signifcant decrease relative to the levels measured in the original version of Marlboro Snus resulted in the lower amount of NNN + NNK present in a single portion of Marlboro Snus, even as the size of the pouches increased over time (Table 1).

It should be noted that while the users of smokeless tobacco products that are sold in loose form, such as many varieties of moist snuff, can select the size of the portion used for a single application; in the case of packaged smokeless products, the manufacturer controls the dose, and the increase of the constituent level per single pouch will most likely lead to an increase in the consumers' exposure to these constituents. Other product characteristics, such as moisture content and tobacco particle size, can affect the degree of constituent extraction from the tobacco pouch and its absorption through the oral mucosa. For example, the observed increase in the moisture content of Marlboro Snus (Table 1) can facilitate the extraction of nicotine and potentially NNN and NNK from the large-pouch version of this product. Tobacco particle size is not measured in our laboratory; therefore, we cannot comment on potential changes of this parameter. Individual consumer characteristics such as pH of saliva and patterns of use are also important determinants of individual exposure to nicotine and TSNA from a smokeless tobacco product. The results of biomarker-based studies might become available in the future, allowing comparison of the relative intake of nicotine and/or NNN and NNK from Camel Snus and Marlboro Snus pouches of various sizes.

The lack of a specifcally designed study to compare the amounts of constituents in pouches of various sizes is the major limitation of this report. The constituent levels analyzed here were originally measured for different studies, without the intention of comparing products purchased in various years. Therefore, there is a large variation in the number of available samples for each pouch size and/or year of purchase. Nevertheless, the number of samples was suffcient to conduct statistically meaningful comparisons among pouches of different sizes.

In summary, we report here our observation of an increase in nicotine content per single pouch of Camel Snus and Marlboro Snus, and an increase in TSNA content in Camel Snus pouches, as a result of an increase in pouch sizes for both products between 2006 and 2010. While the health consequences of these changes are still to be understood, the observed tendency implies that unaware consumers might be exposed to even higher levels of these constituents, as the new oral tobacco products are being further modifed in the future. This fnding stresses the importance of tobacco product regulation, ingredient disclosures, and the provision of accurate information to consumers, so that they can make informed decisions.

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Declaration of Interests

None declared.

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