Smokeless tobacco: is it really safe?

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Abstract

Antismoking campaigns and government legislation have resulted in a decline in smoking. However, the use of smokeless tobacco (SLT) is on the increase. Smokeless tobacco is non-smoked tobacco used either intranasally or intraorally. The increase in its use is possibly due to the perception that SLT is a safe alternative to smoking. SLT includes tobacco products such as snuff (sniffed or placed in the oral cavity) and tobacco leaves (which are chewed). In South Africa, traditional and social practices influence SLT use. While the adverse health outcomes associated with smoking are well established, some health risks attributable to SLT use have not been studied conclusively, especially those that affect the cardiovascular system. Although some studies have found some relationships between SLT use and adverse health outcomes, others have found SLT use to be associated with risks not higher than those in non-users. This article reviews the available literature on the use of SLT, the associated health risks and adverse health outcomes with the aim of providing a scientific basis on which primary care physicians can make rational decisions when confronted with current SLT users or those who contemplate using SLT as a nicotine harm-reduction substance.

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Introduction

Tobacco use predates the arrival of Christopher Columbus in the Americas in 1492. Although the native Indians smoked tobacco then, they also used it in other smokeless forms such as in enemas.[1] Smokeless tobacco (SLT) refers to non-smoked tobacco, used intranasally or intraorally, mainly as "snuff" (dry, moist and fine cut) or chewed tobacco leaves (loose leaf, plug and twist).[2] The types of SLT products used around the world vary according to region (Table I), as do the health risks associated with them.[3]

Table I: Global variation in SLT products

SLT Products	Characteristics	Common users
Moist snuff, US type	Pulverised tobacco, fermented, portion packed	Adolescents, athletes
Moist snuff, Swedish type	Pulverised and non-fermented, semi-sterile tobacco Loose form or sachets; marketed as "snus"	Men and to a lesser extent women. Used also in Norway
Dry snuff	Pulverised, dry tobacco, used orally or sniffed	Women in southern US
Snuff, South African type	Ground tobacco, mixed with other plant products Largely home-made, sniffed and used orally Also available commercially	Mostly among women. Tradition and culture influence use
Toombak	Tobacco mixed with natron powder. Manually prepared by local toombak vendor	Sudan. Used by men more than by women
Betel quid	Made from tobacco, betel leaves, areca nut and slaked lime	South and Southeast Asia

Adapted from Asplund (2003)[8]

Worldwide, tobacco use is an integral part of society and it is the most significant cause of preventable morbidity and mortality. Realising this, Benjamin Waterhouse (1754–1846) commented that "tobacco is a filthy weed that from the devil does proceed; it drains your purse, it burns your clothes, and makes a chimney of your nose".[4] The health implications of tobacco use range from various chronic diseases to death attributable to direct or passive smoking and SLT use. Apart from additives, the major differences between the health implications of cigarette smoking and SLT use lie in the by-products of combustion present in inhaled cigarette smoke.

While the prevalence of cigarette smoking is reducing in the developed world, the use of SLT is on the increase.[5] It has been suggested that this is as a result of smokers switching to the perceived less dangerous SLT, while others have raised concerns that SLT may serve as an entry point to tobacco smoking for young people. About 25% of young men who started with "snus" (a form of SLT used in Sweden) switched to cigarette smoking within a short period of time,[6] and the risk of starting cigarette smoking among a cohort of US Air Force recruits was also found to be twice as high amongst SLT users when compared to non-users of tobacco.[7]

Some studies have shown increased risks of carcinogenesis, dental anomalies and poor pregnancy outcomes among SLT users when compared to non-tobacco users. However, the Swedish studies on SLT use and carcinogenesis have not confirmed this increased risk, suggesting that differences in the composition of SLT across regions may account for variations in the observed health outcomes. While some studies have found increased risks for cardiovascular diseases, others have found SLT use to be associated with risks not higher than those of non-tobacco users.[9]

SLT use is prevalent in South Africa, especially among African women and adolescents, but very few studies have been conducted on the health outcomes associated with the SLT types used. Unlike cigarette smoking, research on the health implications of SLT use is still evolving and some issues remain uncertain. This has serious implications for clinical practice where SLT use is prevalent and used as a smoking harm-reduction substance. This article explores the health implications of SLT use, and provides information for primary care physicians to make rational decisions when confronted with current SLT users or those who contemplate using SLT as a nicotine harm-reduction substance.

Epidemiology of SLT in South Africa

Tobacco products in South Africa are made primarily from the leaves of *Nicotina tabacum.* Traditional, home-made SLT as 'snuff' is commonly used in South Africa and is prepared with local additives, such as *ash* obtained from burning the mukango vegetable plant.[10] Common industrially-made SLT in South Africa includes "Ntsu", "Taxi-Red", "Singleton-Menthol" and "Tobacco-rette original". In developed countries, most urban consumers use industrially manufactured SLT. Apart from the warning sign that tobacco causes 'cancer', SLT manufacturers in South Africa are not mandated by law to disclose the nicotine content of their products. This gap in legislation denies consumers vital information necessary for decision making.

The free nicotine content and amount absorbed vary in close relation to the pH of the tobacco preparation. This nicotine delivery capacity was shown by Ayo-Yusuf et al[10] to be high but variable among the products available in South Africa. Variations also exist among samples manufactured by the same manufacturer in South Africa, and estimates of nicotine delivery vary from values consistent with those found in industrialised nations such as Sweden and the USA, to very high levels found in "toombak", the traditional SLT used in Sudan.

In 1998, the national prevalence of SLT use was estimated to be 6.7%.[11] Across all racial groups, it was estimated that 13.2% of women engaged in the use of SLT, although a more recent study in a rural area, published in 2005, estimated the prevalence of SLT use among black women to be 28.1%.[12] While men smoke cigarettes more than they use SLT, the converse is true for women. This information is in contrast to that obtained in Sweden, Norway and North America, where SLT is predominantly used by men, especially young athletes.[6,13]

Ayo-Yusuf et al10 quoted a 1999 report by Swart and colleagues that suggested a prevalence of 18.6% for SLT use among black South African teenagers, compared to rates of between 11.4% and 19% among American teenagers in the same year.[14,15] Early exposure to the systemic effects of nicotine, risks of nicotine dependence early in life, switching to cigarette smoking and adverse health outcomes are issues of serious concern in this age group. Parental tobacco use influences tobacco use among young people, and paternal snuff use is associated with exclusive use of 'snus' among Swedish boys (OR = 3.0, 95% CI: 1.4–6.4).[16] Very young SLT users also tend to consume more alcohol than non-users and smoking adolescents.[17] The estimated mean consumption of alcohol was found to be five to 10 times higher among Swedish ninth grade tobacco users than non-users. In addition, heavy alcohol drinkers had disproportionately higher odds of reporting SLT use (OR = 16.7; CI: 12.9–21.7).[18] No local study has been done to establish if SLT use among South African adolescents is associated with increased alcohol consumption. Long-term exposure to SLT and increased alcohol consumption could spell doom for young people, as these are risk factors for various chronic diseases, including oral, head and neck cancers.

The "Birth to Ten" study conducted in Soweto, South Africa found that 7.5% of the participants had used SLT, mainly as 'snuff' during pregnancy.[19] Another study reported a prevalence of about 10% for SLT use among pregnant, black South African women.[10] Using snuff during pregnancy demonstrates the nicotine addictive capacity of SLT, which makes it difficult for these women to stop despite awareness of the inherent dangers of tobacco use during pregnancy. Poor knowledge among health care providers about adverse pregnancy outcomes associated with SLT use may also explain why the focus only falls on stopping cigarette smoking during antenatal care.

Nicotine handling, metabolism and dependence

The nicotine content of SLT ranges from 6 to 16 mg/g, and these concentrations vary from two to 15 times those found in cigarettes.[4,10,14] It is logical to assume that SLT users will experience more harmful effects of nicotine than will cigarette smokers. However, cigarette smoking is associated with more health risks than is SLT, suggesting that factors other than the nicotine content may be responsible for the adverse health effects associated with tobacco smoking. Products of combustion, i.e. carbon monoxide, polycyclic aromatic hydrocarbons, tobacco-specific nitrosamine, the sodium content, licorice and other additives are components of tobacco that have been implicated in the various harmful effects associated with its use.[1,20,21]

Nicotine metabolism varies among ethnic groups and, given the same amount of nicotine exposure, the dependency rates tend to be higher for females than males, and for adolescents higher than for adults.[10] Only 2 to 3% of cigarette smokers attempting to quit finally succeed, and fewer than 50% of ever-smokers quit in a lifetime.[22,23] The success rate of quitting among SLT users is not glaringly different. While 67% of SLT users wish to quit, up to 36% of those who made attempts could not. Considering the nicotine content and addictive capability of the SLT products that are available in South Africa, SLT use may fuel nicotine addiction.

SLT use, cardiovascular risks and diabetes mellitus

The majority of the studies in this field have been conducted in Northern Europe, where the commonly used SLT is moist 'snuff'.[8] While some of these studies have shown an increase in cardiovascular risks among SLT users, others have not shown any significant increase in risks.[9] However, nicotine has been implicated in increased ambulatory heart rates and diastolic blood pressure among both cigarette smokers and SLT users compared to non-users ($P < 0.05$).[24] While screening for oral cancers and hypertension in a group of people aged 18 to 25 years in Ohio, USA, the mean blood pressure among SLT users was found to be 143.7/ 80.7 mmHg, compared to 131.6/72.8 mmHg among non-users of tobacco. The mean difference in diastolic pressure between tobacco users and non-users was 7.9 mmHg ($P = 0.01$).[15]

Apart from acute, non-sustained elevation in blood pressure in normal subjects, paroxysms of severe hypertension were described in a patient with phaechromocytoma following snuff dipping.[25] Marked elevations in blood pressure were attributed to an acute surge in catecholamine levels, and these were associated with acute coronary episodes. Nicotine enhances the release of catecholamine and is associated with acute increases in heart rate and blood pressure. Substantial quantities of licorice found in chewed tobacco have also been suggested to cause excessive accumulation of mineralocorticoids, which may result in hypertension, sodium retention, hypokalaemia and myalgia.[21,26] Secondary analyses of data of black South African women during the 1998 National Demographic and Health Survey showed that blood pressure readings were higher in snuff users than in non-users of

tobacco, especially when snuff was dipped more than eight times daily. The increases in blood pressure were however not statistically significant after controlling for confounders (OR = 1.12; 95% CI: 0.84–1.50).[27]

Diabetes mellitus is a known risk factor for cardiovascular diseases and moist snuff dipping in addition to cigarette smoking is associated with an increased risk for diabetes mellitus (OR = 2.7; 95% CI: 1.3–5.5).[28] The consumption of large amounts of SLT at baseline was associated with the development of the metabolic syndrome in a Swedish longitudinal study (OR = 1.6; 95% CI: 1.26–2.63).[29] However, the risks of developing diabetes for ever and current 'snus' users in the Swedish MONICA study were not significantly increased when compared to those of non-users of tobacco (OR for 'ever users' = 1.34; 95% CI: 0.65–2.7, OR for 'current users' = 1.18; 95% CI: 048–2.9).[30]

When compared with cigarette smoking as a risk factor for myocardial infarction in a case-control study in a northern Swedish population, SLT was not predictive of myocardial infarction.[31] Although the authors were unable to demonstrate an increased risk of coronary ischaemia, a large study was needed to exclude any detrimental effects of SLT on the risk for coronary ischaemia. In another Swedish study, on SLT use and cardiovascular mortality among construction workers, workers who smoked 15 or more cigarettes a day and snuff users had relative risks of 1.9 (95% CI: 1.7–2.2) and 1.4 (95% CI: 1.2–1.6) respectively compared to non-users.[32] The risk of dying from cardiovascular disease for SLT users was higher among subjects younger than 55 years old compared to those who were older (RR = 2.1; 95% CI: 1.5–2.9 vs. RR = 1.1; 95% CI: 1.0–1.4].[32] When adjusted for body mass index, blood pressure and history of heart symptoms, the results were unchanged. The authors concluded that both smokers and smokeless tobacco users faced a higher risk of dying from cardiovascular diseases than non-users of tobacco. In interpreting the findings of this study, it was pertinent to consider the "healthy-worker's" effect, which indicates that the working population has a lower total morbidity and mortality than the general population – usually about 70 to 90% that of the general population.[33] The risks in the general population may therefore be higher than these estimates.

In the long term, nicotine adversely affects serum cholesterol and triglyceride levels and promotes platelet aggregation through prostacycline synthesis inhibition. These effects on lipid metabolism and thrombosis increase the risks for adverse cardiovascular events among smokers and SLT users. The promotion of platelet aggregation increases the likelihood of thrombo-embolic events – a key process in the pathogenesis of many cardiovascular diseases. Notwithstanding these possibilities, SLT users do not differ from non-users in adjusted levels of total and HDL cholesterol.[5]

Another Swedish study assessed cardiovascular risk factors among snuff users, smokers and non-users who were younger than 31 years of age. Compared to non-users, SLT users were more likely to consume more alcohol ($p < 0.01$) and less likely to engage in physical exercise ($p < 0.05$). These poor lifestyles are known to increase the risks of cardiovascular diseases. SLT users also had higher plasma fibrinogen levels compared to non-users ($P = 0.07$).[34] Abstinence from SLT use increases weight but, in contrast to smoking cessation, cessation of SLT use does not improve the profile of lipoproteins over time.[35] The risk for increased thickness of carotid artery intima associated with cigarette smoking has not been demonstrated among SLT users,[36] reaffirming the suggestion that inhaled smoke from tobacco combustion, rather than the nicotine content, may be the important aetiological factor in the atherosclerotic process.

Given the inconsistencies in the findings of the available studies on the cardiovascular risks associated with SLT use, and the differences in the types of SLT used in different parts of the world, there is a need for studies on the health implications of SLT used in other parts of the world besides Europe and North America.[23] This need is very critical, as cardiovascular diseases are increasingly more important causes of morbidity and mortality in the developing world as these countries experience ongoing health transition.

SLT use, oral and gastrointestinal diseases

Cigarettes contain many carcinogens, but the carcinogens in SLT are less well appreciated. The carcinogens in SLT include polonium-210, N-nitrosamines (including tobacco-specific nitrosamines), volatile aldehydes and polycyclic aromatic hydrocarbons. These carcinogens are linked to increased risks of oral, cervical, prostatic and pancreatic cancers.[4] SLT use also predisposes to oral lesions, such as gingival recession, gingivitis, loss of periodontal attachment, peridontitis, teeth staining, dental caries and tooth loss.[15] Halitosis, leukoplakia and erythroplasia are also common findings among SLT users. When used over a very long time (more than 40 years), SLT may promote micronuclei formation and, to a lesser extent, loss of cell cohesion and hyperkeratosis – changes that have been associated with oral neoplasia.[4] Vitamin A and beta-carotene have been suggested to reverse these precancerous oral lesions in tobacco chewers.[37]

Differences in additives, patterns of use, modes of preparation and co-morbidities may account for the differences in cancer outcomes in different regions of the world. The use of "snus" (the form of SLT in Sweden and Norway) has not been linked to significantly increased risks for head and neck and other cancers.[1,23] However, the local form of SLT in India is an established risk factor for oral cancers in its users. Similarly, strong associations exist between 'toombak' (a form of SLT used in Sudan) and squamous cell carcinoma of the lip, buccal mucosa and mouth floor (OR = 3.9; 95% CI: 2.9–5.3).[38] The cancer sites correspond to the sites of placement of toombak in the mouth. Similar results were found in North Carolina, USA, where snuff dipping among non-smoking whites was found to hold a greater risk for oral and pharyngeal cancers than in non-users (RR = 4.2; 95% CI: 2.6–6.7).[39] The risk approached 50-fold for cancer of the lips and buccal mucosa. The "Zulu snuff" produced in South Africa contains charred aloe stems, which give high levels of the carcinogenic "benzpyrene". An increased risk for maxillary antrum cancers has also been described among snuff users in South Africa.[23]

SLT use has been linked to gastro-oesophageal reflux disease, peptic ulcer and inflammatory bowel disease.[4] Strong associations of SLT use (for more than 20 years) with lower oesophageal cancers have also been described in studies conducted in India (OR = 1.2; 95% CI: 2.6–14.2 in women and OR = 10.6; 95% CI: 5.6–17.3 in men).[23] The risk for gastric cancers was increased in tobacco chewers compared to non-users in a case-control study in Mizoram, India (OR = 2.6; 95% CI: 1.1–4.2).[40]

SLT use and respiratory diseases

A recent study of data from a nationally representative sample of black South African women reported an association between SLT use (more than eight times per day) and chronic bronchitis (5.3% vs 2.8%; $p = 0.01$). Compared to non-users, this study showed that snuff users were also more likely to present with a history of tuberculosis (23.3% vs 15.9%; $p = 0.06$) and a lower peak expiratory flow rate (237 L/min vs 293 L/min; $p < 0.01$).[11] The mucosal changes in the upper airway secondary to intranasal snuff use, the high potency of nicotine as a bronchial gland stimulant, the increased survival of neutrophils in the presence of nicotine, and the capability of snuff to act as a source of dust and bacteria are factors that could explain the role(s) of snuff in the pathogenesis of chronic bronchitis. Newer, enclosed snuff packages

reduce the possibility of dust inhalation and bacterial contamination. Mortality analyses in two large studies in the US did not show significant mortality risk for chronic obstructive airway disease (COPD) among users of the new package "spit tobacco", introduced after 1982, compared to non-users. In contrast, the old, free spit tobacco had significant mortality risks for COPD.[41] In analysing the effect of switching from cigarette smoking, smokers who switched to spit tobacco had a significantly increased risk for lung cancers compared to smokers who stopped completely (HR = 1.46; 95% CI: 1.24–1.73).[42]

SLT use and exposure to nicotine during pregnancy

Nicotine targets specific neurotransmitter receptors in the fetal brain and may affect neural cell proliferation and differentiation, leading to shortfalls in the number of cells and altered synaptic activity. The consequences of these changes include neurological and cognitive deficits, and nicotine dependence in the offspring. These changes may occur even after a long period of early childhood normality, becoming evident in late childhood and even during the adolescent period.[43]

Increased risks for adverse pregnancy outcomes have been shown with cigarette smoking, although SLT use during pregnancy has also been associated with reduced birth weight (OR = 1.6; 95% CI: 1.1–2.4), pre-eclampsia and an increased risk of preterm delivery (OR = 1.4; 95% CI: 1.0–2.1) in India.[44] Similar adverse pregnancy outcomes were also reported by England et al in a study of 23 524 pregnant women in Sweden.[45] In South Africa, while no study has examined obstetric outcomes associated with SLT use in detail, the "Birth to Ten" study found that though SLT use in the form of snuff resulted in a mean adjusted 17.1 g [95% CI: 69.5–102.7; p = 0.69] lower birth weight compared to non-users of tobacco, this difference was not statistically significant.[19] This finding may not hold for the entire South African population, considering the fact that, while most urban SLT users use industrially manufactured snuff, the majority of rural women use the traditional, home-made snuff. Traditional home-made snuff contains different additives, some of which are known carcinogens, and this difference could change the outcomes if the study were conducted in rural areas.

Conclusions

Adverse health outcomes have been linked to SLT use, but these health risks generally appear to be less than those associated with cigarette smoking. The risks of adverse health outcomes also depend on the type of SLT used in a specific region of the world. Nevertheless, adverse health outcomes associated with SLT use on a global level include increased risks for cancers, poor pregnancy outcomes, nicotine dependence and addiction, and periodontal disorders. SLT use may also be a risk factor for the development of chronic bronchitis and may predispose to tuberculosis infections in South Africa. Cardiovascular risks associated with SLT use are still clouded in uncertainty, but there is a general trend of lower risks compared to cigarette smoking.

To the extent that several adverse health outcomes have been reported with SLT use in studies conducted in South Africa and in other settings, SLT use cannot be regarded as a safe alternative to cigarette smoking. Where feasible, therefore, the cessation of the use of all tobacco products remains the only safe option.

As most of the available literature on the health implications of SLT use are based on studies from Europe and North America, differences in the types of tobacco products, modes of preparation, types of additives, SLT habits of users and types of co-morbidity limit the generalisation of their findings to other contexts. Given the high prevalence of SLT use and a different SLT type in South Africa, more studies on the health outcomes of SLT use are needed in the local context in order to confirm some of the findings of overseas studies.

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