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A Review of the Health Impact of Nicotine Pouches

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ABSTRACT

Introduction and Purpose of Research

Nicotine pouches, popular especially among young people, are smokeless alternatives to traditional tobacco. Placed in the mouth, they release nicotine absorbed through the mucosa, reducing withdrawal symptoms and avoiding harmful tobacco smoke. Often used for smoking cessation, they are considered lower-risk than smoking and may help reduce smoking rates. The aim of this review is to summarize the current knowledge on the impact of nicotine pouches on overall human health.

Review Methods

The review is based on 39 articles found in PubMed databases published between 2006–2024.

Conclusion

While nicotine pouches and snus are marketed as lower-risk alternatives to smoking, their health implications are still significant. These products, popular among young adults and athletes, may help with smoking cessation but carry risks, particularly with long-term use. Research suggests nicotine pouches and snus may have no performance-enhancing effects in sports and could impair physical performance, including endurance and strength. Moreover, their use is linked to various health concerns such as cardiovascular issues, type 2 diabetes, oral mucosal changes, and decreased sperm count. Snus has been associated with a modest increase in cardiovascular disease risk, although the risks are lower than smoking. Additionally, smokeless tobacco use is linked to an increased risk of oral squamous cell carcinoma, especially in women. The use of snus during pregnancy has also been linked to

higher risks of post-neonatal mortality and other adverse outcomes. Despite these findings, there is a need for more extensive, well-controlled studies to fully understand the long-term health effects of smokeless tobacco products and their role in public health.

Keywords: nicotine pouches, smoking, type 2 diabetes, smokeless tobacco, snus, peripheral artery disease, oral mucosal changes

Introduction

Smokeless tobacco also known as Swedish snuff is consumed by more than 300 million people worldwide [31]. Nicotine pouches, unlike Swedish snuff, do not contain tobacco, only nicotine and possibly additional substances. In 2021, the prevalence of nicotine pouches in the European Union (EU) was estimated at 0.3% of the adult population [15]. Nicotine pouches are becoming increasingly popular due to their overall availability [9, 16] . They are very popular among teenagers and young adults [17] . Nicotine pouches are products containing nicotine that are used orally as an alternative to traditional tobacco products, such as cigarettes. These small, convenient pouches are made from a material that allows chemical substances to pass through and contain nicotine, flavor additives, and filler substances [28]. The pouch is placed between the gum and the cheek or lip [33]. The nicotine is gradually released from the pouch through contact with the moist environment of the mouth. The active substance is absorbed through the mucous membrane of the mouth, bypassing the respiratory system. Nicotine then enters the bloodstream, where it affects nicotine receptors in the central nervous system, triggering the release of neurotransmitters like dopamine [37], which induces feelings of pleasure and reduces withdrawal symptoms. Nicotine pouches are used as a smoking cessation aid, helping to reduce nicotine cravings. They can also be used by individuals who wish to avoid tobacco smoke and its toxic components (e.g., tar). Due to their lack of combustion and absence of tobacco leaf, nicotine pouches are likely to be a substantially 'lower-risk product' relative to tobacco smoking [29] [23] . It is believed that substituting

combusted tobacco products with alternative nicotine products may help reduce smoking rates[7].

Nicotine Pouch Awareness and Use Among Youth

Data collected from the 2021 National Youth Tobacco Survey (NYTS) shows that approximately 9.4 million students, or 35.5%, had heard of nicotine pouches. Additionally, 1.9% of students reported having ever used nicotine pouches. Among users, current nicotine pouch use was reported by 13.3% of ever and 41.3% of current smokeless tobacco users, 5.1% of ever and 11.5% of current cigarette users, and 3.2% of ever and 6.9% of current e-cigarette users. Approximately 63.5% of current nicotine pouch users reported using them on 1–5 days in the past month, with 19.3% using them on 6–19 days and 17.2% on 20–30 days). The majority (61.6%) of current users reported using flavored nicotine pouches. While 14.6% exclusively used nicotine pouches, 85.4% reported using at least one additional tobacco product, with 32.8% using one other type and 52.6% using two or more[14].

Transition from Smoking to Oral Nicotine Pouches

The three test products of nicotine pouches, available in retail stores at three nicotine levels—2 mg, 4 mg, and 8 mg (representing low, middle, and high levels of nicotine, respectively)—were compared to select harmful and potentially harmful constituents in adults who smoke and switch to oral tobacco products.

The harmful effects of smoking are mainly caused by exposure to the harmful and potentially harmful substances found in cigarette smoke. For adults who smoke and are either unable or unwilling to quit, switching to oral tobacco-derived nicotine products, such as the test items used in this study, may help reduce harm. The findings from this biomarkers of exposure study indicate that switching from smoking to these products significantly lowers exposure to specific harmful and potentially harmful substances (excluding nicotine) compared to continuing smoking, with reductions similar to those seen in individuals who quit smoking altogether. No significant differences in exposure reduction were observed between the various nicotine levels. While these products are not without risk due to their nicotine content, which is addictive, the most effective option for smokers remains quitting all tobacco products. The study's results are promising and suggest that for those unable or unwilling to completely quit smoking, switching to these nicotine pouches and maintaining this switch

over time may help sustain reductions in exposure to harmful substances, potentially lowering the risk of smoking-related diseases[26].

Snus use in sport

Based on data available for athletic populations, it is estimated that 15-75% of athletes are either current or former users of oral nicotine[2, 5, 22].

The use of snus is prevalent among professional male football players, drawing criticism from healthcare professionals, clinicians, and the media.

Research on snus and nicotine use in sports indicates that their performance-enhancing effects are unlikely, with some evidence suggesting they may even hinder performance. Nicotine might improve cognitive functions such as attention, memory, and fine motor skills while offering temporary stress relief. However, its use is linked to impaired sleep, suboptimal nutrition, and long-term health risks like periodontal disease, cardiovascular issues, and metabolic disorders. Nicotine dependence, increasingly reported among athletes, can also lead to mental health challenges and withdrawal symptoms, potentially harming performance, recovery, and overall well-being[25].

Athletes report that nicotine may aid in managing dry mouth, appetite suppression, concentration, reaction time, and relaxation. However, evidence suggests that nicotine-containing products like snus provide no performance benefits and may even impair aerobic, anaerobic, and strength-based performance. Studies indicate that snus can increase mental fatigue, prolong reaction times, and reduce training readiness, especially in non-habitual users. Negative side effects such as confusion, dizziness, nausea, and tremors have also been observed. Any perceived benefits, such as reduced fatigue, are likely due to withdrawal relief in habitual users[10].

On the other hand long-term daily snuff use does not impact endurance performance in activities involving large muscle groups. VO2max and time to exhaustion during a maximal running test remained unchanged after the snuff cessation period (SCP). The effects on cardiovascular risk factors were mixed, with improvements in heart rate and blood pressure but negative changes in total cholesterol, LDL, and body mass[4].

The research on snus is limited and faces challenges, including individual nicotine tolerance, placebo control difficulties, and health-related stigma. To clarify the potential ergogenic effects of snus, robust, well-controlled studies are needed across various populations.

Risk of Type 2 Diabetes

A cohort of 36,742 participants aged 56–95 years was tracked for new cases of Type 2 diabetes and mortality between 2009 and 2017, using data from the Swedish National Patient, Prescribed Drug, and Death Registers.

Among participants who had never smoked, the use of snus was associated with an increased risk of Type 2 diabetes in the model adjusted for age and sex. However, this association was weakened after further multivariable adjustments[35] .

Peripheral artery disease (PAD)

Peripheral artery disease is a major cardiovascular disease that affected 202 million people worldwide in 2010[34]

The study included participants from the Cohort of Swedish Men (COSM), initiated in 1997, with 100,303 Swedish men aged 45-79 from Västmanland and Örebro counties invited. Follow-up surveys were conducted in 2008 and 2009, with 37,861 and 29,068 men completing health and risk factor questionnaires, respectively. After excluding those who had died before July 1, 2009, those with prior PAD diagnoses, and those with missing snus d ata, 24,085 men were included in the final analysis.

Snus users were younger, had lower education levels, less physical activity, and a history of hypertension, hyperlipidemia, and diabetes. Past snus users had a higher probability of being free from PAD diagnosis compared to never snus users ($p = 0.02$). However, after adjustment, snus use was not associated with PAD risk in either the age-adjusted or multivariable-adjusted models (hazard ratios for past and current snus users were 0.95 and 0.88, respectively). This suggests that although snus use may influence the likelihood of being free of PAD, it does not show a significant association with PAD occurrence after considering other factors [38].

Risk of Cardiovasular Disease (CVD)

The study examines the association between the use of Swedish snuff (snus) and the risk of cardiovascular disease (CVD) and mortality in middle-aged and older adults. It involved over 100,000 participants from the Swedish cohort, with data collected between 1990 and 2012.
Researchers found that snus use was associated with a modestly increased risk of CVD and mortality, although the risks were lower than those associated with cigarette smoking. The study highlights the importance of understanding the health impacts of snus, particularly in comparison to other forms of tobacco use [36].

Decreased sperm count

Men (n = 613) from the general population, recruited 2000-2010, were physically examined and provided urine, blood, and semen samples. Sperm parameters and reproductive hormones were analyzed, along with DNA fragmentation (via Sperm Chromatin Structure Assay). Nicotine exposure was assessed through urinary cotinine levels. General linear models were used, adjusting for cigarette smoking and abstinence time for semen parameters.
After adjustments, total sperm count was 24% lower and testosterone 14% higher (in 109 snuff users compared to non-users. In the general population, the use of smoke-free tobacco (snuff) was linked to a lower sperm count and higher testosterone levels, with the degree of use appearing to influence the results[12]

The spontaneous abortion

The population-based cohort study using data from the national Swedish Pregnancy Register (SPR). The study population comprised women who had their first antenatal visit registered in SPR from January 1, 2014 to July 31, 2018. Criteria for inclusion were singleton pregnancies that ended in SA or childbirth. In total, 525 604 pregnancies were included in the analysis.
Maternal use of snuff was linked to higher risks of post-neonatal mortality, SIDS, and SUID. Stopping smoking and snuff use prior to the first antenatal visit was associated with lower risks of SIDS and SUID compared to ongoing use[32].

Oral mucosal changes

An online survey was conducted from August 2022 to April 2023 in a university student council group (n=50) to assess medical and dental health, dietary habits, and tobacco use. Participants aged 18–35, with no systemic diseases or medications, not pregnant, free of

periodontitis, and using nicotine pouches/smokeless tobacco daily for at least 2 years were selected for further investigation. Seven respondents met these criteria and underwent an oral examination, including dental status, oral cancer check, and basic periodontal assessment
The results indicated that nicotine pouches led to changes in the oral mucosa, manifesting as white, uniform lesions at the pouch placement sites. Histopathological analysis revealed parakeratosis with thickened epithelium, edema in both the epithelium and connective tissue, and chronic inflammation with lymphocyte and macrophage infiltration [19] . The World Health Organization states that oral epithelial dysplasia is linked toa higher risk of developing squamous cell carcinoma[6]

Another research was made with an online retrospective survey - respondents who were 18–35 years old, did not have any systemic diseases or medical conditions, did not take any daily medicine, were not pregnant and had not used antibiotics for at least 6 months were invited to take part in the research and to undergo an oral examination. Overall, 76 respondents underwent oral mucosal examination.
The study found that oral mucosal changes were present in snus users, primarily males, who used at least 5–10 tobacco pouches daily for 5–10 years. All the observed lesions were white and located at the sites where the pouches were placed. Clinical examination, along with the collection of medical and tobacco use history, were essential in identifying these areas [18] . These white lesions are known as smokeless tobacco keratosis [21] . It was concluded that the use of smokeless tobacco is associated with an increased risk of oral squamous cell carcinoma, particularly in women[20].
Németh, Orsolya et al. examines the relationship between snus use and oral health in adolescent athletes, with a particular focus on gum bleeding and dental caries. The results reveal a statistically significant link between snus consumption habits and gum bleeding during toothbrushing. The findings emphasize the combined effects of poor oral hygiene and frequent snus use, which contribute to increased gum bleeding. However, the limited sample size within specific snus user groups means the study highlights trends rather than providing definitive conclusions [24].

Nicotine Toxicity From Repeat Use of Nicotine Pouches

This case report highlights a 21-year-old male who experienced acute nicotine toxicity after consuming 15 extra-strength nicotine pouches (10.9 mg each) within 12 hours. He presented with confusion, tremors, nausea, and hypertension, consistent with moderate nicotine toxicity. Initial evaluation ruled out other causes, including amphetamine use, as the symptoms aligned more closely with nicotine overdose. The patient was treated with fluids and benzodiazepines, recovering fully within 24 hours [11].

The patient's total nicotine exposure of 163.5 mg illustrates the risk of repetitive dosing, as the delayed onset of effects may lead users to consume excessive amounts to achieve the desired outcome. This case underscores the potential dangers of modern nicotine products marketed as safer alternatives, particularly among inexperienced users who may not recognize overdose risks.

Nicotine pouches are increasingly popular, particularly among youth, but their pharmacokinetic properties—delayed peak concentrations and higher systemic nicotine exposure—pose unique risks. Unlike traditional cigarettes, the greater nicotine load can result in inadvertent toxicity, as demonstrated in this case. Further studies are needed to understand real-world patterns of use and improve safety measures, including better labeling and public education on the potential dangers of excessive consumption.

Tobacco-Free Oral Nicotine Delivery Products and Their Association with Acute Renal Tubular Necrosis

Study on tobacco-free oral nicotine delivery products (ONDPs) in pouch shows these products contain no detectable levels of nitrosamines or polycyclic aromatic hydrocarbons (PAHs), and the quantified harmful and potentially harmful constituents (HPHCs) are similar to those in nicotine replacement therapy (NRT) products, with both being significantly lower than in tobacco-based products[3].

Nicotine has been shown to have nephrotoxic effects [8, 27] . In chronic smokers, nicotine accumulates in the kidneys via glomerular filtration and tubular secretion, interacting with nicotinic acetylcholine receptors (nAChRs) in renal proximal tubular epithelial cells (PRTECs). Studies suggest nicotine may induce nephrotoxicity through mechanisms such as activation of the NLRP6 inflammasome and alpha7 nAChRs, leading to increased levels of kidney injury markers like kidney injury molecule-1 (KIM-1) [39] . Additionally, nicotine

triggers apoptosis by generating reactive oxygen species, causing cell cycle arrest. These mechanisms contribute to acute tubular injury and increase the risk of chronic kidney damage over time.

Lactate dehydrogenase (LDH) is a widely recognized marker of cell injury, including renal tubular damage. Elevated LDH levels are often associated with acute tubular necrosis (ATN), particularly following ischemic events in kidney transplant patients, where it serves as a non-invasive indicator of kidney injury and a tool for tracking clinical outcomes[13, 30]. In cases of pre-existing tubular atrophy and interstitial fibrosis, ONDPs may exacerbate renal damage, leading to increased LDH levels[1].

Conslusion

In conclusion, nicotine pouches, tobacco-free products, contain nicotine and additional substances such as flavorings and fillers. Their compact form makes them easy to use – they are placed between the gum and the cheek, where the moist environment allows the gradual release of nicotine and its absorption through the mucous membrane. This process bypasses the respiratory system, making them potentially less harmful than traditional cigarettes, as users are not exposed to toxic substances like tar. Due to these characteristics, nicotine pouches are seen as an alternative to traditional tobacco products and can support smoking cessation by reducing withdrawal symptoms.

The popularity of nicotine pouches is growing, especially among teenagers and young adults, partly due to their accessibility and attractive flavor options. In 2021, 0.3% of the adult population in the European Union reported using nicotine pouches, although studies indicate much higher awareness among youth. According to 2021 data, approximately 35.5% of high school students had heard of nicotine pouches, and 1.9% admitted to using them. Most users consume pouches occasionally (1–5 days per month), with flavored variants being the most popular. However, their rising popularity among teenagers raises concerns about the risk of nicotine addiction and potential health consequences.

Although nicotine pouches are considered lower-risk products compared to smoking cigarettes, they are not entirely safe. Their use can lead to changes in the oral mucosa, such as white lesions at the application sites, which increase the risk of squamous cell carcinoma. Moreover, chronic use is associated with potential health risks, including cardiovascular diseases, type 2 diabetes, and nicotine toxicity. Cases of acute nicotine poisoning have also been reported in users consuming excessive amounts of pouches in a short period. For instance, a 21-year-old man experienced symptoms such as disorientation, tremors, and hypertension after consuming 15 high-nicotine pouches within 12 hours.

Nicotine pouches are also used by athletes, though their effects on physical performance are debatable. Some studies suggest that nicotine may enhance concentration and reaction time, but its use often leads to side effects such as impaired sleep quality and reduced training readiness. In the long term, nicotine can negatively impact oral health, causing periodontal diseases and other dental problems.

In summary, nicotine pouches are perceived as a less harmful alternative to smoking and can support individuals seeking to reduce or quit smoking. However, their growing popularity, particularly among youth, and the health risks associated with long-term use call for further research and public education on the safe use of these products.

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