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A cessation program for snuff-dippers with long-term, extensive exposure to Swedish moist snuff: A 1-year follow-up study

MATS WALLSTRÖM[1], GUNILLA BOLINDER[2], BENGT HASSÈUS[3] & JAN-M HIRSCH[4]

[1]*Department of Oral and Maxillofacial Surgery, Institute of Odontology, Sahlgrenska Academy at University of Gothenburg, Gothenburg, Sweden,* [2]*Department of Medicine, Karolinska Institutet and Karolinska University Hospital, Stockholm, Sweden,* [3]*Department of Oral Medicine and Pathology, Institute of Odontology, Sahlgrenska Academy at University of Gothenburg, Gothenburg, Sweden, and* [4]*Department of Surgical Sciences, Oral and Maxillofacial Surgery, Uppsala University, Uppsala, Sweden*

Abstract

Objective. Smokeless tobacco (Swedish moist 'snus') users are often strongly addicted to nicotine. Compared to the large number of smoking-cessation studies, there have been few evaluated clinical cessation programs in conjunction with nicotine replacement therapy (NRT). The aim of this study was to evaluate a cessation program for snus users with a weekly use of >2 cans/week for >10 years. ***Material and methods.*** A prospective, open, non-randomized intervention trial was undertaken including baseline oral examination and soft tissue biopsy, minor physical examination, brief cessation advice, NRT recommendations and five prospective follow-up visits within 12 months. Individual cessation counseling was given, together with oral examination in the dental office. Fifty snus users with a minimum consumption of 100 g/week who were actively seeking cessation treatment were recruited through advertising. Self-reported abstaining, including random-sample biochemical verification, and NRT use were evaluated at 6 weeks and 3, 6 and 12 months. ***Results.*** At the 3-, 6- and 12-month visits, 58%, 46% and 30% of subjects, respectively were tobacco-abstinent. All nicotine abstinence was randomly controlled during the study except at 12 months, where all subjects claiming abstinence were confirmed biochemically and clinically. ***Conclusion.*** Smokeless tobacco cessation achieved together with suitable NRT seems a promising way to improve a persistent tobacco-free condition.

Key Words: *Cessation, nicotine replacement, oral mucosa, smokeless tobacco, snus*

Introduction

In Sweden today, ≈23% of the male population and 3% of the female population use moist snuff ('snus') on a daily basis. Among young males aged 25–34 years, the prevalence of snus use is as high as 35% [1]. The habit is usually established in adolescence.

Swedish snus consists of finely ground tobacco mixed with water and flavouring. It is marketed as loose snuff and in small pouches containing the average amount consumed by those preferring a loose 'pinch' of snuff. A pouch or a 'pinch' of snus is placed between the upper lip and gum. The amount of snus in a single 'pinch' is usually 1–2 g and the content of nicotine varies between 5 and 11 mg/g, with an extensive variation in the amount of un-ionized nicotine, which is positively correlated with the rate and speed of the trans-mucosal absorption of the nicotine (for a review, see Richter et al. [2]). The average daily exposure time of snus users in Sweden to snus is estimated to be 13 h [3,4].

Continuous exposure to high levels of nicotine is addictive [3] and, in addition, it contributes to a wide range of pharmacological effects on visceral and circulatory functions. Besides nicotine, snus contains >2000 identified chemicals, including carcinogenic tobacco-specific nitrosamines (TSNAs) [5]. Local oral lesions resulting from the use of snus have been demonstrated [3,6–8], as well as general effects such as increased risks of tumor development, cardiovascular disease, and diabetes [9–13]. The negative health consequences of snus use and the increased

Correspondence: Mats Wallström, Department of Oral and Maxillofacial Surgery, Institute of Odontology, Box 450, SE-405 30 Gothenburg, Sweden. Tel: +46 317863199. Fax: +46 31826091. E-mail: mats.wallstrom@odontologi.gu.se

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consumption of snus, especially among adolescents, make it necessary to promote snus cessation. There are few specially designed cessation programs for smokeless tobacco users available [14,15], especially those including nicotine replacement therapy (NRT) [16–19], although there are numerous published smoking-cessation programs [20–23]. A systematic review [24] concluded that interventions conducted by health professionals increase tobacco abstinence rates significantly.

The assistance of NRT has increased the success rate for educational and behavioral smoking cessation significantly, from 10% to 30% [25]. The long-term success rates of smoking-cessation programs normally do not exceed 30% [26]. Smokeless tobacco cessation without NRT has been reported to be successful in 18% of cases [27]. Adding nicotine gum at low doses for short periods resulted in no significant improvement in treatment outcome [17]. It is hypothesized that snuff-dippers with extensive tobacco use are highly nicotine-dependent [28], and generally have higher cotinine blood levels, due to their continuous exposure to tobacco [11,29], and that they have difficulty refraining from tobacco use.

The aim of the present study was to examine in a cohort study whether a 12-month cessation program for extensive snuff users could generate success levels comparable to those of established smoking-cessation programs. The program included a short motivational information-giving session with the unambiguous message that snus is harmful to health, a supply of NRT, a biopsy of the oral mucosa and a minor medical check-up.

Material and methods

Study population

A metropolitan newspaper advertisement and a questionnaire to visitors of a public health anti-tobacco exhibition were used to recruit smokeless tobacco users who were interested in smokeless tobacco cessation. Inclusion criteria were daily snus use of > 2 cans/week (>100 g snus) for ≥10 years, agreement to undergo an optional biopsy and the motivation to give up snus use throughout a 12-month clinical survey. Out of 280 responders, who were screened over the telephone, the first 50 subjects to fulfill the inclusion criteria were entered in the study. All the subjects used loose snus.

Exclusion criteria were ongoing habitual or occasional smoking. Before entering the study, all subjects were informed by telephone about the cessation program and then gave their oral consent to participation.

Study design

The study was designed as a prospective, open-label, non-randomized, interventional trial. All subjects were examined and reviewed by the same investigator (M. W.). A total of six visits were scheduled during a 1-year period (Table I). At the first visit (baseline), medical and tobacco histories were obtained, height and weight were recorded and blood pressure and heart rate were measured after a 5-min rest with the subject in a supine position. Subjects were

Table I. Investigations undergone by the study subjects over the 12-month study period.

	Visit					
	I	II	III	IV	V	VI
	Time					
	Baseline (quit day)	2 weeks	6 weeks	3 months	6 months	12 months
Medical history	x					
Tobacco history	x					
Oral examination	x	x	x	x	x	x
Visual/photographic examination	x	x	x	x	x	x
Biopsy	x				x	
Counseling	x	x	x	x	x	x
Weight	x		x	x	x	x
Height	x					
Blood pressure	x		x	x	x	x
Total cholesterol	x			x	x	x
Withdrawal symptoms	x	x	x	x	x	x
Salivary cotinine	x		x	x	x	x
Expired CO	x	x	x	x	x	x

x = data collection.

permitted to continue eventual ongoing medication. A 20×10 mm^2 biopsy was obtained from the oral snus lesion and sent for routine examination [3]. A venous blood sample was taken for serum cholesterol analysis. The day of the first visit was also designated the quit day and all subjects were recommended NRT (see below under *NRT medication*). Follow-up visits were made at 2 and 6 weeks and at 3, 6 and 12 months. At all visits, body weight was checked and a clinical examination of the oral mucosa at the site of application of the tobacco was done and pathological changes were recorded and photo-documented. Saliva samples were randomly collected for cotinine analysis.

Behavioral intervention

We used a single-cessation technique consisting of primary face-to-face counseling according to Kottke et al. [20], supplemented by medical examinations at five repeat visits and oral screening.

Motivational information was combined with the subjects' own inspection of the residual or former mucosal lesion. In addition, at all visits the participants were given brief information about the health benefits of tobacco cessation.

NRT medication

All subjects were recommended Nicorette® 4-mg chewing gum (10 pieces/day) for a maximum of 3 months. This was followed by an individual tapering period for 3 months when Nicorette 2-mg chewing gum use was recommended up to the 6-month visit. The instruction regarding the chewing method was to chew the gum until a slight tingling sensation was felt in the throat and then to place the gum under the upper lip, where the snus quid is normally placed. Withdrawal symptoms were registered by means of open questions at each visit [30].

Assessments

For biochemical verification of the patients' self-reported tobacco use, saliva cotinine and expired carbon monoxide were analyzed. Saliva samples (1 ml) were taken, frozen at -20°C and transported to Pfizer Health AB (Helsingborg, Sweden) in order to determine cotinine levels by gas chromatographic analysis. Cotinine is the major metabolite of nicotine frequently used to verify cessation compliance. Values exceeding >15 ng/ml were considered to indicate ongoing tobacco use [31]. To verify non-smoking status, a carbon monoxide (CO) analyzer (Bedfont Smokerlyzer; Technical Instruments Ltd, Rochester, UK) was used at all visits. A CO level <10 ppm was considered to indicate a non-smoker. The oral mucosa was examined to trace obvious signs of ongoing snus use by using the Axell classification [32].

Outcome measures

The following definitions were used:

- Success: Continuous, self-reported, complete abstinence from any tobacco use from the second visit until the endpoint at 12 months.
- Failure: Reported tobacco use or cotinine > 15 ng/ml or exhaled CO >10ppm or patients still using NRT at the 12-month visit or subjects lost to follow-up.

Ethics

The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Sahlgrenska University Hospital, Gothenburg, Sweden.

Statistics

The Mann–Whitney U-test was used to detect differences for non-paired data and the Wilcoxon signed-rank test was used for paired data. For correlation analyses, linear regression was used. All analyses were performed using the statistical software SPSS 12.0 (SPSS Inc, Chicago, IL). $P < 0.05$ was considered significant [33].

Results

Subjects

Forty-five of the 50 subjects who entered the study completed the program at the 12-month follow-up; 5 patients were lost to follow-up and were regarded as failures.

Table II shows mean values for medical and anthropometric data and tobacco use measurements. Snus had been used on average for more than two decades and for a maximum of 42 years. The number of hours per day spent using snus varied from 7 to 22.

Cessation outcome

All nicotine abstinence was randomly controlled during the study, except at 12 months where all subjects claiming abstinence were confirmed biochemically and clinically.

Table II. Anthropometric, medical and tobacco use measurements. Subjects lost to follow-up at the 12-month visit ($n = 5$) were excluded.

	Baseline	12 months
No. of subjects	50	45
Age (years)	42.2 ± 10.7	43.2 ± 10.7
Snuff duration (years)	20.8 ± 8.4	n.a.
Snuff duration (h)	15.2 ± 2.1	4.5 ± 6.2
Nicotine (mg/day)	280 ± 144	161 ± 68
BMI (kg/m^2)	25.0 ± 3.4	26.5 ± 3.4
SBP (mmHg)	128 ± 15	127 ± 11
DBP (mmHg)	83 ± 12	81 ± 10
HR (beats/min)	75 ± 11	70 ± 9
Total cholesterol (mmol/L)	5.0 ± 1.5	5.5 ± 1.5

n.a. = not available; SBP = systolic blood pressure; DBP = diastolic blood pressure; HR = heart rate.

Fifteen subjects (30%) were self-reported and biochemically verified as being snus- and NRT-free by the end of the study. At the 3-, 6- and 12-month visits, 58%, 46% and 30% of subjects, respectively were tobacco-abstinent. Table III shows the intervention outcome from the 2-week follow-up until the endpoint at 12 months.

NRT use and withdrawal symptoms

Compliance with pharmaceutical treatment was high, regardless of outcome. NRT was initially used as recommended by 30/41 subjects (73%) attending the visit at 2 weeks, as shown in Table IV. After 3 months, 21/39 subjects (54%) were using NRT. At 6 months after the 3-month tapering period, 12/38 subjects (32%) were still using NRT. At the end of the study, 7/45 subjects (16%) were using NRT. Of these seven subjects, four were tobacco-abstinent but still regarded as failures. Of those who were tobacco-abstinent, 59% were using NRT at the 3-month visit, 35% at the 6-month visit and 21% at the 12-month visit. No correlation was found between the amount of snus use before cessation and the amount of NRT use during the study. Reported side-effects resulting from gum use were hiccupping and gastrointestinal symptoms. Withdrawal symptoms, as registered by craving for snuff, was the predominant symptom. Craving for snuff among the abstinent subjects decreased over time but, by the end of the study, 20% of those in the success group were still subject to cravings.

Table III. Intervention outcome with continuous tobacco abstinence from Week 2 until the endpoint at 12 months.

Visit	Success[a]; *n* (%)	Failure; *n* (%)
6 weeks	31 (62)	19 (38)
3 months	29 (58)	21 (42)
6 months	23 (46)	27 (54)
12 months	15 (30)	35 (70)

[a]Verified with salivary cotinine ≤15 ng/ml and/or CO ≤10 ppm.

At the 12-month follow-up visit, the group of successful nicotine-free subjects and the group of relapsed snus users and/or NRT-using subjects were compared with regard to baseline and endpoint values (Table V). There were no significant differences in age, mean number of snus-using years or amount of daily snus use between the failure and success groups.

Although classified as failures, the failure group reduced their mean snus consumption by 38%, from an average of 5.1 to 3.2 cans/week at 12-month follow-up.

Weight and body mass index

Almost all subjects gained weight during the study: the success group participants gained on average 5.1 kg (minimum −4 kg; maximum +18 kg) and the failure group 2.4 kg (minimum −1 kg; maximum +7 kg). The body mass index (BMI) values in the success group were significantly higher at follow-up compared to baseline, as shown in Table V.

Medical measurements

The physical examination revealed normal blood pressure values (<140 mmHg systolic blood pressure, <85 mmHg diastolic blood pressure) in 88% of the subjects, both at baseline and follow-up. In 12% of the subjects, borderline or slightly hypertensive blood pressures were observed. At follow-up, there was a significant correlation ($P < 0.05$) between an increase in diastolic blood pressure and weight gain in the success group, whereas no significant increase in systolic blood pressure was registered.

Heart rate decreased from a mean of 80 beats/min at baseline to 69 beats/min at follow-up in the success group, although this was not significant. This difference extrapolated to a 24-h mean value corresponds to 10 000 fewer heartbeats in each subject. In the failure group a decrease in heart rate was also found (3 beats/min), but was less pronounced and also not significant.

Total serum cholesterol was measured twice: there was a significant increase in mean cholesterol values in the success group ($P < 0.05$) but not in the failure group. There was also a significant correlation between increase in body weight and cholesterol measurements in the success group ($P < 0.05$), but not in the failure group.

Table IV. Pharmaceutical treatment used during tapering period until endpoint.

Visit	No. attending the visit	NRT use for whole group; *n* (%)	Use of NRT (mg/day)		NRT use for non-tobacco users; *n* (%)
			Mean	Range	
Baseline	50				
2 weeks	41	30 (73)	19.0	6–60	24 (59)
6 weeks	38	25 (66)	17.9	4–60	23 (60)
3 months	39	21 (54)	11.6	2–48	17 (44)
6 months	38	12 (32)	7.3	4–40	8 (21)
12 months	45	7 (16)	16.9	2–40	4 (9)

Table V. Anthropometric, medical and tobacco use measurements in the success group (n = 15) compared to the failure group (n = 30). Subjects lost to follow-up at the 12-month visit (n = 5) were excluded.

	Baseline		12 months	
	Success	Failure	Success	Failure
Age (years)	42.2 ± 9.2	42.5 ± 11.6	43.2 ± 10.7	43.5 ± 11.6
Snuff duration (years)	21.9 ± 7.3	19.3 ± 10.4	21.9 ± 7.3	20.3 ± 10.4
Snuff duration (h)	14.3 ± 3.4	15.2 ± 1.1	0	12.2 ± 3.8
Nicotine (mg/day)	287 ± 176	272 ± 105	0	110 ± 122
BMI (kg/m^2)	24.8 ± 3.6	24.8 ± 2.9	26.6 ± 3.8	25.5 ± 2.7
SBP (mmHg)	126 ± 16	129 ± 15	126 ± 11	127 ± 12
DBP (mmHg)	85 ± 12	82 ± 12	82 ± 10	80 ± 11
HR (beats/min)	80 ± 8	73 ± 9	69 ± 11	70 ± 6
Total cholesterol (mmol/L)	4.9 ± 1.4	5.1 ± 1.2	5.9 ± 1.6	5.3 ± 1.5

SBP = systolic blood pressure; DBP = diastolic blood pressure; HR = heart rate.

Discussion

Treatment outcome

The aim of this study was to evaluate a smokeless tobacco-cessation program in a dental office setting, including both pharmacological and behavioral treatment and repeat follow-up visits over a 1-year period. The endpoint outcome after 1 year showed a success rate of 30%. Data from other smokeless tobacco-cessation studies, both behavioral and pharmacological, are usually limited to 3 or 6 months of follow-up. In the present study, after 3 and 6 months, 58% and 46% of subjects, respectively were abstinent. Ebbert et al. [19] showed similar figures in a smokeless tobacco-cessation trial in conjunction with a 4-mg sublingual nicotine tablet. After 3 and 6 months, 66% and 47% of subjects were abstinent (7-day point prevalences), respectively. Despite the lack of long-term results in previous studies, our 30% rate of prolonged abstinence (from 2 weeks until the endpoint), which was biochemically verified after 1 year, is promising. The results must however be interpreted with caution, as the study lacked control groups and had a relatively small sample size. There could be several reasons for the quite successful outcome, such as the selection of highly motivated subjects, the use of NRT, the individual counseling and the motivational feedback involving a soft tissue biopsy.

Nicotine replacement

Compliance with nicotine replacement use was relatively high. At the 2 weeks follow up with 73% of the study population were using NRT. The mean nicotine consumption (mg/day) during the first 6 weeks of this study was equivalent to the mean nicotine consumption among highly dependent smokers [Fagerström Test of Nicotine Dependence (FTND) score ≥7] in a smoking cessation study [34]. The use of adequate doses of NRT is considered to be of great importance to achieve abstinence in smokers [35]. Compared to 2-mg nicotine gum, 4-mg nicotine gum is effective in highly dependent smokers, is a well-documented and accepted treatment for smoking cessation and is usually recommended to smokers with an FTND score ≥7. Hatsukami et al. [17] published a

study on smokeless tobacco cessation in moderate-to-heavy users comparing the use of 2 mg of nicotine gum versus placebo in conjunction with behavioral treatment or minimal therapist contact and reported unexpectedly that patients assigned to nicotine gum experienced no better success than those assigned to placebo gum. It was concluded that the ineffectiveness of NRT was most probably attributable to the low dosage. Other reports have given the same disappointing conclusion when using the 2-mg nicotine gum [16]. Benowitz [36] showed that mean plasma nicotine concentrations resulting from snuff and cigarettes are approximately equivalent and this was confirmed by Holm [29] among Swedish snuff-dippers, with a small increase in nicotine plasma level in snuff users compared to smokers. However, although they have equivalent nicotine blood levels to smokers, snuff users consume higher total amounts of tobacco due to the continuous supply of tobacco for ≈15 h/day. Substitution with 4-mg nicotine gum in smokers theoretically corresponds to compensation for about two-thirds of the habitual blood nicotine level [37]. So far there have been few smokeless tobacco-cessation studies reporting a higher-dosage regime for nicotine replacement, as reviewed by Ebbert et al. [38].

In this study, the total exposure to nicotine from snuff dipping among the participants was extensive and all snuff-dippers were classified as 'heavy users'. On a pharmacological basis it seemed logical to compare snuff users with highly nicotine-dependent smokers and to recommend all subjects to use the 4-mg nicotine gum. The better long-term success in this study compared to earlier studies on smokeless tobacco cessation is most probably due to the fact that abstinent snuff users did benefit from a higher dose of NRT. The inclusion of a placebo and/or a low NRT dose group could have given information on whether or not the high nicotine content was of importance to the relatively successful outcome.

Intervention

Our intervention design with a face-to-face counseling recall program for reinforcement and relapse prevention has been shown to be effective in a meta-analysis of smoking-cessation programs by Kottke et al. [20]. Therefore, we adapted the method in the present study, using a single-cessation technique but supplemented by a biopsy, medical examinations at five repeat visits (weight, blood pressure, heart rate, cholesterol, oral screening and CO measurements) and random cotinine testing. Motivational information was combined with the subjects' own inspection of the former snuff lesion. The accumulated impression of the investigators was consistent with previous findings of Gordon et al. [39] indicating the effectiveness of repeated professional examinations and care to reinforce cessation success. However, this treatment design creates a time-consuming problem. Altogether, the investigator spent 3.5 h per subject for individual counseling and treatment. Furthermore, the importance of the biopsy taken on the quit day should not be ignored. Shortly following the mucosal biopsy the subjects suffered from moderate pain, swelling and irritating stitches, a discomfort that might have contributed to their readiness not to use tobacco.

The use of the nicotine gum seems important, not only for its delivery of nicotine, but also for the local tactile sensation on the oral mucosa. For some subjects, the feeling of having the gum under the lip, which resemble the feeling produced by a snus quid, seemed important. For others, active chewing of the nicotine gum as a form of oral distraction was crucial, a finding that has previously been reported to promote success [40]. Furthermore, Hjalmarsson et al. [41] reported that the form of nicotine delivery plays a marginal role. The important part was that the nicotine substitution was adequate. The plasma nicotine level of the chewing gum was of the same level as previously obtained with the sublingual tablet [34]. An alternative method of treatment in smokeless tobacco cessation worth studying is the effect of combining the nicotine patch and gum, since data from studies in smokers has shown promising results [42] and the sublingual tablet could also contribute to an increased efficacy of nicotine substitution, as reported previously [19].

Negative outcomes

A problem when designing a functional intervention program for snuff users is the high prevalence of former smokers and the tendency to mix smoking and smokeless tobacco use. Although habitual or occasional smoking was an exclusion criteria when entering the study, 10 subjects reported 'smoking' (eight 'occasional', two 'regular') in the failure group at follow-up. In the success group, craving for nicotine was still present in 20% of the subjects, confirming the strong addictive potential of nicotine. Long-term dependence on nicotine gum has previously been reported [26,43]. Findings in a multicenter intervention study by Murray et al. [44] involving 3094 participants with NRT showed 5% still using 2-mg nicotine gum after 4 years. This indicates that highly nicotine-dependent subjects might benefit from a treatment period longer than 6–12 months in order to achieve and maintain complete abstinence. In the failure group of the present study, 16% were still on NRT at 12 months follow-up, although not using tobacco, and would probably have a higher potential for final success with a more prolonged follow-up period. From a health perspective it is better to continue using pharmaceutical nicotine in

preference to snus or snuff products since the commercial products contain potentially dangerous chemicals such as TSNAs [45].

Smokeless tobacco users show a higher BMI than smokers, despite nicotine increasing metabolic rate, which is considered to contribute to smokers' lower BMI. After tobacco cessation, both smokers and smokeless tobacco users show weight gain, which seems to become more pronounced in smokeless tobacco users, as they start from a higher weight level. The significant increase in metabolic risk factors like serum cholesterol and systolic blood pressure found in this study might be due to this condition, but must be elucidated in studies including behavioral factors [46,47].

Primary prevention

The dental profession has the advantage of regularly meeting a major part of the tobacco-consuming population who are still without clinical symptoms of tobacco-related disease. The dental team provides unique resources to contribute to an improvement in public health by taking an active part in tobacco prevention and cessation assistance. This also signifies great potential to contribute to primary prevention of a large number of fatal and disabling diseases, a fact that should be considered as an important mission for the profession. The provision of knowledge and skills for basic tobacco-cessation treatment should be a compulsory part of the education of dental professionals. The utility for society in terms of cost-effectiveness demands further elucidation, as preventive efforts by the dental team are rarely compensated by the health security systems in most countries.

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