Adverse pregnancy outcomes in snuff users

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OBJECTIVE: The purpose of the study was to evaluate the effects of smokeless tobacco use during pregnancy.

STUDY DESIGN: We examined birth weight, preterm delivery, and preeclampsia in women who were delivered of singleton, live-born infants in Sweden from 1999 through 2000. For each snuff user, 10 cigarette smokers and 10 tobacco nonusers were selected randomly.

RESULTS: After exclusions, 789 snuff users, 11,240 smokers, and 11,495 nonusers remained. Compared with nonusers, adjusted mean birth weight was reduced in snuff users by 39 g (95% CI, 6-72 g) and in smokers by 190 g (95% CI, 178-202 g). Preterm delivery was increased in snuff users and smokers (adjusted odds ratios, 1.98 [95% CI, 1.46-2.68] and 1.57 [95% CI, 1.38-1.80], respectively). Preeclampsia was reduced in smokers (adjusted odds ratio, 0.63; 95% CI, 0.53-0.75) but increased in snuff users (adjusted odds ratio, 1.58; 95% CI, 1.09-2.27).

CONCLUSION: Snuff use was associated with increased risk of preterm delivery and preeclampsia. Snuff does not appear to be a safe alternative to cigarettes during pregnancy. (Am J Obstet Gynecol 2003;189:939-43.)

Key words: Smoking, snuff, fetal growth, preterm delivery, preeclampsia

Cigarette smoking during pregnancy is known to increase the risk of a number of adverse outcomes, such as fetal growth restriction, preterm delivery, placenta previa, and placental abruption.[1] Paradoxically, smoking also reduces the risk of preeclampsia.[2] Unlike smoking cigarettes, the use of smokeless tobacco does not result in exposure to products of combustion; and it has been suggested that the use of smokeless tobacco is safer than smoking.[3,4] The effect of smokeless tobacco use on pregnancy outcomes is unknown.

Sweden has the highest per capita consumption of oral moist snuff worldwide.[5] Swedish snuff is a moist, ground, oral tobacco product that is placed behind the upper lip. It is used regularly by approximately 20% of men and 2% of women and is becoming increasingly popular among adolescents and young adults.[6] We obtained data from the Swedish Birth Registry to compare outcomes for women who used snuff, smoked cigarettes, or used no tobacco products during pregnancy. We focused on the outcomes that have been shown consistently to be affected by cigarette smoking: fetal growth, preterm delivery, and preeclampsia.

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Material and methods

Study design. In Sweden, data from all hospital births, including maternal demographics, tobacco use, reproductive history, complications of pregnancy and delivery, infant sex and birth weight, and gestational age at delivery are collected prospectively and recorded in a register. Information on current tobacco use and tobacco use during the 3 months before pregnancy is obtained by midwives at the woman's first antenatal visit, which occurs before 15 weeks of gestation in 95% of women. Data are recorded by means of check boxes: does not smoke daily, smokes 1 to 9 cigarettes each day, or smokes ≥10 cigarettes each day; does not use snuff daily, or uses snuff daily. Information on tobacco use is collected again in late pregnancy (32-34 weeks of gestation). Data on current tobacco use at the first antenatal visit are available in approximately 95% of deliveries, during the 3 months before pregnancy in approximately 70% of deliveries, and during late pregnancy in approximately 40% of deliveries.

Sweden-born women who were delivered of singleton infants during 1999 and 2000, the years for which snuff exposure data were available, were eligible for inclusion in our analysis. Information on current tobacco use at the time of the first antenatal visit was used to select exposure groups. We selected all snuff users (n = 1322 women); for each snuff user, we randomly selected 10 cigarette smokers and 10 women who used neither product (nonusers). We then excluded from all groups mothers whose infants were stillborn (n = 103 women), had major

congenital malformations (n = 729 women), or for whom gestational age or birth weight were missing (n = 118 women) or implausible (n = 3 women).

We used information on tobacco exposure in late pregnancy, when available, to exclude women whose tobacco exposure status had changed between enrollment into prenatal care and late pregnancy: women who were nonusers at the first antenatal visit but who used snuff or smoked cigarettes in late pregnancy (n = 81 women); women who used snuff or smoked cigarettes at the first antenatal visit but who had quit by late pregnancy (n = 1846 women); and women who, in late pregnancy, had changed from snuff to cigarettes or vice versa (n = 44 women). We also used data on tobacco exposure in the 3 months before pregnancy to exclude from nonusers women who had used tobacco during the 3 months before pregnancy (n = 1132 women), because these women may have been exposed after becoming pregnant. The following groups of women remained for analysis: (1) snuff users (n = 789 women); (2) smokers (n = 11,240 women); and (3) tobacco nonusers (n = 11,495 women). Combined users (those who used snuff and smoked cigarettes at the first antenatal visit [n = 67 women]) were excluded from further analysis because of small numbers. Smokers were divided into light (1-9 cigarettes/d) and moderate-to-heavy users (≥10 cigarettes/d). Information on frequency of use was not available for snuff users.

Preterm birth was defined as delivery at < 37 completed weeks of gestation. Small for gestational age was defined as a birth weight of >2 SD below the mean birth weight for gestational age according to the gender-specific Swedish fetal growth curves.[7] In Sweden, gestational age is assessed by ultrasound scans in >95% of women, usually around the week 17 of gestation.[8] Women with preeclampsia were identified with the use of hospital discharge ICD-10 codes. Preeclampsia in the Swedish version of ICD-10 is defined as ≥1 diastolic blood pressure measurement of at least 90 mm Hg, combined with proteinuria (at least 0.3 g/d or 1+ on a urine dipstick). Eclampsia is defined as preeclampsia with general convulsions. In our study, preeclampsia was determined by the presence of any discharge ICD-10 codes for preeclampsia or eclampsia (any O14 or O15 codes) without accompanying ICD-10 codes for underlying hypertensive disease (any O10 or O11 codes). Previous validation studies have demonstrated that the quality of preeclampsia reporting appears to be accurate in the Swedish Birth Registry.[9]

Statistical analysis. Baseline factors and outcomes among different tobacco exposure groups were compared using *t* tests for continuous variables and chi-squared tests for categoric variables. Analysis of covariance was used to generate adjusted mean birth weights and 95% CIs for women in each of the tobacco exposure groups. Logistic regression was used to compute adjusted odds ratios and 95% CIs for associations between tobacco use and small-for-gestational-age birth, preterm delivery, and preeclampsia. Adjustment factors that were considered were gestational age at delivery (birth weight only), infant sex (birth weight and preterm delivery), maternal age, height, body mass index, and parity and whether the mother was living with a partner (birth weight, small-for-gestational-age birth, preterm delivery, and preeclampsia). The effect of parity on the relationships between tobacco exposure and preeclampsia and preterm delivery was evaluated by stratification into nulliparous and multiparous groups. Living with a partner, an indicator of socioeconomic status,[10] was not associated with any of the outcomes of interest and was dropped from final models; all other variables were included as described. Information on alcohol and illicit drug use, which may be associated with adverse pregnancy outcomes, was not available in the database.

Because late-pregnancy tobacco exposure data were not available for all women and we could not exclude with certainty all quitters from our exposure groups, we repeated the analysis of birth weight after restricting the study population to women whose late-pregnancy tobacco exposure status was known. We did not report the effects of tobacco on preterm delivery or preeclampsia in this restricted population because a disproportionate number of women with preterm deliveries were missing late pregnancy exposure data.

Permission to perform the study was granted by the National Board of Health and Welfare, Sweden, and by the ethics committee at the Karolinska Institutet. This study was determined to be exempt from institutional review board review at the National Institutes of Health.

Results

Baseline characteristics of study subjects differed by tobacco exposure status. Compared with nonusers, both snuff users and smokers were less likely to be living with a partner, were shorter, and had a greater body mass index. Smokers were also younger and more likely to be multiparous (Table I).

Compared with nonusers, adjusted mean birth weight was reduced in snuff users by 40 g (95% CI, 6-72 g), in light smokers by 172 g (95% CI, 158-185 g), and in moderate-to-heavy smokers by 224 g (95% CI, 207-240 g; Table II). After the study population was restricted to women whose late-pregnancy tobacco exposure was known, the adjusted mean birth weight was reduced in snuff users (n = 268 women) by 93 g (95% CI, 38-147 g), in light smokers (n = 2821 women) by 213 g (95% CI, 193-234 g), and in moderate-to-heavy smokers (n = 1638 women) by 250 g (95% CI, 225-275 g).

Smoking was associated significantly with small-for-gestational-age birth, and risk increased as the number of cigarettes smoked per day increased. Snuff use, however, was not associated significantly with small-for-gestational-

Table I. Characteristics of study population by tobacco exposure status

Maternal and infant characteristics	*Nonusers (n = 11,495)**	*Snuff users (n = 789)*	*Smokers (n = 11,240)*
Age (y)†	29.9 ± 4.6	30.0 ± 4.8	28.5 ± 5.8‡
Height (cm)†	167.2 ± 5.9	165.9 ± 6.2‡	166.3 ± 6.0‡
Body mass index (kg/m^2)†	24.2 ± 4.1	24.7 ± 4.7§	24.8 ± 4.7‡
Parity > 1 (n)	6649 (58%)	456 (58%)	6818 (61%)‡
Not living with partner (n)	283 (3%)	45 (6%)‡	1683 (15%)‡
Infant sex male (n)	5931 (52%)	411 (52%)	5782 (51%)

Unknown data were excluded when calculating percentages.
*Reference group.
†Data are given as mean ± SD.
‡$P \leq .0001$.
§$P < .01$.

Table II. Birth weight by tobacco exposure status

Tobacco exposure status	*Mean birth weight**	*Difference in mean birth weight†*	*Adjusted mean birth weight‡*	*Difference in adjusted mean birth weight†*
Nonuser (n = 11,495)	3635 (544)	Reference	3597 (4.2)	Reference
Snuff user (n = 789)	3529 (569)	106 (65-146)	3557 (16.3)	39 (6-72)
Cigarette smoker (n = 11,240)	3410 (571)	224 (210-239)	3407 (4.4)	190 (178-202)
1-9 cigarettes/d (n = 7375)	3428 (569)	206 (190-223)	3425 (5.3)	172 (158-185)
≥10 cigarettes/d (n = 3865)	3376 (573)	258 (239-279)	3372 (7.4)	224 (207-240)

*Data are given as grams (SD).
†Mean birth weight of nonuser minus mean birth weight of snuff user or cigarette smoker; data given as grams (95% CI).
‡Adjusted for maternal age, parity, body mass index, height gestational age at delivery, and infant sex; the adjusted analysis includes women with complete data on covariates (10,318 nonusers, 677 snuff users, and 9947 cigarette smokers). Data are given as grams (SE).

age birth (Table III). Both snuff use and cigarette smoking were associated with preterm delivery. Compared with nonusers, snuff users (after the adjustment) had a 2-fold increased risk of preterm delivery; smokers had a 60% increased risk. The elevated risk of preterm delivery in snuff users was not significantly different from that of smokers.

Compared with nonuser risk of preeclampsia in nonusers, the risk of preeclampsia was reduced in smokers; snuff users had a nearly 60% increased risk (Table III). The relationships of snuff and cigarettes to preeclampsia and preterm delivery were unchanged after stratification by parity (data not shown), which suggests that an adverse obstetric history was not an important confounder in our analyses.

To determine whether the effects of snuff use on the risk of preeclampsia could account for the excess risk of preterm delivery that is observed in snuff users, we evaluated the association between tobacco exposure and preterm delivery after excluding women with preeclampsia. The association between snuff use and preterm delivery was attenuated slightly but similar in magnitude to that seen with moderate-to-heavy smoking (Table IV).

Comment

In this population-based cohort of women, we found that both cigarette smoking and snuff use in pregnancy adversely affected fetal growth and that the effects of smoking were more pronounced. Smoking and snuff use increased preterm delivery risk to a similar extent. Although smoking was protective, snuff use significantly increased risk of preeclampsia.

Because the use of smokeless tobacco does not result in exposure to products of combustion, snuff is considered to be generally less harmful than cigarettes. Compared with cigarette smoking, snuff use appears to have less effect on atherosclerosis,[11] risk of myocardial infarction,[12] and risk of death from cardiovascular disease.[13] The effects of smokeless tobacco on pregnancy outcomes, however, are unclear. Krishna[14] reported a 100- to 200-g reduction in birth weight and an excess of preterm deliveries among Indian women who used chewing tobacco during pregnancy compared with nonusers. Krishnamurthy and Joshi[15] reported a 3-fold increase in low birth weight among Indian women who used mishri, a burnt chewing tobacco. These studies were small and did not include comparisons to cigarette smokers, and the authors were unable to determine if effects on birth weight were independent of effects on length of gestation or to control fully for potential confounders. In the current study, population-based data were used to compare the effects of snuff use and smoking on fetal growth, preterm delivery, and preeclampsia while controlling for a variety of factors.

It has been hypothesized that smoking results in adverse outcomes such as fetal growth restriction as a result of carbon monoxide-mediated tissue hypoxia, nicotine-in-

Table III. Small-for-gestational-age birth, preterm delivery, and preeclampsia status by tobacco exposure status

	Small-for-gestational-age birth		*Preterm delivery*		*Preeclampsia*	
Tobacco exposure status	*N (%)*	*Adjusted odds ratio (95% CI)**	*N (%)*	*Adjusted odds ratio (95% CI)**	*N (%)*	*Adjusted odds ratio (95% CI)**
Nonuser (n = 11,495)	179 (1.6)	Reference	453 (3.9)	Reference	343 (3.0)	Reference
Snuff user (n = 789)	17 (2.2)	1.25 (0.72-2.17)	59 (7.5)†	1. 98 (1.46-2.68)	37 (4.7)‡	1.58 (1.09-2.27)
Cigarette smoker (n = 11,240)	475 (4.2)†	2.99 (2.48-3.61)	666 (5.9)†	1.57 (1.38-1.80)	234 (2.1)†	0.63 (0.53-0.75)
1-9 cigarettes/d (n = 7375)	298 (4.1)†	2.75 (2.24-3.36)	416 (5.6)†	1.50 (1.30-1.74)	169 (2.3)‡	0.71 (0.59-0.88)
≥10 cigarettes/d (n = 3865)	177 (4.6)†	3.50 (2.79-4.39)	250 (6.5)†	1.71 (1.44, 2.04)	65 (1.7)‡	0.48 (0.36-0.64)

*Adjusted for maternal age, body mass index, height, (small-for-gestational-age birth, preterm delivery, and preeclampsia), parity (small-for-gestational-age birth and preterm delivery), and infant sex (preterm delivery); the adjusted analysis includes women with complete data on covariates (10,318 nonusers, 677 snuff users, and 9947 cigarette smokers). An additional 36 births were excluded from analysis of small-for gestational-age birth because of missing small-for-gestational age status.
†$P < .0001$.
‡$P < .01$.

Table IV. Percent of women and adjusted odds ratio for preterm delivery by tobacco exposure status after the exclusion of the women the preeclampsia

Tobacco status	*Preterm delivery*	*Adjusted odds ratio* (95% CI)*
Nonuser (n = 11,152)	388 (3.5%)	Reference
Snuff user (n = 752)	46 (6.1%)†	1.79 (1.27-2.52)
Cigarette smoker (n = 11,006)	602 (5.5%)‡	1.66 (1.44-1.91)
1-9 cigarettes/d (n = 7206)	368 (5.1%)‡	1.56 (1.33-1.83)
≥10 cigarettes/d (n = 3800)	234 (6.2%)‡	1.84 (1.53-2.21)

*Adjusted for maternal age, body mass index, height, infant sex and parity; the adjusted analysis includes women with complete data on covariates (10,006 nonusers, 643 snuff users, and 9737 cigarette smokers).
†$P < .001$, reference is nonusers.
‡$P < .0001$, reference is nonusers.

duced vasoconstriction, or both.[16] Our finding that snuff use was associated with a more modest reduction in gestation-adjusted birth weight than was cigarette smoking suggests that carbon monoxide plays a more prominent role than nicotine in fetal growth restriction among smokers. However, snuff users likely have lower exposure than smokers to a variety of potentially harmful compounds besides carbon monoxide (such as polycyclic aromatic hydrocarbons), which makes it difficult to implicate a particular agent in tobacco-related fetal growth restriction. In addition, although studies in nonpregnant populations have demonstrated that snuff users and cigarette smokers have similar levels of nicotine exposure,[17,18] comparable studies in pregnant Swedish women have not been conducted. Therefore, we cannot be certain that differences in nicotine dose did not contribute to the discrepancies in birth weight that we observed between smokers and snuff users. Finally, there may have been unidentified quitters in the tobacco-exposed groups in our study, which would result potentially in a differential underestimation of the effects of snuff use and smoking on birth weight. After restriction of the analysis to women with late pregnancy exposure data, however, the effect of snuff use on birth weight was still less than that observed from smoking.

In our study, both smoking and snuff use were associated with an elevated risk of preterm delivery. Snuff users were also at increased risk of preeclampsia, which often results in preterm delivery. After the analysis was restricted to women without preeclampsia, the risk of preterm delivery in snuff users persisted and was comparable to that of moderate-to-heavy smokers. This implies that a component that is common to both cigarettes and snuff, such as nicotine, may play a role in tobacco-related preterm deliveries.

The protective effect of smoking against preeclampsia has been well documented,[2] although the mechanism is unknown. Our finding that snuff users were at increased risk for preeclampsia and that smokers were protected raises the possibility that the protective factor that is found in cigarette smoke is a product of combustion rather than nicotine. In the absence of this protective factor, nicotine could raise the preeclampsia risk through effects on the cardiovascular system, such as by causing endothelial dysfunction or raising blood pressure. Alternatively, additives in snuff could act to increase risk. For example, sodium and licorice, both of which can elevate blood pressure, can be found in Swedish snuff. However, most brands of Swedish snuff do not contain licorice; and salt restriction has not been found to prevent preeclampsia.[19] It is doubtful therefore that these additives caused the increase in preeclampsia that was observed in this study.

In summary, both cigarette smoking and snuff use were associated with restricted fetal growth and increased the risk of preterm delivery. Unlike smoking, snuff use was also associated with increased risk of preeclampsia. Pregnant women who smoke should not be encouraged to switch to smokeless tobacco. Complete cessation is the only certain way for tobacco users to reduce their risk of adverse pregnancy outcomes.

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