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Nicotine exposure in breastfed infants

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Aim: To study exposure to nicotine in breastfed infants in relation to parental smoking habits. *Material and Methods:* Forty mother–infant pairs were studied. Twenty non-smoking mothers, 18 smoking (2–20 cigarettes per day) and two snuff-taking mothers were included. All infants were healthy, exclusively breastfed and their postnatal age was 6 wk. During a home visit, parental smoking habits were recorded, and the time of mothers' last smoke or taking of snuff and breastfeeding were recorded. Breast milk and infant urine samples were collected. Concentrations of nicotine and cotinine were analysed with gas chromatography. The amount of milk ingested during the home visit was calculated by weighing the infants. *Results:* Two non-smoking and non-snuff-taking women had milk containing nicotine (28 and 13 μg/l, respectively). Both had smoking spouses. In the smoking and snuff-taking group, the mean (SD) milk nicotine concentration was 44 (38) μg/l ($n = 36$). When milk samples taken 7 h and 0.6 h after smoking were compared, the concentration of milk nicotine increased from 21 to 51 μg/l ($p < 0.01$). The two snuff-taking mothers exposed their children to higher milk nicotine concentrations than all but two of the smokers. The concentrations of the metabolite cotinine in infant urine correlated with the dose of nicotine ingested during the home visit ($r = 0.84$, $p < 0.01$).

Conclusions: Breastfed infants with a smoking or snuff-taking mother are exposed to nicotine in breast milk. The mean intake of nicotine via milk is 7 μg/kg/d. With a shorter time between the mothers' smoking and breastfeeding, the milk nicotine concentration will increase. Both passive smoking at home and snuff-taking were associated with measurable nicotine levels in milk. Healthcare personnel promoting breastfeeding should be aware of these factors influencing exposure to nicotine in the breastfed infant.

Key words: *Breastfeeding, infant, nicotine, parental smoking, snuff-taking*

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In spite of increased knowledge of the adverse effects of nicotine on the foetus and the newborn child (1, 2), 13% of pregnant Swedish women smoke daily and 10% smoke during the lactation period (3). Nicotine exposure early in life may have implications for health and development.

A possible damaging effect on the brain has been suggested by Slotkin and co-workers who, in animal models, have shown that nicotine in doses of 2–6 mg/kg/d causes cell injury in the foetal rat brain (4). Nicotine induced deficits in brainstem M2-receptor in newborn rats were restricted to males (5). We have previously studied some effects of prenatal exposure to cigarette smoking on the autonomous nervous system (ANS). Smoking in mothers of term boys seemed to influence heart rate variability during the first week of life (6). This could reflect a prenatal effect of smoke on the sympathovagal balance in the ANS in the male foetus.

The neuroactive substance nicotine accumulates in breast milk. We have previously found a mean nicotine milk-to-plasma ratio of 2.9 (1.8–4.2) in lactating women 30 min after smoking one cigarette (7). Luck et al. (8) also found a breast milk nicotine concentration of three times that in the blood.

There are many benefits of breastfeeding (9, 10), but when the breastfeeding mother smokes, the situation becomes more complex. Klonoff and co-workers (11) reported that breastfeeding was protective against sudden infant death syndrome (SIDS) among maternal non-smokers (OR 0.37; 95% CI: 0.19–0.72) but not among smokers (OR 1.38; 95% CI: 0.16–12.03).

There is clear evidence that maternal smoking affects the foetus and the newborn. However, it is not clear to what extent the effects can be attributed to postnatal exposure after the immediate neonatal period. We hypothesized that breastfed infants of smoking mothers are exposed to higher doses of nicotine after the neonatal period. The aim of this study was to examine the exposure to nicotine via breast milk in healthy infants, after the neonatal period and in relation to parental smoking habits. Cotinine, the main metabolite

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of nicotine (8) without any known pharmacological effect (12), was also analysed.

Subjects and methods

Subjects

Forty-four healthy infants and their mothers were recruited from child health centres (CHC) for the study. After written information, given to smoking mothers and controls by the CHC nurses, the 44 families were contacted and all gave their consent to participate. Three families decided to withdraw after giving their initial consent, and one child was excluded due to fever on the study day. Thus, 40 infant/mother dyads were examined. Eighteen of the mothers were daily smokers of cigarettes, with smoking habits of 2–20 cigarettes per day, two mothers were taking snuff and 20 mothers were non-smoking/snuff-taking.

All infants were exclusively breastfed, and no mother was on any medication. Five of the 20 non-smoking mothers and 8 of the 18 smoking mothers had smoking spouses (Table 1). The two snuff-taking mothers had non-smoking spouses.

Method

To record the environment of each child and the parents' snuff-taking or smoking habits, and to minimize disturbance of the breastfeeding routines, the studies were conducted in the homes when the children were around 6 wk old. A nurse (CE) and a paediatrician (AD) made a home visit between 09.00 and 13.00 in all cases. The procedural protocol included the timing of breast-feeding and the mothers' smoking and/or snuff-taking habits before and during the visit and our milk sampling times.

Smoking mothers were asked not to smoke during the last 6 h before our visit, and a sample of the smoking mother's milk was collected at the beginning of the home visit. Another milk sample was collected in the middle of the first breastfeed after smoking. Only one milk sample was collected from the non-smoking mothers. A urine sample was collected from each infant with a baby urine collector (COLOPLAST®), carried by the infant during the entire home visit period. To measure the amount of breast milk ingested during our visit, the weight of the child was checked at the beginning and end of the visit, and the total weight gain, including weight gain of disposed diapers, was recorded.

Milk and urine samples were stored at −20°C until analysed. The concentration of nicotine and its main metabolite, cotinine, was determined by gas chromatography, by the method of Curvall et al. (13). The sensitivity of the assay of nicotine and cotinine was 0.1 μg/l in plasma and urine and 1 μg/l in milk. Due to the high lipid content of milk, a re-extraction step was used, as described in our previous report (7).

The taking of snuff exposes the user to nicotine and, consequently, we combined the two snuff-taking mothers with the smokers in our analysis.

Statistical analysis

Student's *t*-test for independent values was used for comparisons between the smoking and non-smoking groups regarding the infants' gestational age, postnatal age, birthweight and weight gain. Wilcoxon's matched pairs test was used to compare the nicotine concentrations in milk samples taken before and after smoking. Correlations were tested by multiple regression. The level of significance was $p < 0.05$. Statistical calculations were performed using the statistical software package Statistica (StatSoft, Tulsa, OK, USA).

The study was approved by the local ethics committee.

Results

There were no differences between the two groups with regard to gestational age, postnatal age, birthweight or gender. Maternal smoking or snuff-taking did not influence postnatal weight gain from birth to the age when the infant was examined ($p = 0.28$) (Table 1).

Table 1. Material. Characteristics of infants, grouped according to maternal smoking/snuff-taking habits (mean values and range).

	Mothers		
	Non-smoking	Smoking or snuff-taking	
		<10 cig./day	> = 10 cig./day or snuff-taking
Number of mother/infant dyads	n = 20	n = 11	n = 9
Number with smoking spouses	5	5	3
Infant characteristics			
GA (weeks)	40.1 (37–42)	39.6 (37–42)	39.2 (38–40)
Postnatal age (weeks)	6.4 (4–10)	5.9 (5–7)	6.7 (5–9)
Birth Weight (g)	3634 (3000–4185)	3458 (2370–4925)	3462 (2885–4115)
Birth Length (cm)	50 (47–54)	49 (47–52)	49 (46–54)
Male/Female(number)	7/13	7/4	4/5
Weight at study (g)	5075 (4045–6360)	4999 (3500–6670)	5025 (3716–6975)
Weight gain/week(g)	235 (116–374)	264 (186–477)	230 (145–297)

Table 2. Nicotine and cotinine concentrations in breast milk from smoking or snuff-taking and non- smoking mothers and in infants' urine (median and range).

	Mother			Infant	
	Non-smokers	Smoke and snuff group		Non-smokers	Smoke and snuff group
	Breast milk	Breast milk 1	Breast milk 2	Urine	Urine
Number of samples	19	18	18	18	18
Time from last nicotine exposure (mean hours)		6.9 (0.8–17)	0.6 (0.1–1.5)		
Number of samples w/o* nicotine	2/17	17/1	18/0	4/14	9/9
Nicotine (μg/L)	0 (0–28)	21 (0–81)	51 (8–192)	0 (0–1.8)	0.7 (0–6.1)
Number of samples w/o* cotinine	1/18	18/0	18/0	13/5	18/0
Cotinine (μg/L)	0 (0–0.9)	325 (39–1397)	233 (95–1265)	0.8 (0–5.2)	61 (17–297)

*with/without.

Nicotine concentrations in milk are presented in Table 2. The mean nicotine concentration in all 36 milk samples from smoking or snuff-taking mothers was 44 μg/l. Two non-smoking women had milk containing nicotine (28 and 13 μg/l, respectively). Both had smoking spouses. The non-smoking woman with the highest milk nicotine concentration had a spouse who was a heavy smoker (>20 cigarettes/d), and the other non-smoking woman with nicotine in her milk had a spouse who smoked 10 cigarettes/d.

The time between smoking or snuff-taking and breastfeeding influenced the concentration of milk nicotine. The median milk nicotine concentration increased 2.4 times from 21 to 51 μg/l ($p < 0.01$) when the time between smoking/snuff-taking and milk sampling decreased from 7 to 0.6 h (Table 2).

Comparing smoking with the taking of snuff, we found that the smokers had a nicotine concentration of 23 (0–80) μg/l (mean and range) in the first milk sample and the two snuff-takers 57 and 47 μg/l. The time from nicotine exposure to milk sampling was 7.2 (0.75–17) h for the smokers and 0.75 and 7.5 h for the two snuff-takers. In the second milk sample, the smokers had nicotine concentrations of 57 (8–192) μg/l and the two snuff-takers 99 and 89 μg/l, and the time span was 0.6 (0.1–1.5), 0.3 and 0.4 h, respectively. Fig. 1 shows nicotine concentrations plotted in relation to the time between smoking/snuff-taking and milk sampling in paired milk samples from nine smoking and two snuff-taking mothers.

The concentrations of nicotine and cotinine in the infants' urine are presented in Table 2. In the smoke and

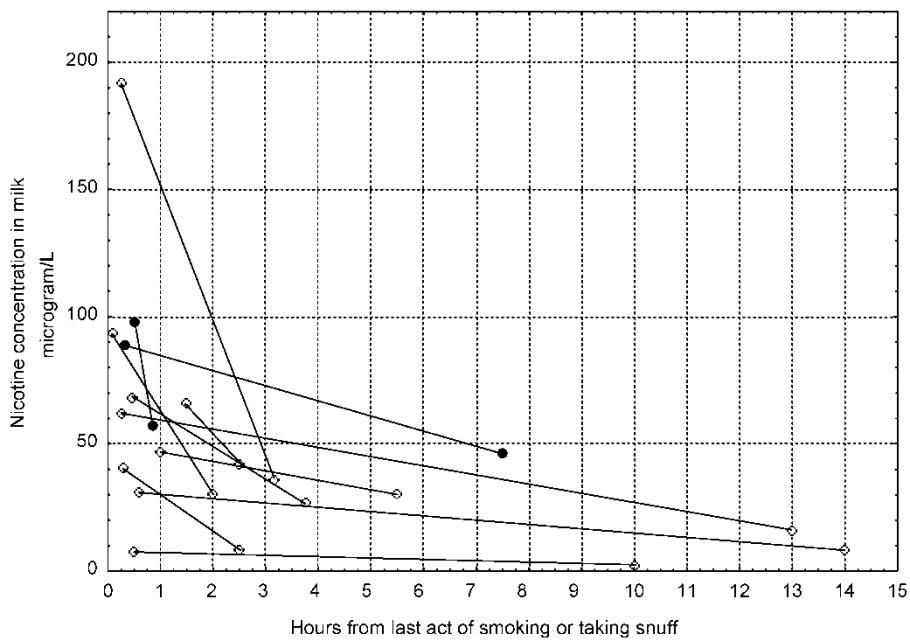

Fig. 1. The effect of the time interval between smoking (○) or snuff-taking (●) and breastfeeding. Nicotine concentrations in milk are plotted against short and long time intervals for 11 individuals.

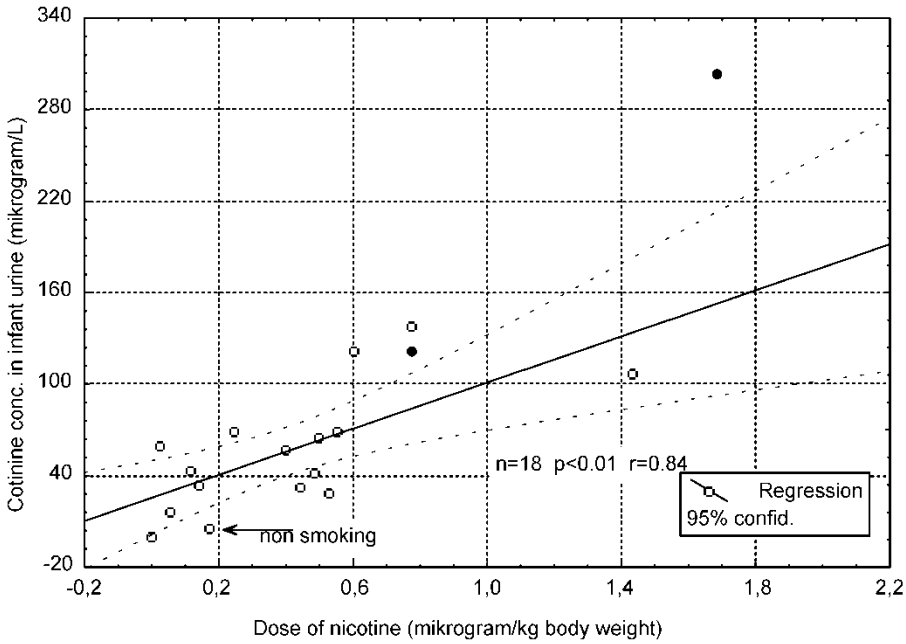

Fig. 2. Cotinine concentrations in infants' urine versus nicotine dose (μg/kg) in breast milk from 15 smoking mothers (○), two snuff-taking mothers (●) and one non-smoking mother (⟶).

snuff-taking group, half of the infants had measurable concentrations of nicotine and all had cotinine in their urine. Among the non-smokers, four out of 18 infants had nicotine, and 13 of 18 had cotinine in urine. The low concentrations found in the non-smoking group could be explained by the normal maternal dietary exposure to nicotine (14), except for the child with the highest urine cotinine value (5.2 μg/l), with a heavy smoking father, already mentioned.

The dose of nicotine to which each child was exposed, during our home visit, was calculated from the amount of breast milk fed to the child, the milk nicotine concentration and the infant's bodyweight. The dose of nicotine correlated with the concentration of cotinine in the infants' urine ($r = 0.84$, $p < 0.01$) (Fig. 2). One extreme value is explained by the combination of a snuff-taking mother with a high milk nicotine concentration (89 μg/l) and a child fed the largest amount of milk (130 ml) in the smoking group during the study hours.

To evaluate the mothers' reports of smoking habits, we tested the correlation between the reported daily consumption of cigarettes and cotinine concentrations in breast milk and found a significant correlation ($r = 0.6$, $p < 0.05$).

Discussion

Today, nearly all Swedish women start out breastfeeding their newborn child. In Stockholm, 73% of all infants are exclusively breastfed at 4 mo of age (15). Due to parental smoking, every fifth child in Stockholm lives in a household with cigarette smoke (15). Furthermore, there is also an unknown number of lactating women who expose their children to nicotine from snuff or the use of nicotine replacement drugs (NRDs). Since 1999, there has been central registration of both smoking and snuff-taking habits among Swedish women before and during pregnancy. Preliminary data show a snuff-taking frequency of 1–2% among pregnant women, but due to a lack of information in 60%, the true frequency may be larger (16).

We chose to examine healthy infants after the neonatal period at a postnatal age of 6 wk, when most babies are exclusively breastfed, have a rapid weight gain and the exposure to breast milk nicotine should be maximal. All infants were considered healthy at the CHC examination, and we did not include individuals with risk factors connected with maternal smoking during pregnancy, such as prematurity and intrauterine growth retardation. We have not found any reports about snuff-taking and breastfeeding in the literature, and decided to include the two snuff-taking mothers and their infants in the smoking group.

By visiting all families at home, we believe we recorded as valid information as possible about the parents' smoking habits and about the environment for the child. We also wanted to disturb breastfeeding routines as little as possible.

There is a close correlation ($r = 0.99$) between cotinine concentrations in milk and plasma (7). In the

present study, we found a significant correlation between maternal smoking habits and milk cotinine concentrations, which supports the notion that the mothers' own reports of the number of cigarettes smoked daily were reliable.

Our instructions to the mothers to refrain from smoking 6 h before our home visit were not always followed. It was our intention that the first milk sample should represent a non-smoking period of at least 6 h. Some of the women did not refrain from smoking during the morning hours before our visit. Consequently, the first milk samples cannot be used as smoke-free morning reference samples.

Other limitations in our report are that we only studied part of a day and do not know how milk quality, infants' eating habits or mothers' smoking habits vary throughout the day and how it could effect infants' intake of nicotine. Neither did we register how mothers inhaled when smoking, nor variations in milk nicotine during breastfeeding. Our information is based on self-reports in both the smoking and snuff-taking and non-smoking groups.

There were significant differences in milk nicotine concentrations depending on the time between smoking and sampling (Fig. 1). This is in agreement with our earlier report, with a tenfold increase in milk nicotine when mothers smoked 30 min before sampling compared to 12 h before (7). Differences in milk nicotine concentrations can also depend on variations in the milk-to-plasma ratio, possibly due to differences in milk pH (7).

Stephan and Wilkerson (17) found a mean milk nicotine concentration of 33 μg/l (range 0–93) in the milk of five smoking women. Smoking habits comprised 10–20 cigarettes per day, but the time between smoking and milk sampling was not stated. In our study, the mean milk nicotine concentration in all 36 samples (before and after smoking) was 44 μg/l, but with a wide range from 0 to 192 μg/l, representing at least 12 h of smoke-free milk production to very frequent and recent smoking.

Steldinger et al. (18) found, in repeated milk and blood samples from nine smoking mothers, the half-life of nicotine in milk to be 95 min and in plasma 80 min. Oscarson and co-workers (19) report that 1% of the Swedish, Finnish and Spanish populations are slow metabolizers of nicotine due to a lack of the enzyme CYP2A6. The smoking mother with the highest milk nicotine concentration of all (192 μg/l) reported smoking 15 cigarettes per day and might represent this group. Her milk cotinine concentration supported her reported smoking habits. Accordingly, a small group of women may expose their infants to considerably higher amounts of nicotine.

Our study allows estimations of the daily oral dose of nicotine for the infants with a smoking or snuff-taking mother. An infant consuming 150 ml milk/kg/d (20), containing an average nicotine concentration of 44 μg/l, will be exposed to a daily dose of 7 μg/kg. A 70-kg person smoking one Swedish Light® cigarette (with a machine tested delivery of 0.7 mg of nicotine) per day will be exposed to the same relative dose. Between 29 and 92% of the nicotine is absorbed when smoking (21), but, to our knowledge, there are no reports on how infants absorb nicotine from the gastrointestinal tract or how infants absorb passive smoke, and first pass metabolism of nicotine in infants is not known. The finding that half of the infants in the maternal smoking group passed urine with measurable amounts of nicotine suggests that the babies have absorbed nicotine during its passage through the gastrointestinal tract. The smoking group infants without nicotine in their urine have probably metabolized it to a larger extent.

Cotinine in the urine is an indicator of active or passive smoking. We found a close correlation between the oral dose of nicotine and the urinary cotinine concentrations in our 3-h sampling model. In the breastfeeding infants, cotinine in the urine also represents cotinine ingested via the smoking mothers' milk (22). The very low concentrations of cotinine in the non-smoking group could represent maternal exposure to dietary nicotine (14), but there is conflicting information about how much dietary nicotine can contribute (23).

Passive smoking is of concern for most parents, who are aware of the risk of exposing their infant to side-stream smoke and will not smoke in the same room as their child. In our study, we found two non-smoking/non-snuff-taking women with nicotine in their breast milk. Provided that the information we have is correct, we believe this is the first report in which a non-smoking woman, exposed to passive smoking at home, has fed her child milk containing nicotine. These two infants passed urine with measurable cotinine concentrations.

Another example of exposing the child to nicotine without cigarette smoke is when the lactating woman uses snuff. We found that the two snuff-taking mothers in our study exposed their infants to higher nicotine concentrations in their breast milk than the majority of the smoking women. This was possibly due to more frequent maternal intake of nicotine (Fig. 1). One of these infants had the highest urinary nicotine concentration in our study. To our knowledge, there are no previous reports about snuff-taking during lactation. The possible risks of using snuff during breastfeeding may not have been sufficiently addressed publicly.

The mean daily nicotine dose to the infant in our smoking and snuff-taking group is 7 μg/kg. Our findings do not support our hypothesis that the exposure of nicotine, measured as weight-adjusted dose, will increase after the neonatal period. The dose might be low, and we do not know the bio-availability of the ingested dose or the first pass metabolism. We do not know at what level nicotine exposure is harmless to the child.

Froen et al. found impaired autoresuscitation among newborn piglets exposed to a single intravenous dose of 5 μg/kg of nicotine (24).

One may speculate that nicotine in mothers' milk may be associated with the finding of Klonoff and co-workers that the protective effect of breastfeeding against SIDS is lost when the mothers smoke (11). During infancy, after the neonatal period when the risk of SIDS is at its highest, the ANS with cholinergic nicotinic receptors is developing (25).

Due to lack of evidence, the American Academy of Pediatrics Committee on Drugs removed nicotine from the list of drugs contra-indicated during breastfeeding (26). Swedish health authorities recommend smoking women to use nicotine drugs and to stop smoking but continue breastfeeding (27). We are not aware of any scientific basis for these guidelines (28). Studies have shown that the total maternal exposure to nicotine can be lowered when using nicotine gum during short-term use in pregnancy instead of smoking (29). On the other hand, when smoking, there is a short peak of high nicotine concentration in plasma with a similar pattern in milk. When using snuff, nicotine gum or dermal patches, the absorption and distribution kinetics are different, with a much broader peak with high levels of plasma nicotine (30). This will probably lead to a higher milk nicotine concentration over a longer period of time, and possibly a higher dose of nicotine to the breastfed infant. NRDs, on the other hand, deliver only nicotine, and can be a temporary bridge to non-smoking.

Our health authorities have been successful at informing parents not to smoke in the same room as the baby. We believe parents are aware of this, but not about the exposure to nicotine when using snuff or NRDs during lactation.

In summary, in a group of 40 mother–child pairs, we have shown that even if the woman is a moderate smoker, the breastfed child is exposed to nicotine in the mother's milk. A non-smoking woman exposed to passive smoking can feed her child with milk containing nicotine. A snuff-taking woman may have more nicotine in her milk than a woman smoker. Nicotine concentration in milk is dependent on the time between smoking and breastfeeding. The longer a mother refrains from smoking, the lower the nicotine concentration in the milk will be.

We need more information to know whether nicotine in breast milk can affect the health of the nursing infant. With the knowledge we have today about the exposure to nicotine in milk, we want to encourage women to stop smoking or taking snuff and avoid all exposure to cigarette smoke and continue breastfeeding. Any intake of nicotine must be considered a potential risk for the infant, since nicotine (5) is a substance with both acute and long-term effects on the developing nervous system. Health authorities should keep on encouraging women to breastfeed and stop smoking.

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