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MATERNAL SMOKING EFFECTS ON INFANT GROWTH

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Abstract

Maternal smoking is known to have adverse effects on birth weight, duration and volume of breast feeding. It also negatively affects maternal body composition and prolactin concentration at the end of pregnancy. The effect of smoking on longitudinal growth has not been studied thoroughly. Sixteen smoking mothers (S) during pregnancy and lactation (7.1 ± 4.4 cigarettes/day) and 22 non-smoking mothers (NS), were selected at delivery time, in Santiago, Chile. Infants were evaluated monthly and volume of breast milk was measured at one month by dose-to-infant deuterium dilution, as well as cotinine levels. The concentration of zinc, copper and iron in milk was measured by atomic absorption spectrophotometry (AAS). Zinc, copper and cadmium were also determined in the infant's hair at one and six months and once in the mother (beginning of lactation). Cotinine levels were determined at one and six months by a radio-immuno-analysis standard kit. In monthly visits to the house, additional formula/food intake to breast feeding was determined in a 48 hours questionnaire to the mother, as well as infant's morbidity was registered.

At birth, weight and height were not significantly different, although higher in NS infants. Cotinine levels were 30 times higher in S-mothers compared to NS-mothers and 12 times higher in their infants. Both S and NS infants grew within normality as defined by the National Centre for Health Statistics (NCHS) in the Z-scores curves (weight/age, height/age and weight/height). Breast milk was similar in a partial group of NS and S groups (730 ± 133 g/d, 736 ± 136 g/d) and there was no difference in the content of zinc, copper and iron in milk or hair, except for cadmium which was higher in infant's hair at one month of age.

Significant differences in height and height/age were found from one to six months of age. Weight/height began to be significantly higher in S-infants from three months onward, due to their slower height growth. Another group of infants (from non-smoking mothers during pregnancy but smokers during lactation) had a growth pattern intermediate to both curves, suggesting the impact of maternal smoking at any period of infant growth. Smoking had a clear effect on infant height during the period of breast feeding, attributable to the effect of the known content of cadmium in smoker's milk, on the bioavailability of essential nutrients such as zinc.

1. SCIENTIFIC BACKGROUND OF THE PROJECT

Smoking effects on infant growth and maternal health, as well as other effects of smoking on later morbidity have been previously studied. Smoking was found to alter body composition in the mother, a trait maintained from the non-pregnant period [1], as well as lowering the level of prolactin at the end of pregnancy, which has implications for the lactation period [2]. A recent paper showed the effect of smoking on growth until the 3rd month in a smaller sample from this same study [3] and the effect of passive smoking in the infants from non-smoking mothers, but with other smoking resident in their house [4]. Using the precise dose-to-mother deuterium dilution methodology, mothers of smokers were found to produce significantly less volume of milk at one month, which correlated with a slower rate of birth [5] at that age. Since then, the Ministry of Health has started a vigorous campaign to stimulate breast feeding until six months of age, and has trained health personnel to support the mother from the moment

of delivery in her feeding procedure. Non-published data from the same Ministry of Health suggests that the source of milk be obtained through breast feeding in 50-60% of the cases.

There is concern that smoking could not only affect birth weight, but also inhibit growth in height, given to the known presence of cadmium in tobacco. Such a study required a bigger sample than the one utilised (10 S and 10 NS) in a previous work [5]. For that reason, the present work was designed to study these objectives.

2. SUBJECTS AND METHODS

2.1. Subjects

Mothers from low socio-economic status were contacted after delivery in a hospital in the South-East region of Santiago (Sotero del Rio), after verifying their normal status and infant's birth weight (3.000-4000 g), no intake of medication or any factor affecting a normal lactation, their intention to breast feed until four months minimum. The study was thoroughly explained to the mother and written acceptance was given before being included to participate. Smoking mothers were selected with the same characteristics and with a smoking pattern of a minimum of five cigarettes daily during pregnancy and lactation. Such dyads of smokers mothers and infants are difficult to find, and a total sample of 20 pairs smoking mothers and their infants (S) were encountered; 35 non-smoking mothers (NS) and their infants were selected to increase the statistical power of the sample.

Of the total group of non-smoking mothers, ten mothers started to smoke from the third month of the lactation period. The non-smoking group during pregnancy and lactation was reduced to 25 cases, and a mixed smoking status group (MSG) was formed with the remaining ten mothers.

Some cases were excluded (2 smokers) for impossibility of the mother to continue the protocol until six months (change of address, starting work), and some others were excluded (2 smokers and 3 non-smokers) as they were found later not to comply with inclusion criteria for birth weight (3.000-4000 g). The final group was comprised then of: 22 non smokers, 16 smokers and 10 mixed smoking status.

2.2. Methods

Infants were measured at their homes monthly until six months of age (weight using a SECA balance for infants and height with an infant stadiometer). Mother's weight was checked at one-month post-partum.

Breast milk production was measured at infant's one month of age, and on those infants still being breast fed at six months of age, by the dose-to-infant deuterium dilution methodology. A dose of 0.2g/kg of 99.9% of deuterium oxide was administered to the infants, after collecting a basal saliva sample of 3 ml. At one month of age, urine samples were collected all days 1-8 after dosing, by a cotton layer over the nappy and careful extraction of the urine; at six months of age, samples were collected at days 1-10. Mothers were well trained to collect urine samples, but to assure the validity of the milk measurement; the field worker personally collected samples of the first two days and the final two days of the sampling protocol. Samples were frozen at -20°C until measured in a Europa Scientific HYDRA continuous flow IRMS at INTA.

Hair from both mother and infant, was collected carefully at one and six months, from the underneath hair in the back of the head, and stored immediately in sealed

plastic bags at room temperature. The mother collected milk from 6-8 feedings along one day, 2 ml before and after each feed on one breast; samples were pooled in one tube to perform micronutrient analysis (copper, zinc, and iron) by AAS (atomic absorption spectrophotometry). The first part was done at INTA, and the cadmium measurements at the Department of Nutrition, Faculty of Medicine, University of Chile.

3. RESULTS AND DISCUSSION

3.1. Results

In Table 1, the description of subjects (mother/infant) at birth is shown. There are no significant differences in any characteristics of the subjects, except for the levels of smoking and cotinine as expected.

TABLE I. DESCRIPTION OF SUBJECTS

	Smokers (n 16)	Non-smokers (n 22)
Mother		
Age (y)	27.1 (5.2)	24.9 (4.3)
WAD(kg)	69.2 (7.4)	68.6 (5.5)
Height (cm)	155.9 (4.3)	154.4 (5.7)
Parity	2.6 (1.0)	2.0 (1.0)
Cotinine (ng/ml)	2694 (2044)*	55 (28)*
Cigarettes (n)	7.1 (4.4)	-
Infant		
Birth weight	3306 (327)	3385 (256)
Birth height	49.5 (1.3)	50.0 (2.6)
Gestational age	39.0 (0.8)	39.1 (0.7)

At one and six months of age in the infant, growth is shown as well as levels of cotinine (Table II). Weight is always higher in non-smokers, without being significantly different, and the difference of 190 g at one month is reduced to 107 g at six months. Height begins to be significantly different at one month of age, and the difference in favour of non-smokers of 0.5 cm at birth (Table I) is increased to 1.3 cm at one month and to 1.5 cm at six months of age. Cotinine levels are statistically different at one and six months, increasing with time in smokers, ratifying a tendency of mothers to smoke more as lactation progresses.

TABLE II. GROWTH AND LEVELS OF COTININE IN INFANTS AT ONE AND SIX MONTHS OF AGE

	Non smokers		Smokers	
	One month	Six months	One month	Six months
Weight (g)	4277 (351)	7886 (684)	4087 (310)	7779 (768)
Height (cm)	53.6 (1.3)#	67.5 (2.1)&	52.3 (1.2) #	66.0 (1.9)&
Cotinine (ng/ml)	12.0 (10.4)*	11.1 (13.8)+	122.6 (78.3)*	149.8 (36.1)+

#p<0.01 &p<0.05 *p<0.0001 +p<0.001

In Table III, levels of zinc, copper and cadmium in infant's hair is shown. No significant difference is observed in zinc and copper between smokers and non-smokers; and zinc diminished with time in both groups. Cadmium is higher in smoker's infant's

hair, but not statistically different given the dispersion of values. Cadmium values increased in a dose-dependent manner from non-smokers, mixed smoking, and smokers. The fact that non-smoker's infants have cadmium in their hair may be linked eventually to passive smoking (from other members of the family, other than the mother). Cadmium levels in smoker's infants diminished at six months, according to a high proportion of these infants not being exclusively breastfed, and reducing their source of cadmium intake.

TABLE III. ZINC, COPPER AND CADMIUM LEVELS IN INFANT'S HAIR AT ONE AND SIX MONTHS OF AGE

	N	Zinc (μg/g)	Copper (μg/g)	Cadmium μg/g
One month				
Non smokers	22	212.3 (104.1)	18.1 (10.0)	0.21 (0.49)
Smokers	16	215.7 (101.8)	23.0 (16.6)	2.09 (8.18)
Mixed smoking	10	237.5 (118.4)	44.7 (45.6)	0.36 (0.39)
Six months				
Non smokers	22	120.8 (72.8)	41.9 (48.7)	0.35 (0.45)
Smokers	16	119.5 (41.3)	27.9 (22.0)	0.73 (1.48)
Mixed smoking	10	144.2 (74.2)	23.2 (14.8)	0.60 (1.33)

In Table IV, the maternal levels of zinc, copper and cadmium in hair are shown. Maternal zinc and copper concentrations do not differ, which agrees with the normal nutritional status of the mothers. Hair levels of cadmium did not differ between the two groups, (a surprising fact), although routes of deposit of cadmium in the body are mainly related to renal via. The low levels could be also attributable to passive smoking.

When comparing infant hair cadmium concentration at one month to maternal cadmium hair content, infants of non-smokers have ten times the concentration of cadmium; this ratio reaches 200 times in infants of smokers compared to their mothers. By six months, this ratio has reached 17 times in non-smokers and 73 times in smokers.

These figures confirmed the accumulation of cadmium in the infant at one month, probably due to in utero contamination and direct and passive ways [6]; the effect of passive smoking in the infants of non-smokers is also evident. Another point is the effect of the detention of breast feeding in smokers, inhibiting acquisition of cadmium from a direct gastrointestinal way.

TABLE IV. ZINC, COPPER AND CADMIUM LEVELS IN MOTHER'S HAIR

	N	Zinc (μg/g)	Copper (μg/g)	Cadmium μg/g
Non smokers	22	167.6 (28.7)	17.06 (9.6)	0.02 (0.03)
Smokers	16	189.8 (47.3)	17.53 (9.7)	0.01 (0.03)
Mixed smoking	10	193.5 (40.2)	14.80 (13.2)	0.04 (0.10)

In Table V, zinc, copper and iron levels in maternal milk are shown; there was no significant difference in any group either, due to the normal nutritional status of mothers. Results for the milk content of cadmium are being processed at present, which will complete the picture and will help to interpret the results in growth; nevertheless, cadmium is a known contaminating factor present in maternal milk of smokers.

Milk production has been determined in part of the sample (16 non-smokers and 10 smokers), showing no significant differences between smokers and non-smokers. Breast milk was similar in a partial group of NS and S groups (730 ± 133 g/d, 736 ± 136 g/d). The introduction of additional formula was done at three months in smokers (10 out of 16) and at five months in non-smokers (6 out of 22).

TABLE V. COPPER ZINC AND IRON LEVELS IN MATERNAL MILK

	N	Copper (mg/100g)	Zinc (mg/100g)	Iron (mg/100g)
Non smokers	22	0.085 (0.039)	0.676 (0.258)	0.595 (0.156)
Smokers	16	0.069 (0.014)	0.572 (0.109)	0.540 (0.162)
Mixed smoking	10	0.074 (0.020)	0.555 (0.167)	0.550 (0.198)

In Tables VI and VII, it is shown that infants of smokers are being fed earlier complementary feeding, and that by fourth months of age, infants are having a significantly greater energy, protein and calcium intake. This fact could be related to the greater weight/height of smokers' infants. Unfortunately, no determination of maternal milk intake was done at three months of age to evaluate the contribution of each type of feeding.

TABLE VI. COMPLEMENTARY FEEDING IN INFANTS OF NON-SMOKERS

Month/ N cases	Energy (Kcal)	Protein (g)	Calcium (mg)	Copper (mg)	Iron (mg)	Zinc (mg)
Three (2)	72 (84)	2 (1.9)	45 (52.8)	0.04 (0.05)	1.00 (1.0)	1.0 (0.6)
Four (4)	221 (272)	5 (5)	174 (225)	0.14 (0.19)	2.28 (3.4)	1.3 (2.2)
Five (4)	339 (311)	8 (5)	224 (307)	0.25 (0.21)	3.80 (3.96)	2.3 (2.6)
Six (3)	333 (184)	9 (7)	207 (228)	0.34 (0.03)	3.81 (2.62)	1.1 (0.6)

TABLE VII. COMPLEMENTARY FEEDING IN INFANTS OF SMOKERS

Month/ N cases	Energy (Kcal)	Protein (g)	Calcium (mg)	Copper (mg)	Iron (mg)	Zinc (mg)
Two (4)	54 (14)	2 (1)	47(22)	0.03(0.01)	0.54(0.35)	0.40(0.11)
Three (6)	271 (255)	11 (12)	345 (415)	0.10 (0.14)	1.29 (2.62)	1.14 (1.57)
Four (8)	421 (267)	20 (16)	653 (518)	0.21 (0.14)	1.24 (1.65)	1.63 (1.18)
Five (9)	528 (333)	23 (20)	354 (321)	0.34 (0.41)	3.95 (3.72)	1.71 (1.09)
Six (9)	673 (382)	30 (19)	717 (569)	0.54 (0.32)	4.94 (3.24)	3.45 (2.18)

In Figures 1a, 1b, 1c the Z-scores for Weight/age (W/A), Height/age (H/A) and Weight/height (W/H) are reported. Height of NS-infants is significantly higher in the whole period (from one to six months of age). Height/age is significantly greater in infants of non-smokers in the period one to fourth months of age (Figure 1.b). Weight/height becomes significantly different in infants of smokers, from the third month onwards, mainly due to the deficit in height growth.

3.2. Discussion

Smoking affects transiently the growth in infant's height, attributable to the transfer of cadmium by tobacco smoking. Chronic contamination of cadmium is known to be caused by smoking or shell food; although the placenta and breast do present a barrier, cadmium has been shown to alter the ratio cadmium/zinc and cadmium/copper in foetal blood, as there is evidence that cadmium is preferably attached to α-Lactoalbumin or low molecular weight fractions in human milk (7,8). The most important interactions are between cadmium and zinc and some results indicate disturbances of the metabolism of zinc, copper and iron, especially when administered at low dose (6). Accumulation of cadmium in the liver and kidney will also increase zinc levels in these organs due to binding to metallothionein. Our hypothesis is that this binding may alter the supply/bioavailability of zinc during breast feeding of smokers, altering growth in height significantly. This problem begins to change after the early introduction of formula feeding in infants from smokers in combination with the slow down of the rate of growth from four months onwards.

Introduction of complementary feeding is done earlier and by four months in infants of smokers; these children received a significantly greater intake of energy, protein and calcium, when compared to infants of non-smokers. The rapid increase of weight for age in smoker's infants could be attributable to the greater intake of complementary feeding. No information was collected on the amount of breast-milk volume, between two and five months included, but only if infants were breastfed.

Further work is necessary to evaluate the differences in intake in both groups, as well as the role of cadmium on metallothionein synthesis and its effect on zinc bioavailability, due to tobacco smoke.

4. CONCLUSIONS

Smoking has been shown to transiently affect growth in height preferentially during the period of breast feeding. This may be due to eventual cadmium transfer by milk, produced by tobacco inhaled by the mother; cadmium has been found to alter zinc and copper metabolism, and zinc in particular has an important role in longitudinal growth. The marked change in longitudinal growth after the ingestion of additional formula in infants of smokers suggests that stronger efforts to be made to convince mothers of stopping smoking during pregnancy and lactation. This campaign should include the effects of the interference of toxic elements in their infant's health and growth. Future studies should look into: cadmium loss in urine, the impact of cadmium in preferential binding of zinc by metallothionein, and relate it to the linear growth of smoker's infants in longer periods.

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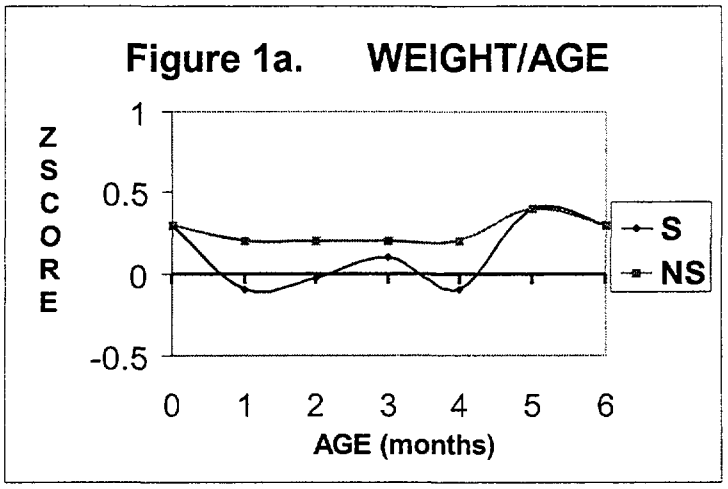
Figure 1a. WEIGHT/AGE
ZSCORE
1
0.5
0
-0.5
0 1 2 3 4 5 6
AGE (months)
S
NS

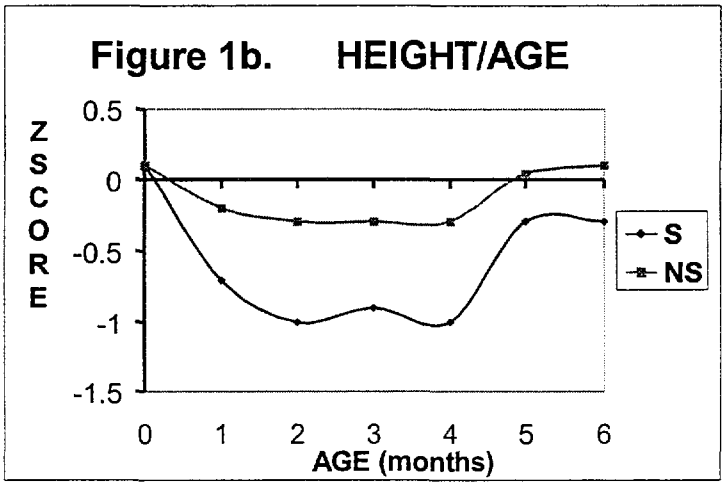
Figure 1b. HEIGHT/AGE
ZSCORE
0.5
0
-0.5
-1
-1.5
0 1 2 3 4 5 6
AGE (months)
S
NS

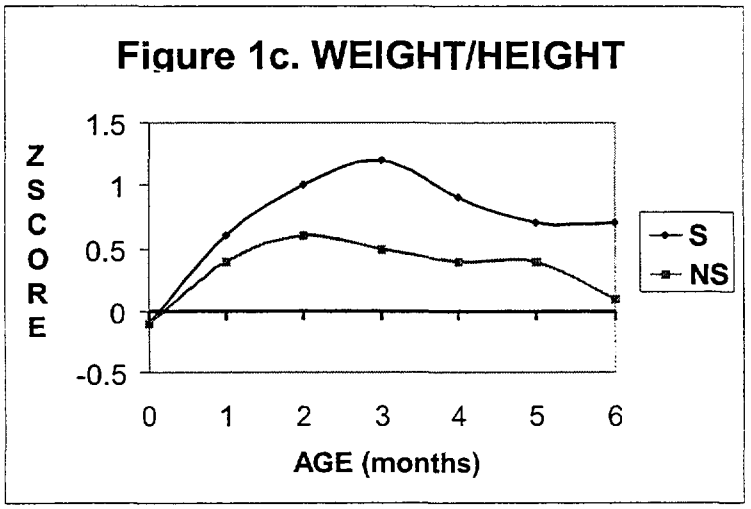
Figure 1c. WEIGHT/HEIGHT
ZSCORE
1.5
1
0.5
0
-0.5
0 1 2 3 4 5 6
AGE (months)
S
NS