EFFECTS OF DIOXINS AND FURANS ON THYROID FUNCTION IN THE HUMAN NEWBORN.

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INTRODUCTION

In western Europe the levels of dioxins and furans (henceforward jointly summarized as dioxins) in breast-milk are rather high, especially in the Netherlands, Belgium and the United Kingdom [1]. Therefore breast-feeding may expose infants to high doses of these compounds. Also before birth fetuses may be exposed to dioxins, since they can pass the placental barrier [2]. From animal studies it is known that these compounds can influence the thyroid hormone status [3]. Because adequate levels of thyroxine are necessary for normal psychomotor development of infants, we investigated the thyroid hormone levels in a population of 38 healthy breast-fed infants in relation to dioxin content of breast-milk.

SUBJECTS AND METHODS

Thirty-eight healthy women volunteered to participate in the study. All participants had a normal pregnancy without use of medicines with known effects on thyroid hormone status. They had the intention to breast-fed for at least three months. In eleven women breast-feeding ceased in the period from four to eleven weeks after delivery.

Plasma from the umbilical cord, taken at the age of one week and at the age of eleven weeks, was used to determine concentrations of thyroxine (TT4), thyroid binding globulin (TBG) and thyrotropin (TSH) in the infant. Breast-milk, sampled four weeks after delivery, was used to measure concentrations of dioxins. TEF values were used to calculate the amount of toxic equivalents (TEQ). The median dioxin concentration in milkfat was used to divide the infants into a high and a low exposure group.

Dioxin concentrations were 8.7 - 28.0 ng TEQ/kg fat (mean 18.6) in the low exposure group and 29.2 - 62.7 ng TEQ/kg fat (mean 37.5) in the high exposure group. Mean gestational age and birthweight were 40.2 $\pm$ 0.3 versus 40.4 $\pm$ 0.3 weeks and 3.64 $\pm$ 0.09

versus 3.65 ± 0.12 kg in the low and high exposure group respectively. Six women (31.6%) had a history of smoking during pregnancy in the low exposure group compared with one woman (5.3%) in the high exposure group.

Table. The influences of dioxins on neonatal thyroid function: the difference between low and high exposure at different ages.

		Low exposure		High exposure		
Age	Item#	Mean ± SEM	N	Mean ± SEM	N	P*
Birth	TT4	122.5 ± 4.1	18	134.3 ± 4.8	15	0.071
	TBG	520.1 ± 27.2	18	589.5 ± 30.5	15	0.099
	TT4/TBG	0.240 ± 0.007	18	0.232 ± 0.008	15	0.45
	TSH	10.4 ± 1.3	14	11.9 ± 1.9	11	0.58
1 week	TT4	154.5 ± 6.3	19	178.7 ± 5.5	19	0.006
	TBG	532.6 ± 16.3	19	546.2 ± 19.1	19	0.59
	TT4/TBG	0.291 ± 0.009	19	0.332 ± 0.011	19	0.006
	TSH	2.93 ± 0.41	15	2.56 ± 0.41	11	0.51
11 weeks	TT4	111.1 ± 4.0	18	122.2 ± 3.0	16	0.033
	TBG	519.0 ± 29.4	18	500.7 ± 13.0	16	0.574
	TT4/TBG	0.220 ± 0.008	18	0.247 ± 0.009	16	0.040
	TSH	1.81 ± 0.19	18	2.50 ± 0.26	12	0.044

* two-tailed paired Student's t-test
# T4 in nmol/L, TBG in nmol/L, TSH in mU/L,

RESULTS AND DISCUSSION

The results are listed in the table. The mean TT4 concentrations at birth and at the age of one week were higher in the high exposure group, but the difference was only statistically significant one week after birth. At this time, also the TT4/TBG ratio was significantly higher in the high exposure group, indicating that dioxins affect the thyroxine metabolism rather than concentrations of the major thyroxine binding protein. At birth and at the age of one week, mean TSH concentrations were similar in the high and low exposure

group, suggesting that the dioxin induced TT4 elevation is caused by an effect on the thyroid hormone regulatory system. Dioxins, which are structurally related to thyronines [4], might act on the level of T4 transport into the cell, 5'-deiodinase, or T3 binding to the nuclear receptor. Therefore higher plasma TT4 levels may be necessary to maintain an adequate T3 concentration on the nuclear receptor. At the age of eleven weeks the mean levels of TT4 and TT4/TBG ratio were still significantly higher in the high exposure group, while now also the mean TSH levels were significantly higher in this group.

The higher TT4 levels can't be explained by differences in gestational age and birthweight, because these were similar in both groups of infants. Neither can they be explained by the difference in smoking habits of the mothers in both groups. In a study of Meberg et al. [5] higher thyroxine levels in cord serum were found in the smoking group compared with the non-smoking group, while in our study six of the seven smokers were in the low exposure group.

The significantly higher TT4 levels and TT4/TBG ratio at the age of one week are most likely the result of intra-uterine exposure to these compounds. In the first week of life, when the infant has a low energy intake and at the same time a high energy need to maintain body temperature, fatty acids are mobilized from (brown) adipose tissue. This will cause a release of dioxins stored in the adipose tissue, resulting in circulating dioxin levels high enough to affect target organs. The higher TT4 levels and TT4/TBG ratios in the high exposure group at the age of eleven weeks, may be prolonged effects of intra-uterine exposure to dioxins, but the additional finding of higher TSH levels in this group suggest that also exposure to dioxins via breast-milk plays a role in the effects found at this age.

We conclude that exposure to higher levels of dioxins, intra-uterine and via breast-milk, appears to modulate the hypothalamic-pituitary-thyroid regulatory system in human newborns.

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