PCDDs and PCDFs in human placental tissue from eutrophic and hypotrophic babies

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Objective

The hypotrophy of many (small for date) newborns remains without explanation with no risk factor or obvious cause being recognizable. The influence of xenobiotics is discussed but has never been investigated. In order to evaluate the possible influence of PCDDs and PCDFs we analyzed placental and pooled chorion tissue from four mothers with eutrophic babies and four mothers with hypotrophic (small for date) babies without any recognizable cause or risk factor.

Introduction

Possible and well established causes for hypotrophy of new-born babies are smoking, alcohol, consumption of various medications and drugs and maternal diseases during pregnancy. Nevertheless there is a large number of hypotrophy cases without any recognizable cause. The influence of persistent xenobiotics like PCDDs/PCDFs, PCBs and others is widely discussed but there is a severe lack of scientific data.
PCDDs and PCDFs are found in placental tissue samples at concentrations, which, on a fat weight basis, mirror the mothers' body burden[1]. However, in two of the eight samples the I-TEQ values in placental fat were 2 to 3 times higher than in the corresponding maternal tissue. As placenta represents fetal tissue, a direct influence of PCDDs and PCDFs on the growth of the embryo and/or fetus a priori does not seem impossible. In order to elucidate this question we chose four mothers who gave birth to babies with weights below the 90th percentile. None of the mothers showed any risk factor which could have caused the hypotrophy of their babies. We measured the PCDD/PCDF-concentrations in each placental tissue and the pooled chorion sample. The same was done with placentae and chorion from four mothers with eutrophic babies.

Material and methods

After separation of chorion and decidua tissue (maternal part of placental tissue) the placental and the pooled chorion tissue samples were freeze-dried and ground finely. All 2,3,7,8-substituted PCDD/F-congeners were added as $^{13}C_{12}$-labeled standards before

soxhlet-extraction with n-hexane was carried out. 10% of each extract was separated and kept for analysis of other xenobiotics. After determination of the fat weight a clean-up with 3 or 4 steps was carried out. Finally HRGC/HRMS-analysis was performed.

Results

The PCDD/PCDF-concentrations (in pg/g fat) of the chorion and placental tissue are shown in table 1 (eutrophic) and table 2 (hypotrophic babies). The placenta samples 1a and 1b in table 2 are from twins; 1a belongs to a eutrophic, 1b to a hypotrophic baby.

1) Placental tissue: The fat content in both groups is similar and range from 0.6 to 1.2% of the wet weight (one exception see below). This is in agreement with [1]. The PCDD/PCDF-concentrations - I-TEQ values as well as the concentrations for the single congeners - of all 8 samples are in the range expected for human adipose tissue.

There is **no** significant **difference** in the PCDD/PCDF-concentrations **between both groups**. The mean values of the I-TEQs are even nearly equal.

2) Placental tissue from twins: The eutrophic placenta (1a) has a significant higher fat content (1.9%) than all other samples. The I-TEQ value of the eutrophic placenta is only about half that of the hypotrophic placenta (1b). This difference is solely due to lower PCDD-amounts.

3) Chorion tissue: The fat content is similar (0.5 and 0.6%) and lower than in corresponding placental tissue. As in placental tissue there is **no** significant **difference** in the PCDD/PCDF-concentrations **between both groups**. All values are in the same range as in the corresponding placental tissue except the concentration of 2,3,7,8-Cl_4DF, which is in both samples about 3 times higher than in placentae. Further the concentration of 1,2,3,7,8-Cl5DF seems to be higher.

Conclusions

In contrast to [1] we could not find increased concentrations of the Cl_4- and Cl_5-congeners in placental tissue. In agreement with the chorion samples we recently found even more increased concentrations for 2,3,7,8-Cl_4DF and also for 1,2,3,7,8-Cl_5DF in human umbilical cord tissue which is connected to the chorion[2]. This seems to indicate that these congeners are enriched in some fetal tissues during pregnancy.

The differences between the placentae of the twins are difficult to explain.

In spite of the limited number of samples the PCDD/PCDF-concentrations between both groups are very similar. We therefore assume that PCDDs and PCDFs at normal human exposure does not represent a significant risk factor for hypotrophy of newborns.

Although the PCDD/PCDF-concentrations in placental tissue are not lower than in adipose tissue of human adults, data for non-human primates[3] and humans[4] indicate that the transfer of PCDDs and PCDFs via mothers' milk is much higher than via placenta. This is confirmed by low fecal excretion rates we recently found in two breast-fed human infants[5].

References

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	Chorion	1	2	3	4	**Mean**	**SD**
Fat content (%)	0.50	0.71	0.77	0.65	0.78	0.73	0.06
2,3,7,8-TetraCDD	2.43	2.46	2.42	3.09	1.60	2.39	0.61
1,2,3,7,8-PentaCDD	5.87	6.22	7.62	8.74	4.62	6.8	1.8
1,2,3,4,7,8-HexaCDD	7.54	6.13	6.78	4.67	9.81	6.85	2.2
1,2,3,6,7,8-HexaCDD	26.3	11.4	21.2	16.2	28.3	19.3	7.2
1,2,3,7,8,9-HexaCDD	6.97	4.99	5.73	3.82	6.38	5.23	1.1
1,2,3,4,6,7,8-HeptaCDD	47.9	30.6	21.0	20.0	69.9	35.4	24
OctaCDD	262	239	130	127	189	171	53
Sum PCDD	359.4	300.7	195.1	183.8	309.5	247.3	67
2,3,7,8-TetraCDF	**10.7**	3.70	4.97	4.99	2.45	4.03	1.2
1,2,3,7,8-PentaCDF	**1.34**	(<1.6)	0.60	0.75	(<1.1)		
2,3,4,7,8-PentaCDF	15.8	13.2	22.2	13.6	11.7	15.2	4.8
1,2,3,4,7,8-HexaCDF	9.38	4.31	6.61	3.88	5.99	5.20	1.3
1,2,3,6,7,8-HexaCDF	7.06	4.42	5.82	4.05	4.67	4.74	0.76
1,2,3,7,8,9-HexaCDF	n.n.	n.n.	n.n.	n.n.	n.n.		
2,3,4,6,7,8-HexaCDF	4.66	3.00	3.74	1.51	5.30	3.39	1.6
1,2,3,4,6,7,8-HeptaCDF	12	11	(<6.0)	(<6.4)	(<4.0)		
1,2,3,4,7,8,9-HeptaCDF	n.n.	n.n.	n.n.	n.n.	n.n.		
OctaCDF	(<4.8)	(<9.5)	(<6.9)	(<9.5)	(<6.5)		
Sum PCDF	61.28	39.92	43.95	28.79	30.08	35.69	7.4
I-TEQ	**21.46**	**16.63**	**23.19**	**18.54**	**16.92**	**18.82**	**3.0**

Table 1: PCDD/PCDF-concentrations in pg/g fat (ppt) of chorion and placental tissue from eutrophic newborns

	Chorion	1a*	1b	2	3	4	Mean	SD
Fat content (%)	0.57	1.87	0.99	1.19	0.88	0.79	0.96	0.17
2,3,7,8-TetraCDD	3.01	2.32	3.68	5.36	4.44	3.23	4.18	0.93
1,2,3,7,8-PentaCDD	7.19	3.85	8.43	8.40	10.2	8.84	8.97	0.85
1,2,3,4,7,8-HexaCDD	7.25	3.03	11.1	(<13)	7.49	6.04	8.21	2.6
1,2,3,6,7,8-HexaCDD	21.9	7.64	26.5	19.1	15.8	14.5	19.0	5.4
1,2,3,7,8,9-HexaCDD	8.04	1.38	13.8	(<13)	6.91	4.29	8.32	4.9
1,2,3,4,6,7,8-HeptaCDD	32.1	4.43	12.8	15.6	39.7	26.3	23.6	12
OctaCDD	220	56.8	153	416	191	129	222	132
Sum PCDD	299.0	79.5	229.7	464.6	275.6	192.1	290.5	121
2,3,7,8-TetraCDF	**10.0**	0.67	(<2.0)	2.38	4.71	2.63	3.24	1.3
1,2,3,7,8-PentaCDF	**1.33**	(<0.39)	(<1.9)	(<2.1)	1.24	0.78		
2,3,4,7,8-PentaCDF	7.61	7.97	6.99	22.5	6.07	7.27	10.7	7.9
1,2,3,4,7,8-HexaCDF	4.07	1.46	1.16	2.06	3.46	1.86	2.14	0.96
1,2,3,6,7,8-HexaCDF	3.17	1.44	1.01	1.46	3.89	1.91	2.07	1.3
1,2,3,7,8,9-HexaCDF	n.n.	n.n.	n.n.	n.n.	n.n.	n.n.		
2,3,4,6,7,8-HexaCDF	2.05	0.79	(<0.95)	2.15	1.96	0.93	1.68	0.66
1,2,3,4,6,7,8-HeptaCDF	(<4.2)	(<1.7)	(<5.0)	(<8.8)	(<3.2)	(<2.6)		
1,2,3,4,7,8,9-HeptaCDF	n.n.	n.n.	n.n.	n.n.	n.n.	n.n.		
OctaCDF	(<6.3)	(<2.5)	(<7.4)	(<13)	(<4.7)	(<3.8)		
Sum PCDF	28.24	12.33	9.16	30.59	21.33	15.38	19.12	9.1
I-TEQ	16.67	9.97	17.02	24.12	17.64	14.93	18.43	4.0

* not included in the mean value

Table 2: PCDD/PCDF-concentrations in pg/g fat (ppt) of chorion and placental tissue from hypotrophic newborns. Sample 1a (eutrophic) and 1b (hypotrophic) belong to twins.