PCDD/PCDF LEVELS IN VARIOUS TISSUES FROM SUDDEN INFANT DEATH SYNDROME (SIDS) CASES

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Introduction

Polychlorinated dibenzo-p-dioxins (PCDD) and dibenzofurans (PCDF) were measured in various tissues (subcutaneous fat, liver, kidney and spleen) from 27 infants who died suddenly and unexpectedly. The cases can be subdivided into two groups consisting of 15 infants who died in 1991/ 1992 and 12 infants who died in 1996/1997. PCDD/PCDF analyses were part of the Westphalian crib death study (1991/1992) and the pilot phase of the BMBF SIDS study in Germany (1996/ 1997). The objective of these surveys were inter alia to examine whether PCDD/PCDF probably influence the risk for the sudden infant death syndrome (SIDS). Moreover, the distribution of PCDD/PCDF congeners between various tissues should be investigated. Finally, it was of interest, whether the remarkable decline of human milk contamination observed in the past few years shows similar effects on the PCDD/PCDF body burden of breast fed children.

Materials and Methods

In all cases an autopsy was performed using a standardized autopsy protocol including extensive histology, toxicology, microbiology, virology and clinical chemistry. An adequate cause of death could not be found in these cases. Subsequently the parents were asked during a detailed interview for the age of the mother at delivery, birth order of the victim, duration of breast feeding (full or partially) and type of additional food.

Analytical determination was performed using validated procedures which had been successfully tested in a number of national and international quality control studies. The tissues obtained during autopsy were ground with sodium sulphate and sea sand followed by column extraction using hexane/acetone. Subsequent analytical steps comprise spiking with ^{13}C-labeled PCDD/ PCDF, clean up using sulfuric acid coated silica gel, Florisil and carbon columns, separation by capillary gas chromatography and determination by high resolution mass spectrometry (HRMS) at a resolution of R=10.000 in the selected ion recording mode (SIR). The longterm stability of the methodology is assured by analyzing three different quality control pools since several years.

Results and Discussion

In all tissues analysed, PCDD/PCDF congeners with 2,3,7,8-chlorine substitution were dominating. Other congeners could only be detected occassionally at concentrations near the detection limit. As anticipated, the pattern resemble pretty much those which are found in human milk or adipose tissue of adults. Table 1 shows the PCDD/PCDF levels determined in various tissues besides some basic data, such as year of sampling, duration of breast feeding as well as sex and age of the victim. While in 1991/1992 kidney was analysed in addition to adipose tissue and liver,

the 1996/1997 survey comprised the matrices adipose tissue, liver and spleen. All PCDD/ PCDF levels are given as ng I-TEq/kg fat. Some of the 1991/1992 data were already reported earlier (1). As can be seen from Table 1, tissues from infants who were partly or exclusively breast fed contain higher PCDD/PCDF levels than tissues from non breast fed victims. The duration of breast feeding was directly and the birth order of the victim was indirectly proportional to the PCDD/PCDF body burden. In single cases of the 1991/1992 survey, the dioxin concentration in adipose tissue distinctly exceeded the mean PCDD/PCDF level measured at that time in human milk samples from nursing mothers in North Rhine-Westphalia (2). Compared to 1991/1992, the body burden of partly and exclusively breast fed infants analyzed in 1996/1997 is remarkably lower. This can be explained by the fact, that the PCDD/PCDF levels in human milk decreased during the same period by approximately 50%, resulting in a significantly lower daily intake of these contaminants via breast feeding.

It is striking that in almost all cases the PCDD/PCDF levels, based on fat weight, in liver, kidney and spleen are higher than those in subcutaneous fatty tissue. This is especially true for OCDD, 1.2.3.4.6.7.8-HpCDD, OCDF, 1.2.3.4.6.7.8-HpCDF, 1.2.3.4.7.8-HxCDF, 1.2.3.6.7.8-HxCDF and 2.3.4.6.7.8-HxCDF which are significantly accumulated in liver fat (Table 2). Similar observations were also made by Beck et al. (3,4) and Wuthe et al. (5). The data summarized in Table 2 even seem to indicate that the accumulation of specific congeners in liver tissue from non breast fed infants is somewhat higher than that from partly or exclusively breast fed victims, although the absolute levels in the former cases are generally much lower. Whether these observations have a pathophysiological significance can not be decided at present. In any case, it has to be mentioned that according to the results of some epidemiological studies, e.g. the Westphalian crib death study where breast feeding could be characterized to be a protective factor against SIDS, it can be concluded that PCDD/PCDF do not seem to influence the risk for sudden infant death (6).

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I-TEq Levels in Different Tissues from SIDS-Cases								
	Breast fed (weeks)		age		ng I-TEq / kg fat			
Year	exclusively	partly	(weeks)	sex	adipose	liver	kidney	spleen
96	0	0	13	m	1.8	2.5	2.1	n.a.
96	0	0	31	f	0.6	1.8	1.2	n.a.
97	0	5	27	m	1.7	4.0	2.9	n.a.
97	1	1	10	f	2.0	2.1	1.6	n.a.
97	4	2	10	m	1.9	1.8	3.1	n.a.
96	6	0	33	f	2.8	3.8	1.9	n.a.
96	13	0	13	m	6.7	6.9	7.5	n.a.
96	0	8	37	f	0.7	1.7	1.4	n.a.
96	2	0	14	m	4.2	8.1	4.3	n.a.
96	16	8	42	m	14.9	24.4	14.8	n.a.
96	3	0	3	f	9.2	9.8	10.5	n.a.
96	11	0	11	m	23.8	25.3	29.8	n.a.
92	0	0	59	m	1.2	6.1	n.a.	1.9
92	0	0	10	m	15.6	15.6	n.a.	17.2
91	0	0	14	m	2.5	6.2	n.a.	3.5
91	0	0	23	m	3.8	11.1	n.a.	3.6
92	0	0	17	m	2.4	8.8	n.a.	3.3
91	0	14	17	m	17.2	31.2	n.a.	27.9
92	0	4	38	m	4.0	18.2	n.a.	6.4
92	0	10	32	f	27.6	71.3	n.a.	55.4
92	0	5	18	m	3.8	17.5	n.a.	5.2
92	25	0	31	m	37.3	215.8	n.a.	84.2
92	30	0	35	f	28.6	114.3	n.a.	40.4
91	17	0	18	m	43.9	n.a.	n.a.	39.0
91	24	0	28	m	87.4	192.0	n.a.	n.a.
91	12	0	12	m	29.1	n.a.	n.a.	29.1
91	5	0	5	m	29.0	26.3	n.a.	n.a

e 1 **m: male** **f: female** **n.a.: not analyzed**

Relative Ratio of Liver / Adipose Tissue Concentrations (Based on Fat Weight)								
	non breast fed				exclusively and partly breast fed			
congener	mean	median	min	max	mean	median	min	max
	19.1	16.7	2.3	50.0	11.2	8.0	2.6	43.9
.6.7.8 - HpCDD	10.4	11.0	2.1	23.1	7.0	5.7	1.7	17.5
.7.8 - HxCDD	1.7	1.6	0.8	3.3	1.7	1.3	0.4	4.5
.7.8 - HxCDD	0.9	0.9	0.6	1.8	1.1	0.9	0.6	2.5
.8.9 - HxCDD	1.2	0.9	0.5	2.6	1.5	1.2	0.6	4.2
.8 - PeCDD	1.0	0.9	0.7	1.4	1.1	1.0	0.6	1.9
- TeCDD	1.2	1.0	0.7	2.1	0.8	0.8	0.2	1.3
	17.7	10.9	3.0	46.1	16.9	12.1	0.8	52.0
.6.7.8 - HpCDF	14.7	16.7	3.6	22.7	9.3	8.0	1.5	27.5
.7.8 - HxCDF	10.3	10.0	2.0	24.7	7.8	5.3	1.1	22.6
.7.8 - HxCDF	12.7	11.8	3.3	28.8	9.9	7.0	1.1	25.5
.7.8 - HxCDF	8.7	9.4	3.3	19.2	7.5	5.7	1.3	23.6
.8 - PeCDF	2.7	2.5	1.1	4.2	2.7	2.1	0.8	8.1
- TeCDF	2.4	1.6	1.0	8.2	1.4	1.3	0.7	2.3
	2.8	2.9	1.0	5.1	2.3	1.9	0.9	5.8

2

Relative Ratio of Liver / Adipose Tissue Concentrations (Based on Fat Weight)								
	non breast fed				exclusively and partly breast fed			
congener	mean	median	min	max	mean	median	min	max
OCDD	19.1	16.7	2.3	50.0	11.2	8.0	2.6	43.9
1.2.3.4.6.7.8 - HpCDD	10.4	11.0	2.1	23.1	7.0	5.7	1.7	17.5
1.2.3.4.7.8 - HxCDD	1.7	1.6	0.8	3.3	1.7	1.3	0.4	4.5
1.2.3.6.7.8 - HxCDD	0.9	0.9	0.6	1.8	1.1	0.9	0.6	2.5
1.2.3.7.8.9 - HxCDD	1.2	0.9	0.5	2.6	1.5	1.2	0.6	4.2
1.2.3.7.8 - PeCDD	1.0	0.9	0.7	1.4	1.1	1.0	0.6	1.9
2.3.7.8 - TeCDD	1.2	1.0	0.7	2.1	0.8	0.8	0.2	1.3
OCDF	17.7	10.9	3.0	46.1	16.9	12.1	0.8	52.0
1.2.3.4.6.7.8 - HpCDF	14.7	16.7	3.6	22.7	9.3	8.0	1.5	27.5
1.2.3.4.7.8 - HxCDF	10.3	10.0	2.0	24.7	7.8	5.3	1.1	22.6
1.2.3.6.7.8 - HxCDF	12.7	11.8	3.3	28.8	9.9	7.0	1.1	25.5
2.3.4.6.7.8 - HxCDF	8.7	9.4	3.3	19.2	7.5	5.7	1.3	23.6
2.3.4.7.8 - PeCDF	2.7	2.5	1.1	4.2	2.7	2.1	0.8	8.1
2.3.7.8 - TeCDF	2.4	1.6	1.0	8.2	1.4	1.3	0.7	2.3
I-TEq	2.8	2.9	1.0	5.1	2.3	1.9	0.9	5.8

Table 2

I-TEq Levels in Different Tissues from SIDS-Cases									
		Breast fed (weeks)		age		ng I-TEq / kg fat			
No.	Year	exclusively	partly	(weeks)	sex	adipose	liver	kidney	spleen
349	96	0	0	13	m	1.8	2.5	2.1	n.a.
356	96	0	0	31	f	0.6	1.8	1.2	n.a.
66	97	0	5	27	m	1.7	4.0	2.9	n.a.
55	97	1	1	10	f	2.0	2.1	1.6	n.a.
17	97	4	2	10	m	1.9	1.8	3.1	n.a.
378	96	6	0	33	f	2.8	3.8	1.9	n.a.
354	96	13	0	13	m	6.7	6.9	7.5	n.a.
297	96	0	8	37	f	0.7	1.7	1.4	n.a.
379	96	2	0	14	m	4.2	8.1	4.3	n.a.
374	96	16	8	42	m	14.9	24.4	14.8	n.a.
311	96	3	0	3	f	9.2	9.8	10.5	n.a.
288	96	11	0	11	m	23.8	25.3	29.8	n.a.
366	92	0	0	59	m	1.2	6.1	n.a.	1.9
12	92	0	0	10	m	15.6	15.6	n.a.	17.2
389	91	0	0	14	m	2.5	6.2	n.a.	3.5
381	91	0	0	23	m	3.8	11.1	n.a.	3.6
26	92	0	0	17	m	2.4	8.8	n.a.	3.3
388	91	0	14	17	m	17.2	31.2	n.a.	27.9
58	92	0	4	38	m	4.0	18.2	n.a.	6.4
133	92	0	10	32	f	27.6	71.3	n.a.	55.4
127	92	0	5	18	m	3.8	17.5	n.a.	5.2
80	92	25	0	31	m	37.3	215.8	n.a.	84.2
211	92	30	0	35	f	28.6	114.3	n.a.	40.4
416	91	17	0	18	m	43.9	n.a.	n.a.	39.0
91	91	24	0	28	m	87.4	192.0	n.a.	n.a.
311	91	12	0	12	m	29.1	n.a.	n.a.	29.1
345	91	5	0	5	m	29.0	26.3	n.a.	n.a

Table 1 **m: male** **f: female** **n.a.: not analyzed**