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Heavy metals, chlorinated pesticides and polychlorinated biphenyls in sudden infant death syndrome (SIDS)

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Summary. The concentrations of lead in blood and of cadmium and mercury in kidney tissue were determined by atomic absorption spectrometry in cases in SIDS and a control group containing cases of known causes of death. SIDS cases were split into groups from urban and rural areas and areas highly polluted with lead and zinc (sites of lead and zinc works). Neither the concentration of lead in blood (median 26.5 to 50.0 μg/l), nor the concentration of cadmium (median 24.0 to 44.0 μg/kg ww) or mercury (43.0 to 69.0 μg/kg ww) showed significant differences between the groups. In addition the concentrations of persistent chlorohydrocarbons (hexachlorbenzene; alpha, beta and gamma hexachlorcyclohexane; heptachlorepoxide; dieldrine; total DDT; polychlorinated biphenyls) were measured in subcutaneous fatty tissue in SIDS cases from rural and urban areas and in a control group. These substances also showed no significant concentration differences in cases of SIDS.

Key words: SIDS – Heavy metals concentrations – Chlorinated pesticides – Polychlorinated biphenyls – Toxic environmental factors

Zusammenfassung. Bei SIDS-Fällen und einer altersgleichen Kontrollgruppe wurden mittels Atomabsorptionsspektroskopie Blei-(Blut), Cadmium-(Niere) und Quecksilberkonzentrationen (Niere) bestimmt. Innerhalb der SIDS-Gruppe wurde eine Unterteilung entsprechend den Umweltbedingungen der verstorbenen Säuglinge – rein ländliche, städtische und besonders schwermetallbelastete Gebiete – vorgenommen. Weder innerhalb der SIDS-Gruppe noch zur Kontrollgruppe konnten signifikante Unterschiede der Schwermetallkonzentration festgestellt werden, sowohl was die gemessenen Einzelwerte, als auch die Mittelwerte und Medianwerte betrifft. Die Medianwerte für die Bleikonzentration im Blut betrugen 26,5 bis 50,0 μg/l; die Medianwerte für die Cadmiumkonzentration 24,0 bis 44,0 μg/kg Feuchtgewicht und für die Quecksilberkonzentrationen 43,0 bis 69,0 μg/kg Feuchtgewicht. Bei den toxikologischen Untersuchungen der persistenten Chlorkohlenwasserstoffe (Hexachlorbenzol, alpha-, beta- und gamma-Hexachlorcyclohexan, Heptachlorepoxid, Dieldrin, Gesamt DDT und polychlorierte Biphenyle) im Bauchgettgewebe von SIDS-Fällen aus ländlichen und städtischen Regionen und einer Kontrollgruppe konnten in den SIDS-Gruppen aus ländlichen und städtischen Regionen keine signifikant erhöhten Schadstoffkonzentrationen festgestellt werden. Die durchgeführten chemisch-toxikologischen Untersuchungen lassen somit keinen spezifischen Einfluß der untersuchten Umweltschadstoffe beim SIDS erkennen.

Schlüsselwörter: Plötzlicher Kindstod (SIDS) – Schwermetallkonzentrationen – Chlorierte Pestizide – Polychlorierte Biphenyle – Schadstoffbelastung

Introduction

In recent years a possible correlation between the level of toxic pollutants in the environment and the incidence of SIDS has often been discussed. Up till now there have only been a few scientific studies about this problem. After statistical investigations Hoppenbrouwers et al. (1981) assumed a link between air pollution in Los Angeles and SIDS. Drasch et al. (1988) analysed the lead concentrations in blood from SIDS cases and a control group of living children. They found no significant differences between the arithmetical means of these 2 groups. However they suspected a correlation between lead concentration and SIDS as the 5 highest concentrations of lead were found in SIDS children. Althoff et al. (1987) found no toxic levels of arsenic, lead, cxadmium, mercury, pentachlorphenol (PCP) and carbon monoxide in various organs and in blood, while Erickson et al. (1983) found significant differences in the levels of lead in liver

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and ribs between SIDS victims and a control group. There were no significant differences between the levels of lead in other organs and no significant differences in the levels of cadmium. The problem of exposure of infants to toxic agents was underlined by the discovery of critical levels of persistent chlorohydrocarbons in mother's milk (Hapke 1985; Ende 1987). The „Deutsche Forschungsgemeinschaft" (DFG) recommended an estimate of the level of toxic agents in mother's milk when the nursing period was longer than 4 months (Mitteilungen XII 1984). Because of their lipophilia, chlorohydrocarbons especially concentrate in fatty tissue, are mobilised during lactation and taken up by the infant through the mother's milk.

To obtain further information about the importance of toxic agents in relation to SIDS those substances that are found as impurities in food, especially in mother's milk were investigated e.g. lead, cadmium, mercury and organic chlorohydrocarbons (DFG-Mitteilungen XII 1984; Hapke 1985; Koransky and Forth 1985). In particular we wanted to find out if there were significant differences between cases of SIDS and cases from a control group with defined causes of death and if there were regional differences in the West German State of Lower Saxony.

Methods

The study was conducted within the scope of the investigation program "Sudden Infant Death Syndrome in Lower Saxony" in the years 1986–1988. All sudden and unexpected deaths in the age group 8 days − 2 years with unclear cause of death by autopsy were defined as SIDS. Infections of the upper respiratory system, although common, were not considered to be a cause of death, because their role in the mechanism of death is still a topic of debate (Althoff 1980; Wilske 1984; Kleemann et al. 1989). The control group consisted of children from the age of 8 days − 2 years with known causes of death, e.g. violent death, cardiac defect or congenital malformation. During autopsy 1 kidney, 5–20 g subcutaneous fatty tissue and 3–5 ml blood from the opened right heart were taken. The specimens were stored at −18°C until the time of investigation. The substances, our abbreviations and the examined organs are shown in Table 1. The concentrations of the heavy metals are given in µg/kg wet weight (ww) or µg/l (Tables 2–4). Samples of kidney were analysed by atomic absorption spectrometry (graphite furnace atomisation) using a decomposition bomb after digestion with nitric acid. The concentration of lead in blood was directly analysed by graphite furnace atomisation. The determination of murcury was performed analogously by cold vaporisation. The analysis of persistent chlorohydrocarbons was performed according to the modified procedure of Stijve and Cardinale (1974).

The following substances were considered: The polychlorinated biphenyl (PCB)- isomers 28, 52, 101, 138, 153 and 180, total PCB-isomers, alpha-, beta- and gamma-HCH, HCB, HepE, dieldrin and total DDT (p,p'-DDT; p,p'-DDE; p,p'-DDD). All concentrations are given in µg/kg fat.

Table 1. Scheme of analysis

Substance	Organ	Analysis method
Lead	blood	atomic-absorption-spectrometry
Cadmium	kidney	atomic-absorption-spectrometry
Mercury	kidney	atomic-absorption-spectrometry
Hexachlorbenzene (HCB)	fatty-tissue	gas chromatography
Alpha-, Beta-, Gamma- hexachlorcyclohexane (α-, β-, γ-HCH)	fatty-tissue	gas chromatography
Heptachlorepoxide (HepE)	fatty-tissue	gas chromatography
Dieldrine	fatty-tissue	gas chromatography
Total dichlordiphenyl-trichlorethane (DDT)	fatty-tissue	gas chromatography
Polychlorinated biphenyls (PCB)	fatty-tissue	gas chromatography

Results

1. *Heavy metals*

The concentration of heavy metals in cases of SIDS were split into 3 groups. The first group contained cases from purely urban areas, the second from rural areas and the third group from the districts of Goslar and Nordenham (Gosl/Nord). In the 2 districts are lead and zinc works which are among the largest in the Federal Republic of Germany, so that the districts are considered to be particularly highly polluted (Thron et al. 1978; Hartmann 1986; Krause et al. 1987a, b). The 3 SIDS groups were compared with each other and with the control group. Such a comparison was possible because all specimens were analysed with identical methods in the same laboratory.

There were no differences in blood lead concentrations between the 4 groups (Table 2). Although the blood lead concentrations from the SIDS cases and from the

Table 2. Comparison of blood lead concentrations from different areas (µg/l). DL = detection limit

	SIDS			Controls
	Urban	Rural	Gosl./Nord.	
n	20	19	7	13
Age	158	145	172	234
Range	DL–75	12–85	DL–70	DL–150
Mean	30.0	39.6	41.6	54.8
Std.-Dev.	18.2	18.6	24.6	41.4
Median	26.5	40.0	50.0	50.0

Table 3. Comparison of cadmium concentration in renal tissue from different areas (µg/kg ww)

	SIDS			Controls
	Urban	Rural	Gosl./Nord.	
n	19	23	12	18
Age	160	158	162	217
Range	3–171	7–423	2–292	1–410
Mean	48.6	68.7	73.7	99.7
Std.-Dev.	54.6	97.1	89.8	137.5
Median	30.0	24.0	44.0	35.0

Table 4. Comparison of mercury concentration in renal tissue from different areas (μg/kg ww)

	SIDS			Controls
	Urban	Rural	Gosl./Nord.	
n	19	23	12	18
Age	160	158	162	217
Range	14–418	12–154	11–5823	DL–3663
Mean	116.4	55.2	615.7	420.7
Std.-Dev.	120.2	33.3	1654.7	1059.0
Median	69.0	47.0	56.5	43.0

Table 5. Persistent chlorohydrocarbons in fatty tissue (μg/kg ww, $n = 23$, age = 163 days)

	SIDS/Urban			
	Range	Mean	Std.-Dev.	Median
HCB	15–225	80.7	64.3	60
α-HCH	DL–2	1.1	0.5	1
β-HCH	5–135	42.6	32.7	36
γ-HCH	5–40	13.3	8.6	11
HepE	DL–5	0.8	1.5	0
Dieldrine	1–24	7.6	6.0	5
DDT	20–787	270.5	215.3	181
PCB	61–1151	273.1	288.4	175

Table 6. Persistent chlorohydrocarbons in fatty tissue (μg/kg ww, $n = 23$, age = 176 days)

	SIDS/Urban			
	Range	Mean	Std.-Dev.	Median
HCB	2–94	44.1	25.6	47
α-HCH	DL–2	1.1	0.5	1
β-HCH	10–149	29.2	29.0	19
γ-HCH	5–93	13.8	18.0	9
HepE	DL–3	0.3	0.9	0
Dieldrine	2–16	5.0	3.4	4
DDT	47–615	187.2	160.5	134
PCB	63–556	148.8	103.6	121

Table 7. Persistent chlorohydrocarbons in fatty tissue (μg/kg ww, $n = 17$, age = 263 days)

	Controls			
	Range	Mean	Std.-Dev.	Median
HCB	24–375	123.5	109.4	71
α-HCH	DL–5	1.8	1.2	2
β-HCH	10–447	83.3	104.2	35
γ-HCH	5–38	14.2	7.4	11
HepE	DL–5	0.6	1.4	0
Dieldrine	2–29	9.3	7.3	7
DDT	38–839	280.1	220.8	215
PCB	65–943	243.1	201.8	194

control cases increased with age, no clear dependence on age could be seen. The correlation coefficient (r) of the total group was 0.48, with no differences between the groups. There were also no significant differences in cadmium and mercury concentrations between the 4 groups (Tables 3, 4).

Although the concentration of mercury showed no dependence on age in all groups ($r = 0.27$), the cadmium concentration in kidneys in all groups increased with age ($r = 0.76$). There were higher levels of mercury in the Goslar/Nordenham group and in the control group and the 2 highest concentrations were measured in these 2 groups. Excluding these 2 highest values, the mean for the group of Goslar/Nordenham was 77.3 μg/kg ww (wet-weight) and 75.1 μg/kg ww for the control group.

2. Persistent chlorinated hydrocarbons

SIDS cases were divided into an urban group and a rural group. These groups were compared with each other and with a control group of mainly urban cases (Tables 5–7). No dependence on age could be detected for all substances analysed ($r = 0.02–0.21$). No significant differences could be found between the rural and the urban group of SIDS nor between the urban group and the control group. The concentrations of HCB, alpha and beta HCH and dieldrin were significantly lower in the rural group than in the control group ($P = 0.05$). No significant differences were seen for gamma HCH, HeptE, total DDT and PCBs. The highest concentrations of chlorohydrocarbons were determined for PCBs, total DDT and HCB. Also beta HCH, which has a liposolubility higher than that of alpha and gamma HCH, was found in higher concentrations.

Discussion

Good corroboration was found between our results for harmful substances and the literature despite different analytical methods (Althoff et al. 1987; Drasch et al. 1988; Köhler-Schmidt and Bertram 1988). The special importance of lead lies in its neurotoxic effects on the pre- and postnatal development of the child. Correlation between disvolution of infants and increased levels of lead in blood have been described (Bellinger et al. 1987). On the other hand Thron et al. (1978) could not prove any malfunction of the peripheral nervous system when investigating the distal N. ulnaris of patients of varying ages including infants aged 3–6 years with lead levels of 100–200 μg/l. Lead absorption by the foetus starts in the 12th weeks of pregnancy (Barltrop 1969). Intestinal resorption by children can amount to 50% of the lead uptake whereas for adults it is only 10% (Bernard and Lauwerys 1985). The blood lead concentrations of 41 SIDS cases and living children from a control group, found by Drasch et al. (1988) are similar to our results. However we cannot confirm the correlation between high lead levels and the occurrence of SIDS. In our studies the highest lead concentration of the SIDS-group (75 μg/l) was only 50% of the highest concentration in the control group (150 μg/l). According to standards (Bewertungsmaßstäbe) of the "Institut für Wasser-, Boden-, und Lufthygiene", which are the most rigorous, blood lead concentrations lower than 150 μg/l are regarded as quite safe for the health of children and women in child-bearing age. Monitoring is recommended at concentrations of 150–250 μg/l, although a danger to health is not discernible. A long term danger to health is not excluded if concentrations exceed 250 μg/l and it is recommended to eliminate or reduce sources of pollution (Krause et al. 1987a). No concentrations higher than 150 μg/l were found in our samples. The concentrations of the SIDS group generally reached approx. 25% of this value.

Cadmium is found in concentrations of 22–33 μg/kg wet weight (ww) in kidneys of foetuses and newborn children (Schulte-Löbbert et al. 1978) and occurs as the second most frequent heavy metal in the air after lead („Umweltbundesamt UBA" 1977). However, the main intake of cadmium occurs with food (Forth 1983). The highest concentrations of cadmium are found in the kidneys, especially in the renal cortex (Pesch 1988). Our results for cadmium in renal tissue correspond with those of Althoff et al. (1987), who found a mean of 73.09 μg/kg ww with a minimum of 5 and a maximum of 816 μg/kg ww. Our results also correspond with the concentrations measured by Köhler-Schmidt and Bertram (1988), who reported a minimum of 4.38 and a maximum of 358 μg/kg ww. The standard value for cadmium is 3000 μg/kg ww (Merian 1984) and concentrations of 200000–300000 μg/kg ww are considered to be critical. At these levels irreversible malfunction of the kidneys occurs (WHO 1977; Schaller et al. 1980; Ryan et al. 1982). Even though these values apply only to adults, no toxic influences of cadmium on the death of infants can be deduced.

Althoff et al. (1987) found the mean concentration of mercury to be 76.93 μg/kg ww with a maximum at 552 μg/kg ww (mean 50.00 μg/kg ww). These values correspond with our measurements if the 4 highest values of the control group and the group Goslar/Nordenham are excluded. The standard value for mercury concentration in the renal tissue of adults ranges from 200–2600 μg/kg ww. In cases of death after intravenous injection or ingestion of $HgCl_2$, 56900 and 13600 μg ww respectively were measured after a survival time of 2 h (Baselt 1982; Dittmann and Pribilla 1985). No explanation for these increased values could be found. However similar values in a control group of adults with no known health problems were observed.

The persistent chlorohydrocarbons are used as pesticides or in industry (PCBs). These substances are very problematic because they accumulate in fatty tissues due to their high liposolubility. While the concentrations of the pesticides – which were forbidden in West Germany a few years agoe – have decreased, the polychlorinated biphenyls show no such changes ("DFG-Mitteilungen" XII 1984). No other bibliographical data is available, about concentrations of persistent chlorolhydrocarbons in fatty tissues of infants except for Lenz and Köhler-Schmidt (1988), who investigated the PCB concentrations of SIDS cases and of a control group without finding any significant differences. A comparison between mother's milk from 308 mothers of a nursing group and the fatty tissues of 117 mothers showed that the concentrations of HCB, beta-HCH, DDT and PCB in the fatty tissues of these children were 5–6 times lower than the concentrations in mothers' milk or in the mother's fatty tissues. There were no differences between the milk and the fatty tissues of the mothers ("DFG-Mitteilungen" XII 1984). It is striking that the mean concentrations of persistent chlorolhydrocarbons are higher in the urban cases and in the control group – which also included urban cases – than in rural cases. This difference can be explained for the polychlorinated biphenyls with higher concentrations of these substances in industrial areas (Juszkiewicz et al. 1977 cited by Hahne 1985, Dillon et al. 1981). But for the pesticides, these differences are surprising, although a similar observation has been made for mother's milkd ("DFG-Mitteilungen" XII 1984). This may be caused by the different nutritional behaviours of the rural and the urban population. While the urban population often consumes food from foreign countries, where these pesticides are still used in agriculture, the rural population consumes more home-produced food, which is less contaminated with such residues because those compounds are prohibited in the western industrial nations.

It is not possible to determine whether the toxic agents measured are a danger to the health of an individual and could eventually appear after decades but critical toxic concentrations can be excluded as the cause of death in these children.

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