

Current level of 2,2',4,4'-tetrabrominated diphenyl ether in human adipose tissue in Sweden -a risk factor for non-Hodgkin's lymphoma?

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Abstract

Levels of the tetrabrominated diphenyl ether, 2,2',4,4'-TeBDE, in the adipose tissue in 1995-1997 of 77 individuals from Sweden were determined. The individuals, both men and women ranging from 28 to 85 years in age, represent 19 patients with non-Hodgkin's lymphoma (NHL), 23 patients with malignant melanoma, 8 patients with other cancers or in situ changes and 27 persons without cancer. The mean levels of 2,2',4,4'-TeBDE was 5.1 ppb (range 0.6-28) on lipid basis for the 27 persons without malignancies. For NHL patients the mean level was 13 ppb (range 1.0-98). A dose responsive elevated risk, OR 2.7 (95% CI 0.5-18) and 3.5 (95% CI 0.7-22), respectively, was found for NHL when the cases and controls were compared in the two highest concentration groups with the lowest group.

Introduction

The aim of this study was to determine levels of PBDEs, represented by 2,2',4,4'-TeBDE, in the adipose tissue of patients with NHL and malignant melanoma and also in the adipose tissue of persons with no cancer malignancy. Further correlation of levels with cancer, age and sex as well as with occupational form of activity was studied. The occupation aspects will be reported later.

The monitoring of levels in humans is an important undertaking when making estimates concerning the population's exposure to persistent halogenated compounds, both known and unknown. The ultimate aim of the monitoring of these compounds in any product, process or activity emitting to the environment is the environmental contamination and thereby a potential human exposure and a consequent health risk.

The occurrence of polybrominated diphenyl ether, PBDE, in the environment has been known since the early 80's (1). The origin of this group of compounds in the tissues of humans is a consequence of the physical, chemical and biological properties of PBDE, many of which are shared with the other persistent organohalogenes, and the extensive past and present use of PBDE mainly as a flame retardant. The total exposure path-way to humans is believed to

consists of varying degrees of food-chain exposures, skin contact and inhalation (2,3). Until today only a few reports on the levels in human tissue have been published and more data is urgently needed to answer questions on the present exposure and the consequent risks (4,5).

Among the polybrominated diphenyl ethers, PBDEs, the 2,2',4,4'-TeBDE congener, also denoted BDE #47 in accordance with the PCB notation, is the one which is most prevalent, present at the ppb level, in human tissue. In 1997 we reported for the first time, in connection with a feasibility project on determination of halogenated persistent compounds in the adipose tissue of patients with non-Hodgkin's lymphoma in Sweden, on the identification of PBDE #47, an other TeBDE, two PeBDEs and one HxBDPE isomer in human tissue (4).

There is a typical pattern of PBDEs in biological tissues with distinct profiles for the different homologue groups. Out of the total 209 theoretical isomers we have recently detected 19 tetra to hexa isomers in the blubber of pilot whale (6) and one can expect to find at least half of these in human tissue if a method detection level on ppt is used. This current study uses a method detection level on ppb level and therefore PBDE #47 is the only isomer we here report on.

Material and Methods

The human adipose tissue samples. Adipose tissue samples, 1-10 grams, were taken in 1995-1997 from 77 Swedish males and females between the age of 38 and 85 years. The persons were either newly diagnosed cases with NHL (n=19), malignant melanoma (n=23), other cancer malignancy or cancer in situ (n=8) or healthy persons (n=27) hospitalised for benign diseases. None of the patients had yet received medical treatment for their cancer.

Chemical analyses of PBDE. The 77 coded samples were analysed with GC-MS, R=500, EI ionisation, SIM mass spectrometry of M (m/z 483.7) and M+2 (m/z 485.7) using deca PCB (m/z 509.7, m/z 511.7) as the internal standard. Quantification was done by comparing the relative response of the target compounds against the internal standard in both the sample and in a known standard solution of 2,2',4,4'-TeBDE. Sample clean-up was performed by SFE, supercritical fluid extraction, using CO₂ as the extraction media (7). The PBDEs were collected in the pesticide fraction following LC separation from the trapping column. This fraction was analysed for tetra PBDEs as described above and also for pesticides and PCBs, to be reported separately.

Statistical analyses. Logistic regression analyses was used (SAS/STAT) to estimate the odds ratio (OR) and the 95% confidence interval (CI). The data treatment took in consideration age and gender.

Results and Discussion

The presence of 2,2',4,4'-TeBDE was confirmed in all 77 samples. In table 1 the levels in ng/g lipid and mean ages for both males and females in the four different groups (NHL, melanoma, other cancers or cancer in situ and no-cancer) are given. The levels are expressed as mean and median levels, and the ranges are given for the different categories as well as for age.

The levels of 2,2',4,4'-TeBDE were higher for men than for women in all categories. The highest levels were seen in patients with NHL. The patients with malignant melanoma did not differ from the controls.

Table 1. Mean and median levels expressed in ppb, ng/g lipid, of 2,2',4,4'-TeBDE in the adipose tissue of 77 Swedish individuals in four different categories of cancer and no-cancer.

Categories		Age (y)		2,2',4,4'-TeBDE		
		mean	range	mean	median	range
NHL	(n=19)	63	42-77	13.0	5.3	1.0-98.2
-Men	(n=12)	63	42-77	16.0	6.9	1.1-98.2
-Women	(n=7)	64	57-70	7.8	3.3	1.0-22.3
melanoma	(n=23)	62	28-85	4.8	1.9	0.6-32.4
-Men	(n=15)	63	28-85	6.7	2.6	0.6-32.4
-Women	(n=8)	62	46-82	1.5	1.3	1.1-2.4
other cancers	(n=4)	70	64-77	7.1	4.6	2.2-17.2
cancer in situ	(n=4)	64	61-66	5.1	4.4	3.1-8.2
no-cancer	(n=27)	64	38-79	5.1	3.2	0.6-27.5
-Men	(n=17)	66	38-79	5.8	3.9	0.6-27.5
-Women	(n=10)	63	47-74	3.8	2.0	0.7-11.8

In table 2 the risk for NHL is accounted for. This is based on the comparison of the cases with the controls in three groups, with nine individuals in each, depending on the levels of 2,2',4,4'-TeBDE.

Table 2. Odds ratio (OR) and 95% confidence interval (CI) for NHL in relation to levels of 2,2',4,4'-TeBDE in the adipose tissues of 19 individuals with diagnosed NHL and 27 individuals with no-cancer complaints.

Categories	< 2.05	2.05-<4.91	≥ 4.91 ppb
NHL patients	3	7	9
no-cancer patients	9	9	9
OR	(1.0)	2.7	3.5
CI	-	0.5-18	0.7-22

Conclusions

The results show that PBDE, here represented by 2,2',4,4'-TeBDE, has found its way to humans and is now present in the adipose tissue of the general population in Sweden. The correlation between age and levels of 2,2',4,4'-TeBDE is obscure, and does not follow the trend usually seen for the persistent organochlorine compounds. Further, a connection with NHL can not be excluded at this moment.

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References

1. Andersson Ö and Blomqvist G. Polybrominated aromatic pollutants in fish in Sweden. *Chemosphere*, **1981**, 10, 1051.
2. Bergman Å, Österman C, Nybom R, Sjödin A, Carlsson H. *Organohalogen Compounds*, **1997**, 33, 414.
3. Jansson B, Andersson R, Asplund LT, Litzén K, Nylund K, Sellström U, Uvemo UB, Wahlberg C, Wideqvist U, Odsjö T and Olsson M. Chlorinated and brominated persistent organic compounds in biological samples from the environment. *Environ Toxicol Chem*, **1993**, 12, 1163.
4. Lindström G, van Bavel B, Hardell L and Liljegren G. Identification of the flame retardants polybrominated diphenyl ethers in adipose tissue from patients with non-Hodgkin's lymphoma in Sweden. *Oncology Reports*, **1997**, 4, 999.
5. Klasson Wehler E, Hovander L and Bergman Å. New organohalogens in human plasma - Identification and quantification. *Organohalogen Compounds*, **1997**, 33, 420.
6. Lindström G, Wingfors H, dam M and van Bavel B. Identification of 19 Brominated Diphenylethers in Long-Finned Pilot Whale (*Globicephala melas*) from the Atlantic. **1998**, *submitted*.
7. Lindström G, van Bavel B and Broman C. Determination of chlordane in human adipose tissue by SFE-LC off-line MS. *Organohalogen Compounds*, **1996**, 27, 253.