

Biomonitoring of PCDD/Fs in populations living near portuguese solid waste incinerators: Levels in human milk

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Abstract

In the context of two Environmental Health Surveillance Programs, launched in response to public and scientific concern in relation to waste incinerators located near Lisbon and in Madeira Island, two human biomonitoring projects have been started in Portugal, focussed in dioxins and dioxin-like compounds in human milk. Results from the undertaken studies have already provided data on the extent and pattern of dioxin body burden of both studied groups as well as a preliminary temporal trend of dioxin levels for the population residing near Lisbon incinerator. The present paper investigates difference between exposed and non-exposed subjects under study and, from a preventive perspective, possible covariates of the dioxin levels in human milk. Emissions from both incinerators appear to be well controlled as there is no increase of human body burden of dioxins as measured in human milk of individuals living near these facilities. Concerning other determinants of dioxin levels, results suggest confirmation of previously found significant age-dependent trend towards higher levels of dioxins in aged subjects. On the contrary, association between mother's levels of dioxins and parity lost significance. Apart from the issue of incineration, the general conclusion for the general population is that living in Lisbon as compared to Madeira results in higher milk dioxin levels and possible health risks. The profile of the single congeners for PCDD/Fs in human milk from Madeira and Lisbon shows similar contributions for 12378-PCDD, 23478-PCDF, 123678-HCDD and 2378-TCDD, that account altogether for about 84% of the total identified dioxin body burden in the studied groups.

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1. Introduction

Dioxins and dioxin-like compounds are among the most toxic environmental pollutants that can be produced through waste incineration (either hazardous, municipal, or from hospital or slaughterhouse). Studies of human exposure to this kind of compounds have shown dioxin blood

and milk levels as significant biomarkers of exposure (Deml et al., 1996; Glynn et al., 2003; Bocio et al., 2004; Cerna et al., 2004; Pirard et al., 2004; Schuhmacher et al., 2004; Wittsiepe et al., 2004; Yang et al., 2004; Agramunt et al., 2005; Kumagai and Koda, 2005). Therefore, human milk as well as blood or its components have been widely used in biomonitoring programs to assess human exposure to dioxins and dioxin-like compounds (Wittsiepe et al., 2000; Lakind et al., 2001; Joas et al., 2004; Schecter et al., 1994).

Compared to blood, milk has particular advantages in dioxin exposure monitoring: no invasive sampling

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techniques are needed and the higher lipid level facilitates analysis of the lipid-soluble compounds. However, the use of mother's milk in probability-based surveys to extract results for the general population is questionable, since only a specific demographic segment (women, at reproductive age, breast-feeding, and thus non-representative of the general population) is being considered. For biomonitoring programs, carried out to provide data on dioxin exposure (particularly where there is little or no information), to evaluate temporal and spatial trends, and ultimately to assist in policy design to improve public health and safety, it is appropriate and very important to monitor dioxin exposure through human milk due to several reasons: (1) milk reflects maternal body burden of lipophilic chemicals during pregnancy and thus a measure of critical foetus' exposure to those compounds; (2) being a human food and the first and main foodstuff for most newborn babies, milk can be a very significant pathway for infant exposure to dioxins. As such, human milk levels of these compounds may reflect the cumulative exposure during a determinant although short period (breast-feeding period) within individual lifespan; (3) because large volumes can be collected non-invasively, milk is also a convenient sampling specimen for biomonitoring purposes if it is collected taking into consideration all the relevant factors influencing fat content and thus levels of lipophilic compounds, namely the time of sampling during lactation, breast-feeding patterns and maternal characteristics (Needham and Wang, 2002).

The WHO European Centre for Environment and Health has conducted several studies (Brouwer et al., 1998; Solomon and Weiss, 2002; Malisch and van Leeuwen, 2003) in human milk, designed to assess levels and changes in levels of polychlorinated dibenzo-*p*-dioxins (PCDDs), polychlorinated dibenzofurans (PCDFs) and selected dioxin-like polychlorinated biphenyls (PCBs) in countries worldwide.

There is limited information on the dioxin body burden of the general population or specific groups in Portugal. Reis et al. (2002, 2004a,b); and Sampaio et al. (2004a,b) reported levels of PCDD/Fs and PCBs in whole blood and human milk from people residing in the vicinity of one from two incineration facilities: a municipal solid waste incinerator operating in the Metropolitan Area of North-Lisbon since 1999, and an updated incinerator at Meia Serra, Madeira Island, that recommenced operating in June 2002 to process solid waste, either municipal, or from hospital or slaughterhouse. Data were produced in the context of two Environmental Health Surveillance Programs launched in response to the existing public and scientific concern in relation to waste incinerators and in the perspective that, in relation to suchlike facilities, this kind of data are of utmost relevance in environmental health.

The main goal of each Program has been to monitor magnitude as well as spatial and temporal trends of specific indicators of both the exposure to the environmental agents of greater concern and the potential adverse health

effects in subjects living in the area under influence of the corresponding facility. Several human biomonitoring projects have therefore been started, some of them focussed in dioxins and dioxin-like compounds and using human milk levels as biomarkers of exposure.

Supposing emissions from these incinerators under control, the hypothesis of investigation was: (i) the dioxin internal dose of subjects living in the area under potential influence of each facility is not different from that of individuals with similar characteristics but farther place of residence and work; (ii) dioxin environmental levels, as determined by adequate biomarkers, do not increase along each facility's life. Therefore, in a first phase, baseline levels for dioxin exposure have been established in human milk from two well defined groups, for comparison: breast-feeding women living in the area under potential influence of each facility and women of similar background but residing and working farther from the incinerator. In order to monitor time trends, measurements have been (and still continue to be) repeated periodically.

Ultimately and relatively to each facility, results of dioxin milk levels from the undertaken studies provided *first indicative data* on the extent and pattern of dioxin body burden of the studied populations. For the incinerator near Lisbon, a preliminary temporal trend in milk dioxin levels has been obtained, which enabled provisional conclusions on dioxins source control effectiveness. However, full exploration of results has not yet been performed to investigate: (i) maintenance of non-significant difference between exposed and non-exposed individuals when an enlarged group composed by all subjects from both studies is considered; (ii) possible covariates of the dioxin levels in this whole group, for prevention priorities. These investigations are the objective of the present work.

2. Experimental

2.1. Sampling

Apparently healthy pregnant women, not-known occupationally exposed to dioxins, primiparous and/or breast-feeding first child or, at least, 3 years after breast-feeding the last child, living at residing area for more than 1 year, volunteered to participate in the biomonitoring study after written informed consent. Altogether, study group included 181 volunteers, being 123 from Lisbon area (*Lisbon community*) and 58 from Madeira (*Madeira community*). In relation to specific living area, 73 (potentially exposed) reside at a maximum distance less than 5 km from an incineration facility and 108 (controls) live and/or work far from the plant for more than 5 km. Exposed and non-exposed women are as much as possible similar in relevant socio-demographic characteristics, in order to avoid between-group bias.

Between 1999 and 2003, human milk samples (≈ 40 ml) were collected in decontaminated vials and through breast-pumps provided to volunteers, during a morning visit to

the women's residence 30 days after delivery. For gathering relevant information to identify parameters that might have influenced the individual PCDD/Fs body burden, a questionnaire was applied. In addition to personal data, residence, parity, number of breast-fed children and breast-feeding duration of previous children, profession, smoking habits, use of medicines, and specific dietary habits (mainly consumption of meat, fish, dairy and local food) have been evaluated. Samples were frozen ($-20\text{ }^{\circ}\text{C}$) until analysis.

2.2. Analytical procedures

Milk was collected in chemically cleaned glass bottles and frozen within the next few hours. All samples were shipped on dry ice by an international courier to ERGO Research Laboratory in Hamburg, Germany for dioxin analysis. The samples were stored frozen until analysed. Seven dibenzodioxin, and ten dibenzofuran congeners were analysed by high resolution gas chromatography coupled with high resolution mass spectrometry. All analyses were performed following the isotope dilution method. The 17 native and ^{13}C labelled standards used were obtained from Cambridge Isotope Laboratories, USA and from Wellington Laboratories, Guelph, Canada.

Solvents were supplied by Promochem (cyclohexane, hexane and dichloromethane), Baker (diethyl ether), and Mallinckrodt (ethanol, toluene). Silica gel, alumina oxide, sodium sulphate, potassium oxalate, sulphuric acid and potassium hydroxide were obtained from Merck. The method is described in detail by Fürst et al. (1992).

Levels of dioxin compounds are reported in pg/g, or parts per trillion (ppt), lipid, and in World Health Organization (WHO) dioxin toxic equivalents (TEQs). In addition, lipid content in each sample was gravimetrically measured. Pooled milk samples and method blank samples were also analyzed as part of a quality control procedure (QA/QC).

Before extraction all 17 2,3,7,8 substituted ^{13}C -labelled PCDDs/PCDFs are added to the samples. After spiking, the samples are extracted with adequate solvents using a liquid/liquid extraction for milk. The clean up is done on multicolumn systems involving carbon-on-glass fibre. The measurement is performed by means of high resolution gas chromatography/high resolution mass spectrometry (HRGC/HRMS) on a Micromass AutoSpec operating at a resolution of 10000 using a DB-5 capillary column. The quantification is carried out by the isotope dilution method.

The analytical method applied for human milk was successfully tested in various national and international quality control studies and proficiency tests (WHO, 1995; ICDF, 2001).

2.3. Statistical analysis

Data base management was performed using Microsoft Access 2000 (9.0.3821 SR-1) and, for the statistical analyses, SPSS software version 12.0 for Windows was used.

Significance level was generally fixed at $\alpha = 0.05$. To describe categorical variables, counts and percentages have been used. Numerical variables were described by their arithmetic means, medians, standard deviation and range of variation. Since PCDD/F levels suggest some deviation from normal distribution, appropriate test (Mann–Whitney) was used for comparative analysis across areas of residence, communities and types of parity. The relationship between age and PCDD/F levels was estimated by computing Spearman's correlation coefficient.

When PCDD/F levels were recoded to percentage of results above median or 75th percentile, Chi-Square test was used to study relationship between these variables and area of residence, community and parity and Mann–Whitney test for the relationship with age. In order to estimate magnitude of statistical association through odds ratio adjusted for covariates, multiple logistic regression has been used, considering as dependent variable PCDD/F levels with cut-off in median and in 75th percentile. To decide on variables to enter and stay in the multiple model, environmental health relevance in bivariable analysis and missing values lesser than 1% were the criteria.

3. Results and discussion

Analysis performed in the studied variables such as age, main professional activity, relevant dietary and smoking habits has shown that differences in relation to specific living area (exposed versus control area) were not statistically significant. These findings led to the conclusion that the results to be obtained from the present study are not likely to be confounded by a selection bias.

To investigate possible influencing factors on dioxin body burden as determined in human milk, living area of the subjects, community, age, parity and several other personal and environmental variables (namely professional activity and hobbies considered risky for higher exposure, present or past smoking habits, intake frequencies of fruit and vegetables, and preferential consumption of meat or fish) have been studied. From all statistical analyses performed, only living area, community, parity and age have been identified as relevant factors in the relationship with dioxin body burden.

Table 1 summarizes comparative analysis of PCDD/F human milk levels across areas of residence (exposed and non-exposed or control), communities (Lisbon and Madeira) and types of parity (primiparae and multiparae), as well as correlation between age and dioxin levels. Results are given in pg WHO-TEQs per gram of fat. In relation to the participants' specific living area, median and mean PCDD/F levels are practically identical for exposed and non-exposed (control) women (Table 1 and Fig. 1), with differences not statistically significant ($p = 0.659$). These results indicate that dioxin milk levels of the group living in the area of potential influence of each incinerator are not significantly increased by their PCDD/F stack emissions. This is both an important

Table 1
Comparative analysis of WHO-TEQs (pg/g fat) in human milk across areas of residence, communities and types of parity, and correlation between age and dioxin levels

Variables		<i>n</i>	Median	Mean	SD	Min.	Max.	R_s	<i>p</i>
Area	Exposed	73	9.1	9.5	3.9	2.8	20.9	–	0.659 ^a
	Control	108	9.3	9.1	3.3	3.0	19.9		
Community	Lisbon	123	10.6	10.6	3.1	4.4	20.9	–	<0.001 ^a
	Madeira	58	5.8	6.5	2.4	2.8	13.7		
Parity	Primiparae	98	9.2	9.2	3.7	2.8	20.9	–	0.618 ^a
	Multiparae	75	9.3	9.4	3.4	3.7	16.9		
Age (years)		181	30.0	29.7	6	18	52	0.351	<0.001 ^b

R_s – Spearman's correlation coefficient.

^a Mann–Whitney U-test.

^b Spearman's correlation analysis.

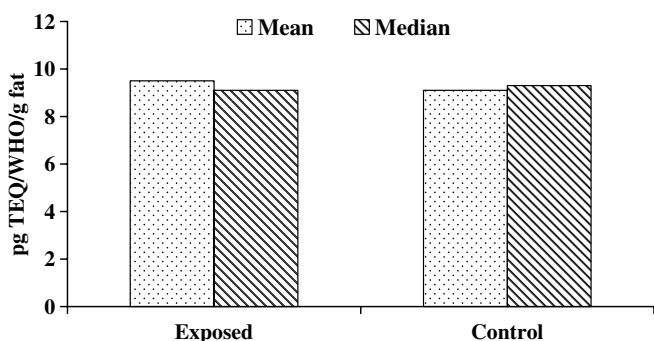


Fig. 1. Comparative analysis of PCDD/F milk levels across area of residence in relation to incinerator.

finding and accurate statement, supporting the dioxin sources control effectiveness.

Still from Table 1 and also from Fig. 2, it can be observed that, concerning studied communities, women from Lisbon show considerable higher median PCDD/F levels in comparison with those from Madeira (10.6 and 5.8 pg WHO-TEQ/g fat, respectively), being differences statistically significant ($p < 0.001$).

Overall mean age of studied breast-feeding women was about 30 years with standard deviation of 6 years within a range of variation from 18 to 52 years. The results for total TEQs in human milk were positively associated with

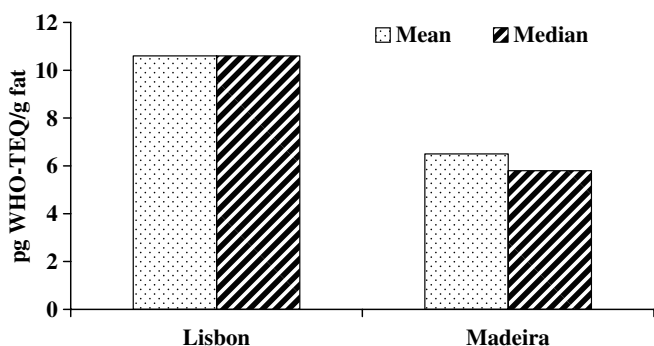


Fig. 2. Comparative analysis of PCDD/F milk levels across Lisbon and Madeira communities.

age of women (Table 1), showing a significant correlation for the whole group ($R_s = 0.351$; $p < 0.001$).

When parity is considered, it can be seen that median and mean PCDD/F levels are quite similar for primiparae and multiparae mothers (Table 1), with differences not statistically significant ($p = 0.618$). Although same results have also been found by other authors (Focant et al., 2002), they are not in accordance with the well documented expected decrease of PCDD/F concentrations in milk from primiparae to multiparae (Fürst et al., 1992; Kiviranta et al., 1999; Clewell and Gearhart, 2002), suggesting that other variables besides number of children might be controlled when multiparae are included.

Table 2 shows comparative analysis of breast-feeding women with higher versus lower dioxin body burden in relation to area of residence, community, parity and age. As can be observed, statistical associations presented in Table 1 are maintained when cut-off in median and in 75th percentile of PCDD/F levels are considered. From these results it is interesting to notice that despite higher percentage of exposed women with more extreme dioxin milk levels (cut-off in 75th percentile: 46.7% versus 37.8%), differences are not statistically significant ($p = 0.292$). Considering the median cut-off, a slightly higher percentage of exposed women was found for the lower PCDD/F levels group (42.2% < median versus 38.5% \geq median), being the difference not statistically significant ($p = 0.606$). From all these results it can then be assumed that the exposure was relatively homogeneous in the different PCDD/F level groups identified through cut-offs, suggesting no association between exposure from incinerators and dioxin levels, as expected.

As shown in Table 1, total WHO-TEQs in human milk were positively associated with age of women, showing a significant correlation for the total population ($R_s = 0.351$; $p < 0.001$). However, when women's age is analysed by area of residence, community and parity (Table 3), differences are not statistically significant for community ($p = 0.848$), meaning that age is not a confounding factor for the dioxin levels of women from Lisbon and Madeira. Concerning parity, although (as expected) associated with age ($p < 0.001$), it can not be considered a confounding

Table 2

Comparative analysis of breast-feeding women with higher and lower dioxin body burden (pg WHO-TEQs/g fat) in relation to area of residence, community, parity and age

Variables		PCDD/ Fs < Median		PCDD/ Fs ≥ Median		<i>p</i>	PCDD/Fs < 75th percentile		PCDD/ Fs ≥ 75th percentile		<i>p</i>
		<i>n</i>	% ^a	<i>n</i>	% ^a		<i>n</i>	% ^a	<i>n</i>	% ^a	
		Area	Exposed	38	42.2		35	38.5	0.606 ^b	51	
	Control	52	57.8	56	61.5		84	62.2	24	53.3	
Community	Lisbon	41	45.6	82	90.1	<0.001 ^b	80	59.3	42	93.3	<0.001 ^b
	Madeira	49	54.4	9	9.9		55	40.7	3	6.7	
Parity	Primiparae	49	57.6	49	55.7	0.794 ^b	75	58.1	23	53.5	0.594 ^b
	Multiparae	36	42.4	39	44.3		54	41.9	20	46.5	
Age	Median	27.0		31.0		<0.001 ^c	28.0		32.0		<0.001 ^c
	Mean	28.2		31.2			28.7		32.4		
	SD	6.0		5.3			5.8		5.0		
	Min–Max	18–52		19–42			18–52		20–42		

^a Percentages within PCDD/Fs groups defined by median and 75th percentile cut-offs.

^b Chi-Square test.

^c Mann–Whitney U-test.

Table 3

Comparative analysis of age (years) in relation to area of residence, community and parity

Variables		<i>n</i>	Median (years)	Mean (years)	SD (years)	Min. (years)	Max. (years)	<i>p</i>	
Age (years)	Area	Exposed	73	29	30	6	18	42	0.809 ^a
		Control	108	30	30	6	19	52	
	Community	Lisbon	123	29	30	6	18	42	0.848 ^a
		Madeira	58	30	30	6	20	52	
	Parity	Primiparae	98	27	27	5	18	40	<0.001 ^a
		Multiparae	75	33	33	6	21	52	

^a Mann–Whitney U-test.

factor for the women dioxin body burden since, as can be seen from Table 1, it is not associated with PCDD/F levels in human milk ($p = 0.618$).

From the several personal and environmental variables analysed for contribution to the PCDD/Fs concentration in human milk, only area of residence (or participants' specific living area), community, parity and age have been considered to include in the multiple regression model mainly due to their environmental health relevance and also missing values lesser than 1%. As can be observed from Table 4, identified statistical association of Lisbon community with higher PCDD/F levels is confirmed (OR = 16.13 for cut-off in median; OR = 22.17 for cut-off in 75th percentile),

meaning that even controlling influent variables such as age, Lisbon still presents higher probability for the occurrence of more elevated dioxin levels. This finding is in agreement with the expected higher environmental pressure of dioxins in Lisbon (as a large urban industrialized centre) when compared with Madeira, assuming effective control of PCDD/F emissions from both the incineration facilities operating in Lisbon and in Madeira.

The pattern of the single congeners for PCDD/Fs in human milk from Lisbon and Madeira (Fig. 3) was very similar being the highest contributions, in descending order, from 12378-PCDD, 23478-PCDF, 123678-HCDD, and 2378-TCDD. Altogether, these four individual

Table 4

Multiple logistic regression analysis relative to higher dioxin levels in human milk (pg WHO-TEQ s/g fat)

Covariables	PCDD/Fs ≥ Median			PCDD/Fs ≥ 75th percentile		
	OR	<i>p</i> _{OR}	IC _{OR} (95%)	OR	<i>p</i> _{OR}	IC _{OR} (95%)
Area (Exposed vs. Control*)	0.66	0.272	0.32–1.38	1.54	0.294	0.69–3.42
Age – in years	1.15	<0.001	1.07–1.24	1.18	<0.001	1.08–1.29
Community (Lisbon vs. Madeira*)	16.13	<0.001	6.36–40.94	22.17	<0.001	4.45–110.99
Parity (Primiparae vs. Multiparae*)	1.58	0.291	0.68–3.70	1.74	0.249	0.68–4.47
Model <i>p</i> value	<0.001			<0.001		
Hosmer and Lemeshow <i>p</i> value	0.108			0.964		
Predicted %	74.6			79.1		

* Reference category; OR: Odds ratio adjusted to covariables.

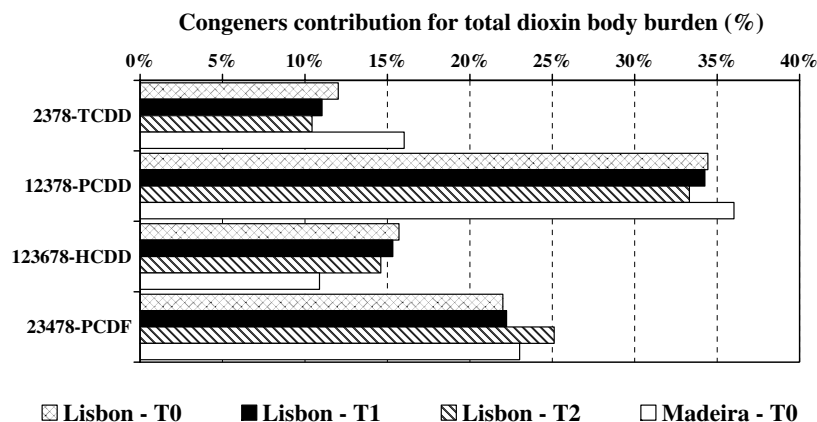


Fig. 3. Contribution (%) of most relevant individual congeners for the total identified dioxin levels in human milk samples.

congeners accounted for about 84% of the total identified dioxin body burden in the studied groups and moments of observation, within a range from 83% to 86%.

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