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Human biomonitoring of polychlorinated biphenyls (PCBs) in plasma of former underground miners in Germany – A case-control study

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ABSTRACT

Polychlorinated biphenyls (PCBs) are very persistent organic pollutants of severe environmental concern due to their toxic properties. Former underground miners might have been exposed to this substance group due to the widespread use of PCBs in hydraulic oils from the late 1960s to the mid 1980s. We have conducted a blinded case-control study in order to evaluate the possibility of retrospective exposure assessment of PCBs using human biomonitoring in former underground miners decades after the last possible exposure.

We have identified n = 34 male former underground miners and n = 136 age-matched male control persons from the database of patients of our occupational outpatient clinic aged between 47.9 and 83.7 years at the time of sampling (June 2006–June 2016). These archived plasma samples have been blinded and analysed for 21 different PCB-congeners using a validated and quality controlled procedure using GC/MS (LOQ: 0.01 µg/L).

Highly significant differences between cases and age-matched controls were only found for the PCB-congeners PCB 74 and PCB 114. The median (95th percentile) levels of PCB 74 in cases and controls were 0.126 µg/L plasma (0.899 µg/L plasma) vs. 0.058 µg/L plasma (0.368 µg/L plasma) and the 95th percentile levels for PCB 114 were 0.039 µg/L plasma vs. 0.017 µg/L plasma. Linear regression models revealed that this difference in plasma levels was unequivocally attributed to the underground mining activity. Thus, retrospective exposure assessment for underground miners by use of human biomonitoring seems feasible and further studies with a particular focus on this special group of workers should be performed.

1. Introduction

Polychlorinated biphenyls (PCBs) are technical mixtures of 209 possible theoretical congeners with varying chlorine content that have been extensively used in the past due to their excellent technical properties, e.g. flame resistance, thermal stability and low electrical conductivity (Frame et al., 1996). PCBs are highly persistent in the environment and especially the higher chlorinated congeners were shown to bioaccumulate in the food chain, leading to an age-dependent body burden in the general population, mainly in industrialised countries (Becker et al., 2002; Xue et al., 2014; Schettgen et al., 2015). This led to a ban of the production and use of PCBs (or PCB-containing products) in Germany in 1989 (in the late 1970s in the United States) and finally worldwide with the Stockholm Convention, which came into force in 2004 (Stockholm convention on persistent organic pollutants (POPs)). More recently, inadvertent formation and distribution of some PCB-congeners (e.g. PCB 11) has been reported in the production of paints and pigments (Vorkamp, 2016).

PCBs are considered to be carcinogenic to humans (Group 1) by the International Agency for Research on Cancer (IARC) (Lauby-Secretan et al., 2013). The Deutsche Forschungsgemeinschaft (DFG) has classified them in category 4 of the carcinogenic substances (non-genotoxic carcinogen) (DFG, 2017).

There are numerous reports on the toxicological effects of exposure to PCBs (IARC, 2013). One of the longest known effects of PCBs are skin alterations in persons with direct contact to PCB-containing oils (Rogan et al., 1988). However, there are strong hints that PCBs might also have immunotoxic, neurotoxic and endocrine disrupting properties (Grandjean et al., 2001; Seegal, 2000; Harper et al., 1995; Heilmann et al., 2010; Gaum et al., 2016). A possible link between the development of diabetes and internal exposure to PCBs is also currently under discussion (Lee et al., 2006; Esser et al., 2016) as well as a causal relationship between exposure to PCBs and non-hodgkin-lymphoma (Kramer et al., 2012). Furthermore, especially lower chlorinated PCB-congeners (and their metabolites) are discussed to have genotoxic and cancer initiating properties and are responsible for shortened telomere lengths in lymphocytes of exposed workers (Lehmann et al., 2007; Ludewig and Robertson, 2013; Ziegler et al., 2017).

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Large amounts of PCBs had been used since the late 1960s in underground mining after a severe accident in a Belgian coal mine in 1956, where mineral oils caused a fire and death of 267 miners. They were mainly used in hydraulic fluids that were for example applied to run the large coal cutters. Due to the flame retarding properties of PCBs, their use was especially advantageous in the potential explosive underground atmosphere (Reichel, 1973). In the mid 1980s PCBs were replaced by other less persistent flame retardants until the final ban of PCB usage in 1989 in Germany. Many of these coal mines are now no longer operative in Germany; however, many machines and PCB-containing devices are still underground. In combination with the mining companies' plan to slowly reduce the water pumping in these abandoned mines (leading to a rise in groundwater level), the (unknown) load of PCBs in these mines and the potential release into rivers and groundwater is currently under intensive discussion in Germany.

Underground miners might have been exposed to these hydraulic fluids not only in repair tasks, but also in regular operation, as they often report leakages in the hydraulic pipes or alignments with intensive skin contact to the oils at these damp and narrow working places in their anamnesis. Consequently, a considerable amount of underground miners might have been exposed to PCBs during their work in the time between the late 1960s and the mid 1980s, when PCBs had been gradually replaced by Ugilec®, a structurally similar, but far less persistent flame retardant. With respect to the toxic potency of PCBs and the long latency of potential diseases, a quantitative exposure assessment for these workers would be favourable. However, retrospective exposure assessment for these workers using human biomonitoring is connected with several difficulties: first, the PCB-mixture formerly used in these hydraulic fluids (Clophen A30 – Clophen A60; Aroclor 1016 – Aroclor 1254) is widely unknown (even for the mining company and producers of hydraulic fluids) and therefore, a specific congener pattern that could be used to retrospectively quantify the exposure to these mixtures is also unknown.

Secondly, the time since last exposure is extremely long. At best, the last exposure occurred more than 30 years ago. Although the plasma half-life for some higher chlorinated PCBs has been reported to be in the range of 15–25 years, it is questionable whether the internal exposure of former underground miners might still be significantly above the continuously decreasing background exposure of the general population. Furthermore, it is not known whether miners have indeed been exposed to these higher chlorinated congeners.

Thirdly, these former underground miners are now very old, aged between 60 and 85 years. There are hardly any data available on internal exposure to PCBs of a non-exposed comparison group, as most studies have only collected data from persons to the age of 65 years.

In order to overcome these problems and to clarify the question whether it is feasible to retrospectively quantify the potential PCB-exposure of underground miners in Germany, we decided to conduct a blinded case control study using archived plasma samples from patients of our occupational outpatient clinic. To our knowledge, this is the first study that assesses the internal exposure to PCBs in former underground miners in Germany.

2. Materials and methods

2.1. Study groups

From the database of patients in our occupational outpatient clinic, n = 34 male patients (= cases) were identified who reported to have formerly worked in underground mining during their anamnesis. The age of these persons at the visit of our clinic ranged between 47.9 and 83.8 years (median: 72.4 years).

From the same database, two of the authors (AE and CS) have compiled a age-matched control group (n = 136, meaning a 1:4 match) from male patients of the same age who did not report to have worked in underground mining or as electrician where they could have been exposed to PCBs in the past. In addition to age, the date of blood sampling for cases and controls was also matched with a subordinated priority in order to account for the decreasing background exposure to PCBs and potential effects of long-term storage of the samples in this period of time. The age of the control persons ranged from 47.9 to 83.7 years (median: 72.3 years). The age distribution of both groups is summarised in Table 1.

Table 1
Age distributions for the group of former underground miners and controls in our study.

		Former underground miners	Controls
n		34	136
mean age		71.16	71.10
median age		72.36	72.26
std. deviation		8.29	8.20
minimum age		47.92	47.85
maximum age		83.77	83.73
percentiles	25	66.04	66.53
	50	72.36	72.26
	75	77.86	78.04
	95	82.53	82.45

All of those persons have attended our outpatient clinic between June 2006 and June 2016. Plasma samples were collected at the visit, immediately aliquoted and stored at −80 °C in Eppendorf caps until analysis. All persons gave written consent about the donation of blood samples for scientific purposes. An approval of the ethics committee of the RWTH Aachen University (EK 206/09) is available for the collection of these blood samples.

The laboratory staff including the corresponding author (TS) has been blinded with respect to the information on group membership until all analyses were finished. After that, results were decoded and evaluated by AE and CS.

2.2. Analysis of PCBs in plasma

These plasma samples were not only analysed for the 6 indicator congeners (PCB 28, 52, 101, 138, 153 and 180) and the 12 dioxin-like congeners (PCB 77, 81, 105, 114, 118, 123, 126, 156, 157, 167, 169, 189), but also for three additional congeners (PCB 66, 74, 99) that were previously found in elevated concentrations in plasma of former capacitor workers (Seegal et al., 2011) as well as in persons with high indoor exposure to PCBs (Meyer et al., 2013). We used a slightly modified method approved by the Deutsche Forschungsgemeinschaft (DFG) described previously (Schulte et al., 1993; Schettgen et al., 2011).

A 2 ml sample of the plasma was deproteinised using formic acid. The PCBs were then extracted with n-hexane (containing PCB 54 as internal standard for the non-dioxin-like congeners as well as $^{13}C_{12}$-labelled PCBs for all 12 dioxin-like congeners), cleaned up on a silica gel column and analysed by GC/EI-MS in Selected Ion Monitoring-Mode (SIM). We used a matrix-matched calibration curve prepared in bovine serum in the range of 0.04–3 µg/L. The limit of quantification (based on a signal-to-noise ratio of 6) was determined to be 0.01 µg/L plasma for all analytes investigated. For quality control purposes, bovine serum was spiked with all analytes at a concentration of 0.4 µg/L and included in every analytical series. The between-day imprecision in this period of time (August 2016–November 2016, n = 23) has been determined to be in the range of 3.2%–9.9% for all analytes.

Furthermore, a reagent blank was included in every series. Due to an accurate cleaning of reagents and glassware, no PCBs could be detected in these reagent blanks. Accuracy of our results is checked by biannual successful participation in a round robin for the determination of the indicator-PCBs in plasma in the environmental concentration range organised in Germany (www.g-equas.de).