POLYCHLORINATED BIPHENYLS AND SEMEN QUALITY IN YOUNG HEALTHY MEN LIVING IN A CONTAMINATED AREA IN BRESCIA, NORTH ITALY

Rota Matteo[1], Ceretti Elisabetta[2], Calza Stefano[1], Viola Gaia Claudia Viviana[2], Marullo Monica[2], Zani Danilo[2], Amoresano Angela[3], Fontanarosa Carolina[3], Lorenzetti Stefano[4], Montano Luigi[5,6], Donato Francesco[2]

[1] Unit of Biostatistics and Bioinformatics, Department of Molecular and Translational Medicine, University of Brescia, Brescia, Italy.
[2] Unit of Hygiene, Epidemiology and Public Health, and Unit of Urology, Department of Medical and Surgical Specialties, Radiological Sciences and Public Health, University of Brescia, Brescia, Italy.
[3] Department of Chemical Sciences, University of Naples Federico II, Naples, Italy.
[4] Department of Food Safety, Nutrition and Veterinary Public Health, Italian National Institute of Health (ISS), Rome, Italy.
[5] Andrology Unit and Service of Lifestyle Medicine in UroAndrology, Local Health Authority (ASL) Salerno, Coordination Unit of the network for Environmental and Reproductive Health (EcoFoodFertility project), "Oliveto Citra Hospital", Salerno, Italy.
[6] PhD Program in Evolutionary Biology and Ecology University of Rome Tor Vergata, Rome, Italy.

INTRODUCTION

Polychlorinated biphenyls (PCBs) are a group of 209 compounds (congeners) produced in the past century up to the 1970s-1980s, when they were banned in most countries due to their toxicity and environmental persistence [1]. PCBs are classified as persistent organic pollutants (POPs) and due to their toxicity they have been banned under the Stockholm Convention in 2001 [1]. Despite their banning in most countries, they are still found all over the world, and high levels of these compounds have been found in people who live or work in areas where electronic wastes are collected and managed [2,3].
Several studies on humans have shown an association between PCBs and metabolic and endocrine diseases, damage to nervous systems, development, immunological, and cardiovascular diseases. PCBs have been classified by the International Agency for Research on Cancer (IARC) as carcinogenic to humans [4]. A heavy decline in semen quality has been observed in both high and medium-low-income countries in last decades, and exposure to endocrine disruptors, including PCBs, has been considered to play a role. Recently, various studies found that PCB levels in serum and/or seminal plasma were associated with the quality parameters of human semen (i.e., sperm count, morphology, and motility) [2,3].
A chemical factory (Caffaro) located in Brescia, North Italy, produced organochlorine compounds, including PCBs, from the 1930s to 1984. PCBs were discharged in irrigation channels and thence accumulated in the soil of a nearby agricultural area and entered the food chain. Investigations carried out in 2001–2003 showed a high PCB concentration in the soil, surface water, animals, and vegetables, and in humans, mainly in people who had consumed locally produced animal food [5,6]. A second survey showed persistence of high serum levels of various PCB congeners and total PCBs in some people living in Brescia in 2013-14 [7].

AIMS

This study aimed i) to quantify PCBs serum and semen levels in a healthy sample of young men and to ii) investigate the relationship between several PCB congeners, functional groups, and total PCB with sperm concentration, total motility, and proportion of normal morphology cells in a contaminated site in Brescia, North Italy.

MATERIALS AND METHODS

A prospective study within the FAST randomized trial [8] was conducted between April 2018 and June 2019. Serum and semen PCBs concentration and semen quality parameters were assessed at the enrollment (baseline) and after 4 and 8 months. Each semen sample was collected in a sterile container through masturbation, after at least 3 days and at most 5 days of abstinence from sexual activity. The semen sample was delivered to the laboratory within 30–40 min after collection, whereas a portion of semen (<50 µl) was processed immediately for the spermiogram. A 20 ml blood sample was collected for each subject under fasting conditions.

PCBs were measured in serum and semen using mass spectrometry in the Department of Chemical Sciences, University of Naples Federico II, Italy. A minimum concentration equal to half the quantification limit (0.0005 ng/ml) was assigned for congeners detected in at least 30% of the subjects.

Functional PCBs groups were classified as follows: congeners with immunotoxic activities (PCB 138, 153 and 180); low-chlorinated PCBs with pseudo-oestrogen activity (PCB 28, 52 and 153); high-chlorinated PCBs with anti-oestrogenic activity (PCB 170, 180 and 194) and PCBs that can induce phenobarbital (PCB 101, 153, 180 and 194).

Due to the longitudinal nature of the data, a linear mixed model with robust variance estimation was fitted to assess the relationships between PCBs congeners, functional PCBs groups and total PCBs with sperm concentration, while a generalized linear mixed model with Poisson family was used to evaluate cells' total motility and normal morphology counts, with overall cells number as offset. A Bonferroni correction was applied to account for test multiplicity. Since estimates by univariate and multivariable models provided similar results, only the former are shown here.

RESULTS

A total of 143 young healthy men (median age 20 years, IQR 19-21 years) participated in the study. The geometric mean of total PCBs was 3.90 ng/mL (median 3.85, range 3.43-4.56 ng/mL).

Main results are shown in Table 1. A standardized unit increase in semen immunotoxic PCBs concentration was associated with a 5% and 6% reduction in sperm total motility and count of cells with normal morphology, respectively. For such outcomes, an inverse association emerged also for semen total PCBs.

Table 1. Results of univariate mixed model of serum and semen PCB congeners, functional PCB groups and total PCBs on sperm concentration, total motility and cell with normal morphology.

	Sperm concentration (10^6/ml)	Total motility (%)	Cell with normal morphology (%)
	$\widehat{\beta}$ (95% CI)	IRR (95% CI)	IRR (95% CI)
Serum PCB concentration			
Immunotoxic PCBs	0.08 (-1.8, 2.0)	0.98 (0.97, 0.99)*	0.99 (0.96, 1.01)*
Pseudo-oestrogen PCBs	0.45 (-1.2, 2.1)	0.97 (0.96, 0.98)*	0.98 (0.96, 1.00)*
Highly chlorinated anti-oestrogenic PCBs	-0.88 (-3.2, 1.5)	1.06 (1.05, 1.08)*	1.09 (1.06, 1.13)*
Total PCBs	-0.07 (-0.3, 0.2)	1.00 (1.00, 1.00)	1.00 (1.00, 1.01)
Semen PCB concentration			
Immunotoxic PCBs	2.5 (-0.6, 5.6)	0.95 (0.93, 0.96)*	0.94 (0.90, 0.99)*

Pseudo-oestrogen PCBs	-0.03 (-2.2, 2.1)	0.97 (0.95, 0.98)*	0.95 (0.92, 0.98)*
Total PCBs	0.45 (-0.4, 1.3)	0.99 (0.98, 0.99)*	0.98(0.97, 0.99)*

*Statistically significant after Bonferroni correction for test multiplicity.

CONCLUSIONS

We found that various PCB congeners and some functional groups, though not total PCBs, were associated with a decreased sperm motility and count of sperm cells with normal morphology in young healthy men living in a high industrialized and PCB contaminated area in Italy.

REFERENCES

1. Porta M, Zumeta E. Implementing the Stockholm Treaty on Persistent Organic Pollutants. Occup Env Med. 2002 Oct;59(10):651–3.
2. Yu YJ, Lin BG, Qiao J, et al. Levels and congener profiles of halogenated persistent organic pollutants in human serum and semen at an e-waste area in South China. Environ Int. 2020 May;138:105666.
3. Lin BG, Chen CR, Chen XC, et al. Effects of organochlorine exposure on male reproductive disorders in an electronic waste area of South China. Environ Int. 2021 Feb;147:106318.
4. International Agency for Research on Cancer (IARC). Polychlorinated Biphenyls and Polybrominated Biphenyls, VOLUME 107. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Lyon, France, 2016.
5. Apostoli P, Magoni M, Bergonzi R, et al. Assessment of reference values for polychlorinated biphenyl concentration in human blood. Chemosphere. 2005 Oct; 61(3): 413-421.
6. Donato F, Magoni M, Bergonzi R, et al. Exposure to polychlorinated biphenyls in residents near a chemical factory in Italy: the food chain as main source of contamination. Chemosphere. 2006 Aug; 64(9):1562–1572.
7. Magoni M, Donato F, Speziani F, et al. Substantial decline of polychlorinated biphenyls serum levels 10years after public health interventions in a population living near a contaminated site in Northern Italy. Environ Int. 2016 Oct;95:69-78.
8. Montano L, Ceretti E, Donato F, et al. Effects of a Lifestyle Change Intervention on Semen Quality in Healthy Young Men Living in Highly Polluted Areas in Italy: The FASt Randomized Controlled Trial. Eur Urol Focus. 2022 Jan;8(1):351-359.