



Review

Do polychlorinated biphenyls cause cancer? A systematic review and meta-analysis of epidemiological studies on risk of cutaneous melanoma and non-Hodgkin lymphoma



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HIGHLIGHTS

- In 2015 IARC upgraded the classification of PCBs to carcinogenic to human.
- The studies on PCB exposure and risk of cancer provided discrepant evidences.
- Our results don't support the hypothesis that PCBs cause melanoma and/or NHL.

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ABSTRACT

In 2015 a IARC Working Group upgraded the classification of PCBs to Group 1 “Carcinogenic to humans”, also on the basis of evidence from epidemiological studies showing an excess risk for melanoma. Increased risks for non-Hodgkin lymphoma (NHL) and breast cancer were also reported though the evidence was limited. However, some recent reviews of studies on PCB exposure and risk of cancer provided discrepant findings. Therefore, we re-evaluated the association between exposure to PCBs and risk of melanoma and NHL by a systematic review and meta-analysis. We retrieved 11 independent cohort studies on occupationally exposed workers. About half of them showed increased standardized mortality or incidence ratios (SMRs or SIRs) for melanoma and none for NHL. The pooled SMRs were 1.32 (95% CI: 1.05–1.64) for melanoma and 0.94 (0.73–1.23) for NHL. Among population-based cohort and case-control studies with individual measures of PCB exposure, one only study was carried out on PCB exposure and melanoma, showing an odds ratio (OR) of 6.0 (2.0–18.2) for the highest compared to lowest quartile of PCB distribution. 13 cohort and case-control studies evaluated the association between NHL and PCB concentration in blood or subcutaneous fat, with summary OR = 1.5 (1.1–1.7) for the highest vs lowest quartile of PCB distribution. However, two cohort studies on people intoxicated by rice oil containing PCBs found no excess of deaths for skin cancer and inconsistent results for NHL. In conclusion, these findings do not provide a strong evidence that PCB exposure can increase the risk of melanoma and NHL in humans.

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1. Introduction

Polychlorinated biphenyls (PCBs) are organic compounds containing from one to ten chlorine atoms attached to a biphenyl nucleus, including 209 different congeners, largely produced as dielectric fluids in capacitors, transformers and other materials since the 1930s to the 1980s (ATSDR, 2003). After that date, their negative impact on the environment was apparent and subsequently their production and use were banned in most countries. Due to their long persistence in the environment and their bioaccumulation along the food chain, they have diffused everywhere and have contaminated virtually all human populations. Their possible effects on human health are a matter of concern and a large bulk of epidemiologic and toxicological research is available at present.

In 2016, the International Agency for Research on Cancer (IARC) upgraded the classification of the PCBs to Group 1 “Carcinogenic to humans” from the previous Group 2A classification “Probably carcinogenic to humans” (IARC, 2016). These compounds were classified in Group 1 on the basis of sufficient evidence of carcinogenicity in humans and experimental animals, and of the evidence of an aryl hydrocarbon receptor (AhR)-mediated mechanism of carcinogenicity for some PCB congeners similar to 2,3,7,8-tetrachlorodibenzopara-dioxin (dioxin-like PCBs) in both humans and experimental animals (Lauby-Secretan et al., 2013; IARC, 2016). The IARC Working Group concluded for sufficient evidence of PCB carcinogenicity for melanoma and limited evidence for non-Hodgkin lymphoma (NHL) and breast cancer. However, a recent meta-analysis found no evidence of association between PCB exposure and the risk of malignant melanoma (Boffetta et al., 2016). Two reviews on PCB exposure and the risk of NHL found contrasting results (Golden and Kimbrough, 2009; Freeman and Kohles, 2012). Another review of epidemiological studies on PCB exposure and risk of cancer showed some evidence for a possible role of PCB exposure in the development of NHL but inconsistent results for other cancers (Zani et al., 2013).

Because of these discrepancies between the IARC evaluation and the results of some reviews, we aimed to re-evaluate the association between exposure to PCBs and risk of cutaneous melanoma and NHL by a systematic review and meta-analysis.

2. Methods

We updated our previous search (Zani et al., 2013) considering also the studies cited in the IARC Monograph. The methods of this systematic review matched those described in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

The literature search covered the period January 2013–December 2016 and it was carried out using electronic databases of scientific research (PubMed, Scopus, Web of Science).

We conducted the bibliographic search using the following query strings for each electronic database: PubMed: (((PCB[All

Fields] OR (“polychlorinated biphenyls”[MeSH Terms] OR (“polychlorinated biphenyls”[All Fields] AND “biphenyls”[All Fields]) OR “polychlorinated biphenyls”[All Fields]) OR organohalogen[All Fields]) AND (((“tumours”[All Fields] OR “neoplasms”[MeSH Terms] OR “neoplasms”[All Fields] OR “tumors”[All Fields]) OR (“neoplasms”[MeSH Terms] OR “neoplasms”[All Fields] OR “cancer”[All Fields]) OR (“neoplasms”[MeSH Terms] OR “neoplasms”[All Fields] OR “neoplasm”[All Fields]))) AND (((cohort[All Fields] OR case-control[All Fields]) OR follow-up[All Fields]) OR longitudinal[All Fields]) AND (“2013/01/01”[PDAT]: “3000”[PDAT]) AND english[Language]))

Web of Science: (TOPIC:((((PCB OR polychlorinated biphenyls) OR organohalogen) OR organochlorine) AND ((tumours OR cancer) OR neoplasm)) AND (((cohort OR case-control) OR follow-up) OR longitudinal)) AND LANGUAGE:(English))

Scopus: ((PCB OR polychlorinated biphenyls OR organohalogen OR organochlorine) AND (tumour OR cancer OR neoplasm) AND (cohort OR case-control OR follow-up OR longitudinal))

We selected articles according to the following criteria: studies performed in humans, written in English, full text available, key terms present anywhere in the paper, articles with original data. We considered only a) occupational cohort studies and b) population-based cohort or case-control studies with direct measures of exposure to PCBs (in biologic samples) that allowed the computation of standardized mortality or morbidity ratios (SMR), relative risks (RR), odds ratios (OR) or other measures of association. Therefore we excluded studies with only indirect measures of exposure, such as place of residence, occupational history or PCB measurements in environmental matrices, animals or plants.

Studies investigating various chemicals, including PCBs, dioxins or other organochlorine, were considered only if separated measures for PCBs were available. We considered only studies that showed data on melanoma and Non Hodgkin Lymphoma.

We also included two cohort studies of Asian people undergoing mass poisoning by PCBs because both measures of total intake and of serum concentration of these chemicals were available, though not for each individual. Therefore, these cohorts were considered separately from the cohort and case-control studies with individual measures of PCBs.

Related articles were also searched for, so as the cited papers in the articles retrieved and in reviews. Two authors (C.Z. and F.D.) examined separately titles, abstracts and each paper included.

To avoid duplicate data, we considered only the most recent update or the most complete of two or more studies performed on the same population.

Among occupational cohort studies, only those reporting standardized mortality ratio (SMR), proportional mortality ratio (PMR) or standardized incidence ratio (SIR) were used for the meta-analysis, with a summary SMR based on the number of observed and expected deaths or cases in each study, as suggested by Wong and Raabe (1996). Studies reporting no case or death could not be used for calculating the combined SMRs. Studies that provided data only for all lymphopoeitic malignancies together, including leukemias, were excluded, whereas those reporting lymphomas (NHL

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