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Benzene and other solvents exposure and incidence of hematologic malignancies

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Introduction

Benzene and other solvents are widely distributed environmental contaminants known to cause cancer namely hematologic neoplasms [1]. Organic solvents, aliphatic and chlorinated hydrocarbons have also been linked to the development of leukemias [2, 3].

The International Agency for Research on Cancer (IARC) concluded that there was enough evidence that benzene exposure had carcinogenic effects in both humans and animals [4]. In fact, it was found a strong evidence that benzene exposure caused myeloid malignancies and there was also a positive association between benzene exposure and lymphoproliferative disorders [5]. Despite this, few epidemiologic studies have been able to address a relationship between the extent of benzene exposure and the risk of developing blood related malignancies.

We performed a systematic review and meta-analysis in order to clarify the current evidence of benzene/other solvents exposure and the development of hematologic malignancies.

Material and Methods

A literature search using PubMed was performed independently by each author (May 2019). Search terms used: (Lymphoid OR Myeloid cancers) AND (benzene OR solvents OR chemical). Relevant titles or abstracts were screened to determine the suitability of each publication, and full-text articles were retrieved.

Studies included in this meta-analysis had to meet all the following criteria: one of the exposures of interest was benzene or other solvents; the outcome of interest was the incidence of hematologic malignancies; a cohort or case-control design; the risk and corresponding 95% confidence intervals (CIs) or data to calculate these items had to be provided.

Data were collected independently by two authors. The following data were extracted from each study and included in the final analysis: the first author's name, year of publication, country of origin, gender, age, source of patients, number of cases/controls and risk factor assessment.

To determine whether to use the fixed- or random-effects model, we measured statistical heterogeneity. The homogeneity of odds ratios (ORs) across individual studies was quantified by the Q statistic and the I² score. Potential publication bias was assessed by using Begg's funnel plots and Egger's bias test. Sensitivity analysis was conducted, in which the meta-analysis estimates were calculated by sequential omission of every study in turn, in order to reflect the influence of the data from individual studies on the pooled ORs and evaluate the stability of results. Subset analyses were performed by disease subtype and geographic region. P<0.05 was considered statistically significant.

Results

A total of 2901 patients with lymphoid disorders and 7371 controls, 545 patients with myeloid disorders and 5626 controls were included in the present meta-analysis. Among the chosen studies, two were conducted in Europe, two in USA, and three in China.

We observed a significant adverse association between benzene and other solvents exposure and incidence of myeloid malignancies (OR = 2.14. 95%IC 1.64-2.80, I²=0%, P<0.55). Results for lymphoid

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malignancies were not significant, however Egger's bias test ($P = 0.003$) indicated a potential presence of publication bias.

The sensitivity analysis displayed that no study of myeloid malignancies disproportionately affected the summary risk estimates in this meta-analysis. The six specific studies ORs ranged from a low of 2.04 (95%CI 1.55–2.69) to 2.24 (95%CI 1.70–2.96), with no omission of any individual study.

In the subset analysis stratified by geographic region, the results are concordant with the main analysis.

Discussion

Human exposure to benzene/other solvents has been associated with a range of acute and long-term adverse health effects and diseases, including aplastic anaemia and hematologic malignancies of myeloid and lymphoid origin.

We attempted to clarify this possible relationship through a meta-analysis of seven case-control and cohort specific studies.

We demonstrated a significant adverse association between benzene/other solvents exposure and myeloid malignancies. However, contrary to other studies [6, 7], we could not demonstrate a relationship between benzene/other solvents exposure and lymphoid malignancies, possibly due to an observed publication bias. Correcting the observed asymmetry (through Trim and Fill method), a significant association is detected.

Our subset analysis according to geographical region, noted a higher risk of developing hematologic malignancies in China and USA than in Europe.

Considering the systematic review and the meta-analysis results, the authors emphasize that public health actions are needed to reduce the exposure of both workers and the general population to benzene [8], and other solvents.

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