

Effects of Indoor Endocrine-Disrupting Chemicals on Childhood Rhinitis

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Endocrine-disrupting chemicals (EDCs) are ubiquitous in our environment and pose a threat not only to the indoor environment but also to public health [1,2]. Despite the widespread presence of these chemicals indoors, our understanding of the extent and the health effects of exposure is limited by insufficient data on exposure patterns and the action of EDCs over a person's lifespan [3,4]. Previous evidence suggested that both individual and coexposure to low concentrations of EDCs in classrooms were associated with an increased risk of asthma, obesity, and an increased prevalence of nasal obstruction in the previous 3 months among children [5]. Furthermore, we found that exposure to EDCs was also associated with changes in the autonomic nervous system, specifically parasympathetic dysautonomia, thus suggesting that EDCs may increase parasympathetic activity, resulting in a subsequent increase in the risk of asthma, respiratory symptoms, and obesity [5]. In addition to the observed effect of EDCs on nasal obstruction [5], ie, one of the defining symptoms of rhinitis, asthma frequently coexists with allergic rhinitis (AR), which is a risk factor for the development of asthma [6,7]. However, no studies have yet addressed the effects of exposure to EDCs on rhinitis. Therefore, we aimed to assess the effect of indoor individual or combined exposure to EDCs on rhinitis in schoolchildren.

Data from a cross-sectional analysis of 845 participants from 20 schools in Porto, Portugal were analyzed. The evaluation included a self-administered ISAAC-based questionnaire [8] and a physical and clinical assessment (Supplementary file). Children were considered to have AR if

there was a positive answer to the question "Has your child ever had a problem with sneezing, or a runny nose or blocked nose when he/she did not have a cold or the flu?" combined with positive skin prick test results to common allergens. Current allergic rhinitis (CAR) was defined as a positive answer to the question "In the past 12 months, has your child had a problem with sneezing, or a runny nose or blocked nose when he/she did not have a cold or the flu?" [5]. The University Health Ethics Committee approved the study, and informed consent was obtained from the children's legal guardians. Among the 845 children included (49.2% girls), the prevalence of AR and CAR was 13.4% and 10.4%, respectively.

The indoor levels of 13 volatile organic compounds and 2 aldehydes identified as EDCs (toluene, o-xylene, m/p-xylene, hexane, ethylbenzene, styrene, cyclohexanone, butylated hydroxytoluene, benzene, benzaldehyde, tetrachloroethylene, 2-butoxyethanol, 2-ethyl-1-hexanol, formaldehyde, and acetaldehyde) were measured in 71 classrooms over 1 week during regular daily activities and under representative conditions of occupancy and use of the classrooms in winter. The complete sampling methodology has been described previously [5]. Principal component analysis (PCA) was used to identify major EDC patterns based on the 15 compounds. The PCA divided the EDCs into 2 principal components (PC1 and PC2). Generalized linear models and multinomial logistic regression models were used to measure the effect of individual or combined EDCs on AR and CAR. Analyses were performed without adjustment (model 0) and adjusted for age, sex, asthma, exhaled NO, and body mass index (model 1). PCA and mixed effect models were analyzed using RStudio, version 1.0.

A higher number of children with CAR was recorded in classrooms with higher median levels of formaldehyde (16.83 [13.3-25.1] $\mu\text{g}/\text{m}^3$ vs 14.93 [12.3-20.1] $\mu\text{g}/\text{m}^3$, $P=.018$) and higher PC2 scores (0.02 [-0.35 to 0.77] $\mu\text{g}/\text{m}^3$ vs -0.12 [-0.61 to 0.35], $P=.014$). A positive association was found between PC2 and the risk of CAR (OR, 1.44; 95%CI, 1.11-1.89). After adjustment, the effect size estimates were similar (OR, 1.35; 95%CI, 1.02-1.80). No significant associations were observed between individual EDCs and AR and CAR or between PC1 and rhinitis (Figure). In addition, levels of individual EDCs and PC1 scores were negatively associated with constriction velocity and baseline pupil diameter. Moreover, a positive association was found between constriction velocity and amplitude and baseline pupil diameter.

Our findings suggest that exposure to combined EDC levels in classrooms is associated with an increased risk of CAR. Similar to our previous study [5], these findings suggest that exposure to combined EDCs may have an effect on the respiratory health of children, thus increasing the risk of 1 or more symptoms including sneezing, runny nose, and blocked nose in the previous 12 months; these results also contribute to our understanding of the potential health risk of coexposure. Additionally, EDCs represented by PC2 showed that the compounds may interact within or between classes, with different and even opposite effects, suggesting that combinations of low doses of EDCs that are individually inactive may cause a biological effect [9]. EDCs represented by PC2 may act through pathways or mechanisms other

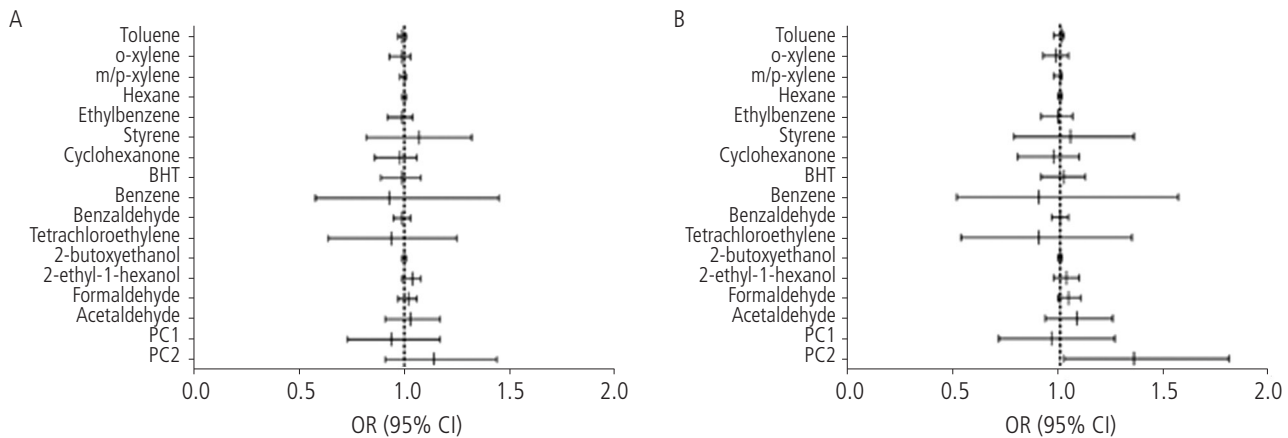


Figure. Association between endocrine-disrupting chemicals and (A) allergic rhinitis and (B) current allergic rhinitis (results adjusted for age, sex, asthma, exhaled NO, and body mass index). BHT, indicates butylated hydroxytoluene; PC1, principal component 1 (toluene, o-xylene, m/p-xylene, ethylbenzene, styrene, and benzene); PC2, principal component 2 (cyclohexanone, BHT, benzene, benzaldehyde, formaldehyde, and acetaldehyde).

than those represented by PC1, suggesting that children may respond differently when exposed to different combinations of EDCs. As previously proposed for asthma [5], changes in the autonomic nervous system (eg, ECD-induced parasympathetic dysautonomia) assessed through pupillometry may also play an important role in the development of CAR. However, the cross-sectional design does not allow us to establish a causal relationship between exposure to EDCs and rhinitis. Furthermore, on-site monitoring of indoor air pollution levels was not applied in the analysis. Although several studies have identified the role of the environment in the development of allergic rhinitis [10-12], the association between exposure to combined EDCs represented by PC2 and the increased risk of current allergic rhinitis is expected to be independent of other indoor exposures. Indicators of the severity of allergic rhinitis [13]—including sleep disturbance, impairment of daily and school activities, and symptoms—and severity of asthma were not taken into consideration. Thus, it will be important to assess the effect of long-term exposure to the school indoor environment to understand the extent of health effects. In conclusion, the present study highlights the negative effect of coexposure to EDCs in CAR. Our findings facilitate the implementation of recommendations to minimize exposures and to promote a healthy indoor environment.

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Conflicts of Interest

The authors declare that they have no conflicts of interest.

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