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Volatile organic compounds of possible microbial origin and their risks on childhood asthma and allergies within damp homes

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ABSTRACT

Background: Risk of indoor exposure to volatile organic compounds of purported microbial origin on childhood symptoms of wheezing, rhinitis, and/or eczema, and doctor-diagnosed asthma, rhinitis, and eczema, respectively, remain unclear.
Objective: To test hypotheses that total sum of 28 microbial volatile organic compounds (Σ26 MVOCs): 1) poses independent risk on doctor-diagnosed asthma, rhinitis, and eczema, respectively, as well as multiple symptom presentation with a minimum of the two of the above conditions (i.e. case); 2) is associated with significant interaction with absolute humidity (AH) on additive scale.
Methods: In a case-control investigation, 198 cases and 202 controls were examined during November 2001 – March 2002 period through home indoor air sampling, air quality inspection, and health outcome ascertainment.
Results: Not only the Σ28 MVOCs but also the global MVOC index were significantly higher within the homes of the cases with a high AH, compared to the controls with a low AH (all Ps < 0.001). Only the cases, but not the controls, were associated with a dose-dependent increase in the exposure variables of interest (Σ28 MVOCs) per quartile increase in AH ($P < 0.0001$ for the cases; $P = 0.780$ for the controls). Only among the children who live in a high AH homes, a natural log (ln)-unit of Σ 28 MVOCs was associated with 2.5-times greater odds of the case status (95% CI, 1.0–6.2; $P = 0.046$), compared to 0.7-times the odds (95% CI, 0.4–1.0; $P = 0.074$) of the same outcome among the low AH homes. Specifically, joint exposure to a high MVOCs and high AH was associated with 2.6-times greater odds of the doctor-diagnosed asthma status (95% CI, 0.7–8.91; $P = 0.137$).
Conclusion: Joint occurrence of high Σ28 MVOCs and AH was associated with a significant increase in the case status and asthma risks in an additive scale.

1. Introduction

Microbial volatile compounds (MVOCs) refer to a group of gaseous compounds, which are argued to be emitted during metabolic digestions by microbes (Korpi et al., 2009; Thrasher and Crawley, 2009; Van Lancker et al., 2008). Ever since their discovery during the 1990s, MVOCs have been proposed as sentinel markers of microbial infestation on hidden building surfaces (Wilkins and Larsen, 1995). At the same time, MVOCs may be a misnomer because, a growing body of evidence suggest that they are produced by not only by microbes, but also by synthetic building materials (Choi et al., 2016; Kim et al., 2007; Korpi et al., 2006; Malysheva et al., 2014; Matysik et al., 2008; Sahlberg et al., 2013; Schuchardt and Strube, 2013). Synthetic sources include recently painted indoor surfaces (Järnström et al., 2008), cleaning agents, automobile emissions (Nalli et al., 2006; Singer et al., 2006). Human behavior choices within indoor space, such as cigarette smoking, cooking, closing windows, also contribute to the generation of the putative MVOCs (Korpi et al., 2009; Newsome et al., 1965; Schleibinger et al., 2008). For example, professional building painters are exposed to a high concentration of 1-octen-3-ol, well-known MVOC, in conjunction with glycol ethers and other plasticizers, 2,2,4-trimethyl-1,3-pentanediol monoisobutyrate (TMPD-MIB) (Wieslander and Norback, 2010). On the other hand, laboratory experiments on microbial cultures

Abbreviations: Σ 28 MVOCs, Total sum of 28 purported microbial volatile organic compounds; aOR, adjusted odds ratio; BBzP, Benzylbutyl phthalate; DBH, Dampness in Building and Health; DEHP, di-(2-ethylhexyl)phthalate; ETS, environmental tobacco smoke; MVOC, microbial volatile organic compound; NILU, Norwegian Institute for Air Research; OR, odds ratio; PFT, perfluorocarbon tracer; PVC, polyvinyl chloride; RERI, relative excess risk due to interaction; TMPD-MIB, 2,2,4-trimethyl-1,3-pentanediol monoisobutyrate; TMPD-DIB, 2,2,4-trimethyl-1,3-pentanediol diisobutyrate; VOC, volatile organic compound; 95% CI, 95% confidence interval.

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on common building materials under various humidity levels have failed to produce clear VOC markers of microbial growth (Korpi et al., 1998; Schleibinger et al., 2008).

Indoor human exposure to putative MVOCs represents a growing public health concern in not only developed, but also developing countries for at least two reasons. First, some purported MVOCs, such as 1-octen-3-ol and 2-pentanol are significantly associated with ocular and nasal mucosa irritation (Elke et al., 1999; Wålinder et al., 2008), asthma and respiratory symptoms, including nocturnal breathlessness in children (Kim et al., 2007), allergic rhinitis (Araki et al., 2012), and sick building syndrome (Araki et al., 2010; Takeda et al., 2009), enhanced nasal lavage-myeloperoxidase and nasal patency reduction in a group of house painters (Wieslander and Norback, 2010), respectively. Human exposure to MVOCs under controlled setting could elicit eye and respiratory irritations and discomfort (Wålinder et al., 2008). Second, MVOCs occur at a higher concentration within damp spaces or those with a history of water damage, compared to the non-damp indoor spaces (Choi et al., 2016; Wieslander et al., 2007). As an estimated 25—50% of the residences in US and in Europe are damp (Lanthier-Veilleux et al., 2016), residents within damp indoor environments are likely to be exposed to MVOC mixture for an extended period (Araki et al., 2012; Araki et al., 2010).

To date, the toxicological properties of many compounds commonly accepted as MVOCs remain unknown (Korpi et al., 2009). Only a handful of studies have examined chronic exposure to MVOC within the home environment and their effects on respiratory health status (Araki et al., 2012; Billionnet et al., 2011; Choi et al., 2010; Sahlberg et al., 2013). While preliminary evidence suggest that joint effect of a complex mixture of the putative MVOCs could be synergistic (Cometto-Muñiz et al., 1997; Korpi et al., 1999), the combined risk of the putative MVOC mixture has never been systematically investigated, particularly in children. As such, there is a critical knowledge gap regarding childhood exposure to MVOCs and their role in asthma initiation and/or exacerbation.

Within the Dampness in Building and Health (DBH) study, we have investigated the indoor sources of 28 putative MVOCs (Choi et al., 2016). Here, we examine the same group of compounds: 1) for the independent risk of the total MVOC concentration on multiple symptoms of wheezing, rhinitis, and/or eczema (i.e., case status), as well as respective doctor-diagnosed status of asthma, rhinitis, and eczema; and 2) modification of MVOC risk by a composite index of absolute humidity. We test a hypothesis that the total concentration of 28 MVOCs (Σ28 MVOCs) is associated with a significantly larger risk within the damp homes on our health outcomes of interest, compared to the non-damp homes.

2. Material and methods

The participant enrollment and methods of an on-going Dampness in Buildings and Health (DBH) study have been described (Bornehag et al., 2004; Bornehag et al., 2005a; Bornehag et al., 2003a; Bornehag et al., 2005b; Bornehag et al., 2003b; Bornehag et al., 2005c; Choi et al., 2010; Holme et al., 2010). Present analysis focuses on Phase II case-control study ($n = 400$).

2.1. Health outcome measurements

The Phase II study incorporates both cross-sectional and nested components within its exposure assessment strategy. The nested component incorporate Phase I (March–April 2000) as well as the Phase II surveys (November 2001 – March 2002) within a case definition (Hasselgren, 2005). Specifically, four health outcomes are considered. To qualify as a 'case', parental reporting of a minimum of two symptoms of wheezing, rhinitis, and/or eczema without a cold within the last 12 months within two repeated surveys (Phase I and II) across 1.5-year period was required. Additional clinical examination was conducted to validate current clinical conditions of asthma ($n = 121$), rhinitis ($n = 99$), and eczema ($n = 129$), respectively. Diagnostic criteria for asthma include: a) at least three wheezing episodes prior to or since age 2; b) an observation of wheezing in addition to other atopic diseases; c) asthma medication use at any age; and d) clinical validation of asthma symptoms at any age. Diagnostic criteria for rhinitis required: a) ever having allergic rhinitis symptoms without a cold; b) mucosal tearing and/or watering symptoms following a contact with furred animals or pollen; c) present use of rhinitis medication. Eczema case definition required that the child have at least six months of remitting itching and redness in common body locations. For the control children, only those whose parent reported an absence of any allergy symptoms during both Phases I and II were invited. The controls were recruited from 1100 children, who are free of wheezing, rhinitis, and/or eczema, registered within local primary care clinics. The doctor-diagnosed cases represent subset of the questionnaire-based cases. That is, the cases children who do not meet the diagnostic criteria of given outcome were excluded ($n = 77$ for asthma; 99 for rhinitis; and 69 for eczema).

The cases and controls were further excluded if: (i) the home was renovated or remodeled due to water damage; and (ii) family relocated to a new residence between phase I and II. The medical examinations of the 400 children as well as the air, dust sample collection, and home inspection were completed concurrently during November 2001 and March 2002 period. A team of four pediatricians, allergists, and nurse practitioners examined all children following a structured anamnesis (Hederos et al., 2007). Allergy positive status was examined by screening the children's blood sample for IgE antibodies to 10 airborne allergens (Phadiatop®, Pharmacia & Upjohn Diagnostics, Uppsala, Sweden), including timothy, mugwort, birch, cat, horse, dog, house dust mites (*D. pteronyssinus* and *D. farinae*), and two mold genera (*Penicillium* and *Cladosporium*). The IgE-positive status was defined using a cut-off value at 1.2 kUA/l. Institutional ethical committee in Örebro, Sweden, approved the study.

2.2. Home exposure assessment by professional inspectors

Cross-sectional exposure assessment component include biological and air and dust samples sample collection as well as a comprehensive walk-through home inspections at the time of health outcome ascertainment (Choi et al., 2014). Average ventilation rate was measured in the room in which the index child spent most time, using validated perfluorocarbon tracer (PFT) technique (Nordtest, 1997; Stymne et al., 1994). Within the same location, temperature (°C) and relative humidity (%) were also measured instantaneously (VL2000 Temperature & Humidity Sensor, Vaisala, Helsinki, Finland) and continuously at every hour for a week (Mitec Satelite-TH, Mitec Instrument AB, Säffle, Sweden).

2.2.1. Air monitoring

The inspectors collected an air sample with SKC pocket pumps (Model 210-1002, SKC Blandford, Dorset, UK) in child's bedroom at 80 ml/min for 60 to 90 min (5 to 8 l) through Perkin Elmer adsorption tubes (glass, 300 mg Tenax TA). Sampling was conducted in a manner consistent with the family's lifestyle and habits in all children's homes. In order to monitor the extent of water damage, windows and doors were maintained shut during air sampling in the homes of cases and the controls. Samplers were placed 1 m above the floor in the room. Upon completion, the sampler was sealed with PTFE stoppers, shipped, and analyzed in Norway Institute for Air Research Norway within two weeks of collection. Use of adsorbent, preparation of adsorbent tubes, sampling equipment, sampling flow and safe sampling volumes, analytical methods, and analytical equipment follow international standards on ambient air quality DIN EN 14662-1 (DIN ISO 5725-2 and 3) with demonstrated reliability (Wu et al., 2004). Temporal reliability of Tenax TA for indoor air analysis was discussed elsewhere (Helmig, 1996; Klenø et al., 2002; Uhde, 2009).

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