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Exposure to inhaled THM: Comparison of continuous and event-specific exposure assessment for epidemiologic purposes

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ABSTRACT

Trihalomethanes (THMs) (chloroform, bromoform, dibromochloromethane, and bromodichloromethane) are the most abundant by-products of chlorination. People are exposed to THMs through ingestion, dermal contact and inhalation. The objective of this study was to compare two methods for assessing THM inhalation: a direct method with personal monitors assessing continuous exposure and an indirect one with microenvironmental sampling and collection of time–activity data during the main event exposures: bathing, showering and swimming. This comparison was conducted to help plan a future epidemiologic study of the effects of THMs on the upper airways of children. 30 children aged from 4 to 10 years were included. They wore a 3M™ 3520 organic vapor monitor for 7 days. We sampled air in their bathrooms (during baths or showers) and in the indoor swimming pools they visited and recorded their time–activity patterns. We used stainless steel tubes full of Tenax® to collect air samples. All analyses were performed with Gas Chromatography and Mass Spectrometry (GC-MS). Chloroform was the THM with the highest concentrations in the air of both bathrooms and indoor swimming pools. Its continuous and event exposure measurements were significantly correlated ($r_s = 0.69$ $p < 0.001$). Continuous exposures were higher than event exposures, suggesting that the event exposure method does not take into account some influential microenvironments. In an epidemiologic study, this might lead to random exposure misclassification, thus underestimation of the risk, and reduced statistical power. The continuous exposure method was difficult to implement because of its poor acceptability and the fragility of the personal monitors. These two points may also reduce the statistical power of an epidemiologic study. It would be useful to test the advantages and disadvantages of a second sample in the home or of modeling the baseline concentration of THM in the home to improve the event exposure method.

1. Introduction

The most prevalent process of water disinfection is chlorination with hypochlorous acid. The trihalomethanes (THMs)—chloroform, bromodichloromethane, dibromochloromethane, and bromoform (respectively $CHCl_3$, $CHBrCl_2$, $CHClBr_2$ and $CHBr_3$)—are major disinfection by-products (DBPs) (Kim et al., 2002), with chloroform the most abundant (Uyak et al., 2008). They are formed by reactions between the hypochlorous acid and the natural organic matter present in treated water (Rook, 1974). Their concentrations vary in time and across drinking-water distribution networks since they depend on a variety of factors, including but not limited to the composition of natural organic matter, pH, temperature, pipe length, and the chlorine dose (Yang et al., 2007). People are exposed to THMs during activities involving chlorinated water: drinking, showering, bathing, washing dishes, doing laundry, and going to swimming pools; baths or showers and swimming pool attendance appear to be the most important sources of exposure (Whitaker et al., 2003b; Nuckols et al., 2005b; Gordon et al., 2006a). The high volatility of these substances makes inhalation a potentially important pathway of exposure, but the relative importance of ingestion, dermal absorption, and inhalation has not been clearly established (Weisel and Jo, 1996; Aggazzotti et al., 1998; Gordon et al., 2006a; Caro and Gallego, 2007).

In addition, the human health effects of THM exposure are still an active research field. Some epidemiologic studies show weak associations between THM exposure and cancer of the bladder, the colon, and the rectum (Morris et al., 1992; Morris, 1995; Villanueva et al., 2007a). Chloroform and bromodichloromethane are classified as possibly carcinogenic to humans, while bromoform and dibromochloromethane cannot be classified for carcinogenicity (IARC, 1999). THM exposure also seems to be associated with adverse birth or pregnancy outcomes (Jo et al., 1990; Reif et al., 1996; Hinckley et al., 2005).

No studies have thus far assessed the local effects of chronic THM exposure on the upper airways. Such a study would require a specific exposure assessment focused on inhalation (even if other routes may have a significant contribution to the body burden). Two possible methods might include a direct and an indirect (Lioy, 1995) one, respectively continuous exposure to THM in personal air measured by a passive VOC badge, and an event-specific exposure assessment using

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an active sampling in microenvironments with Tenax® tubes. Assessing event exposure could be very costly and difficult to implement in practice regarding the number of potential sources of exposure mentioned upwards. Conversely it could be feasible if limited to the main sources of exposures: bathing/showering and pool attendance. The objective of this study was to compare continuous exposure to inhaled THM with the main event-specific (showering/bathing at home and in indoor swimming pools) exposure.

2. Methods

2.1. Data collection

Thirty children aged from 4 to 10 years from the families of staff at the EHESP School of Public Health in Rennes were recruited for a seven-day observation period. Each child's home was visited in March 2008. Bathroom air was sampled when they entered to bathe (bath or shower) until they left. Indoor air of each attended swimming pool was sampled for 1 hour, on a beach near the basin at 1 m height. We used stainless steel tubes filled with Tenax® TA 60/80 mesh (Supelco) and LFS-113 DC Gilian pumps (GE Sensing) with an output of 30 mL/min for bathrooms and 10 mL/min for swimming pools following recommendations of the standard method TO-17 (U.S. Environmental Protection Agency, 1999). Tubes were kept at room temperature with long-term storage brass caps and combined Teflon® ferrules until analysis, as suggested by Volden (2005). Time activity diaries reported the time spent in the bathroom and swimming pool during the study week.

For simultaneous personal air continuous monitoring, children continuously wore charcoal-based passive air samplers—organic vapor monitors (model 3520, 3M™) badges—according to the manufacturer's recommendations (3M Co., 2002). At the end of the study week, parents brought the badge back to the lab after snapping the closure cap onto the passive monitor body. Samples were frozen (−18 °C) until analysis. Badges with torn diffusion barriers were discarded.

2.2. Chemical analysis

2.2.1. Personal 3M™ organic vapor monitors (continuous exposure)

Diffusion rates through the monitor's membrane can be measured only for chloroform and bromoform. Data for other THMs are therefore not presented. THMs passively trapped in these 3M™ organic vapor monitors were eluted with 1 mL of carbon disulfide (CS_2) spiked with 1,2 dibromoethane (Aldrich, internal standard) with a final concentration of 0.5 mg/L in CS_2, in accordance with the procedure recommended by 3M™. A HP6890 gas chromatograph and an Agilent 5975C mass spectrometer were used for the analyses. 1 µL of the elution was injected through a split/splitless injector (split mode, ratio 1:5) into a silica capillary column (HP5MS fused, 30 m × 0.25 mm, 25 µm film thickness, J&W Scientific). The temperature program ran from 40 °C (5 min) to 80 °C at 5 °C/min steps, then from 80 °C to 200 °C at 15 °C/min steps and finally 200 °C for 2 min. The carrier gas was helium at a flow rate of 1.0 mL/min. We used MSDChemstation® software for data analysis. The mass spectrometer (electronic impact—70 eV) was operated in ion monitoring mode with a source temperature of 230 °C. THMs were detected with two specific ions per molecule (chloroform: m/z 83 and 85 ; bromoform: m/z 173 and 175; 1,2 dibromoethane (internal standard): m/z 107 and 109). We used external standards for calibration and an internal standard (1,2 dibromoethane) for correction. The calibration range (7.10^{-2} µg/m³ to 3 µg/m³) was prepared from a methanol solution of THM (LGC Promochem) at 100 mg/L each. The detection limit (DL) and quantification limit (QL) were respectively $0.9.10^{-2}$ µg/m³ and 0.3 µg/m³.

2.2.2. Tenax® tubes (event exposure)

The THMs, actively trapped in Tenax® tubes, were analyzed with an ATD 400 automated thermal desorber (Perkin Elmer) and a GC 8000 Series gas chromatograph (Fisons) coupled with an MD 800 mass spectrometer (Fisons). The primary desorption temperature was 180 °C for 10 min with a 30 mL/min flow of helium. Desorbed THMs were trapped in Tenax® at −30 °C. The trap was then heated from −30 °C to 320 °C (at 40 °C/s steps) with a 2 mL/min outlet split flow. The extracted THMs were transferred to the gas chromatograph (DB-624 capillary column, 30 m × 0.25 mm, 1.4 µm film thickness, J&W Scientific) with a 1 mL/min helium flow. The temperature program ran from 50 °C (5 min) to 120 °C (1 min) at 5 °C/min steps, and finally to 200 °C (5 min) at 40 °C/min steps. Data were analyzed with Masslab® version 1.3 software. The same detection method (two specific ions per molecule) as described above for the organic vapor monitors was used. Calibration was conducted with external standards. Tenax® tubes spiked with increasing volumes of standard solutions (prepared by dilution of a methanol solution of THM (LGC Promochem) in pentane (Fluka, ≥99.0% (GC)) at 100 mg/L each (quantity deposited: 0.05 to 128 g/m³)) were used for the calibration range. The quantification limits were 0.13 µg/m³ for chloroform ($CHCl_3$) and 0.05 µg/m³ for bromoform ($CHBr_3$).

2.3. Data analysis

Continuous exposure (personal air concentration) was calculated from measured masses, diffusion coefficients and extraction rates as described by 3M™ (3M Co., 2002).

Event exposure (Ei, µg/m³) was calculated with Eq. (1):

$$\mathrm{Ei} = \frac{Cb \times Tb + Csp \times Tsp}{T}, \quad (1)$$

where *C*b and *C*sp are THM concentrations (µg/m³) in the air of the bathroom (with bath or shower) and swimming pool respectively, *T*b and *T*sp are the time (in min) spent by the child in the bathroom and swimming pool, and *T* is the total time (min) of the experiment (sampling duration).

Excel® was used for the statistical analysis: Spearman correlation coefficient between continuous and event exposures, and their differences and ratios for each child.

3. Results and discussion

Only 26 children were finally included, because four 3M™ monitors were deteriorated (external diffusion barrier thorn) during the sampling week. Six of these children visited an indoor swimming pool as a leisure activity ($N = 3$, several children attended the same pools). On average, the children took five baths or showers during the sampling week. Mean time in the bathroom was 23 min (SD: 15 min), 16 min (SD: 8 min) when showering and 30 min (SD = 17 min) when bathing. Mean time at the swimming pool was 102 min (SD: 27 min). These time–activity data were consistent with the Exposure Factors Handbook (US E.P.A., 2007), except for swimming pools, but we had very few swimmers.

The THM concentrations in air were dominated by $CHCl_3$ in bathrooms: median is 7.3 µg/m³ for $CHCl_3$, while respectively 0.2, 1.7 and 0.5 for $CHBr_3$, $CHBrCl_2$ and $CHClBr_2$).

Table 1
Continuous and event inhalation exposures to chloroform.

	N	$CHCl_3$	
		Median	P25; P75
Air concentration (µg/m³) in bathroom	26	7.3	2.9; 14.48
Shower	12	7.3	2.7; 20.3
Bath	14	7.3	2.9; 11.0
Air concentration (µg/m³) in swimming pool	3	81.3; 29.5; 17.5	
Event exposure (µg/m³)	26	0.1	$0.4.10^{-1}$; 0.2
Children not attending swimming pool	20	$6.7.10^{-2}$	$0.4.10^{-1}$; 0.1
Children attending swimming pool	6	0.3	0.3; 0.6
Continuous exposure (µg/m³)	26	0.5	0.2; 1.0
Children not attending swimming pool	20	0.4	0.3; 0.8
Children attending swimming pool	6	1.0	0.9; 1.2
Difference (µg/m³) between continuous and event exposures	26	0.4	0.2; 0.8
Ratio continuous/event exposures	26	5.6	3.1; 10.9

Rennes, France 2008.

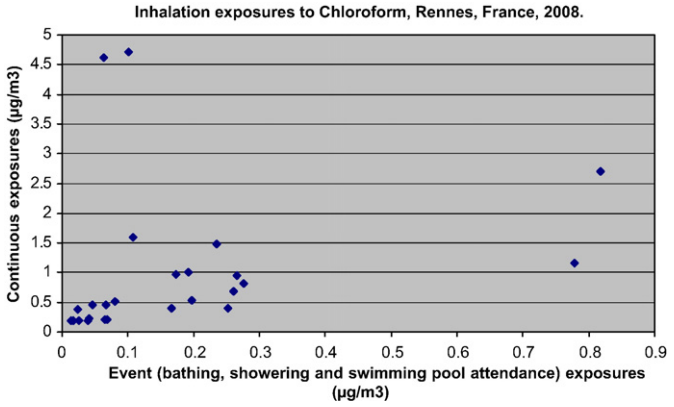

Fig. 1. Children inhalation exposures to chloroform, Rennes, France. 2008.

Min–Max values are respectively: 1.5–36.7 µg/m^3 for $CHCl_3$, while respectively 0.09–0.6, 0.3–11.5 and 0.1–1.4 for $CHBr_3$, $CHBrCl_2$ and $CHClBr_2$. $CHCl_3$ is also predominant in swimming pools (17–81 µg/m^3 for CHCl3 while respectively 0.5–0.6, 1.5–2.8, and 1.0–1.3 µg/m^3 for $CHBr_3$, $CHBrCl_2$ and $CHCLBr_2$), that is consistent with its higher concentration in water and volatility. Table 1 presents chloroform air concentrations in bathrooms and swimming pools, continuous and event exposure measurements, their matched differences and ratio. Air concentrations in bathrooms during shower or baths were lower than other estimations (Keating et al., 1997; Kerger et al., 2000; Levesque et al., 2002; Backer et al., 2008). Those, however, were conducted in the USA where higher chlorine doses are used for tap water disinfection than in France (2–20 µg/L in this study). $CHCl_3$ air concentrations were higher during showers than baths, as Gordon et al. (2006b) observed as well. THM concentrations in the air of swimming pools (with water concentrations from 20 to 70 µg/L) were consistent with previous findings in the same area (Hamel, 2007; Villanueva et al., 2007b). The continuous exposures were lower (mean:1.0, SD:1.2 µg/m^3 for $CHCl_3$) than those reported in earlier studies that used the same personal monitors (Clayton et al., 1999; Adgate et al., 2004a,b), but conducted in North America (with higher chlorine doses). Concerning a possible underestimation of the THMs concentrations when sampling in humid atmospheres, the comprehensive evaluation of the 3M badge (Chung, 1999) depicts a slight recovery decrease with increasing humidity but that chloroform extraction efficiencies do not depend upon ambient humidity.

Chloroform appears to be the most interesting THM for testing an association between THM exposure and respiratory effects because of its abundance, but we certainly cannot rule out the possibility that other compounds are hazardous. The continuous exposures were higher than the event-specific ones. Median exposures, whatever the method, were higher for the children attending a swimming pool, which is consistent with findings from Whitaker et al. (2003a).

A significant correlation between the continuous and event-specific has been found for chloroform exposures ($r_s = 0.69$ $p < 0.001$, cf. Fig. 1) but not for bromoform (data not shown; the other THMs could not be tested for correlation because 3M™ did not provide their diffusion coefficients), that may be partially explained by a lower variability of bromoform concentrations. No correlation was observed between shower, bath, and swimming duration and ages of participants ($r_s = 0.08$), nor between ages and continuous exposure ($r_s = 0.04$). A correlation ($r_s = 0.59$, $p < 0.05$, with 2 outliers excluded) was found between shower, bath, and swimming duration and continuous exposures. The Spearman correlation coefficient between continuous and event exposures was slightly higher than in a similar study (Clayton et al., 1999) that compared chloroform exposure measured with 3M™ badges worn by children with exposure assessed by badges placed in the room where the child spent the most waking time ($r_s = 0.59$ $p < 0.01$). The unexplained variability may be due to our small sample size, which resulted in a lack of statistical power. Another possible explanation is that unmeasured microenvironments (house baseline exposure and during other uses of hot water such as hot beverage, hand, dish or clothes washing (Nuckols et al., 2005a; Gordon et al., 2006b) might have caused the difference between continuous and event-specific chloroform measurements.Dodson et al. (2007) showed that models that include three or more microenvironments provide an unbiased estimate of chloroform exposure. Consequently, although bathrooms and swimming pools have been confirmed to be the predominant microenvironments for THMs, it could be worth testing the utility of taking into account the baseline of exposure with an additional sample in the home because, as can be read in Table 1, this difference is not constant. This second sample would nonetheless imply a longer sampling period, which would not necessarily match real exposure (children would not stay in the room throughout the sampling time), greater inconvenience to participants, and higher costs. Modeling the house baseline of exposure could be an alternative, and is an ongoing pursuit of this work. Considering additional microenvironments in baseline exposure may be considered in case of particular sources of THMs.

In an epidemiologic study focused on the relation between THM inhalation and respiratory effects in children, the event-specific exposure approach could cause a non differential misclassification of exposure. Because exposure appears to be underestimated by the event-specific method, exposed subjects may be classified as unexposed. Thus the strength of association between exposure and illness would be underestimated. This loss of power can be evaluated (Hemon, 1995) by the Pearson correlation coefficient (r) between the two method. After excluding the two outliers (no explanation for their very elevated value and necessity of a normal distribution to calculate r), r equals 0.76 (very close to the previously calculated Spearman correlation coefficient $r_s = 0.69$). The loss of statistical power would thus be about 2 ($1/r$ (Hemon, 1995)) so statistical power would be cut in half if this method was used in an epidemiologic study. At the same time, the use of continuous exposure could also reduce statistical power if used in an epidemiologic study, because acceptance and compliance would be lower than in our convenience population study and because the monitors are subject to deterioration (15% in our study). Many of the subjects complained about the bother of wearing personal monitors for children: thinking to monitor when changing clothes or taking care not to damage it when playing or in case of rainy weather. Furthermore, as it was a convenience sample from colleagues, we can expect a lower acceptability and compliance to procedures in "real" conditions.

The aim of our work was to compare continuous and event-specific exposures to THM for inhalation only, in the perspective of studying their local (and not systemic, that would require to encompass all pathways of exposure with ideally biological measurements of exposure) effects. We observed a significant correlation between continuous and event-specific exposures to chloroform. Both measurement methods may reduce statistical power of an epidemiologic study, but for different reasons (acceptability of sampling and the fragility of the personal monitors for continuous measurements, and exposure misclassification error for the event-specific method). Both methods fail in taking into account ventilation rates (that may be important during swimming). The event-specific method might be improved by considering a supplementary sample in the home or by completing the samples from the bathroom and swimming pool with a modeled baseline THM air concentration in the home.

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