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Total body burden from inhalation during showering with benzene-contaminated drinking water: implications for cancer risk

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Abstract

Currently, the United States Environmental Protection Agency (USEPA) bases risk assessments on air or water contaminant concentrations and exposure durations, but neglects to consider total body burden (TBB). The amount of a contaminant in the body at any given instant is especially important when assessing risk due to inhalation. The purpose of this paper is to compare (1) benzene TBB inhalation cancer risk to ingestion cancer risk and (2) the benzene TBB inhalation cancer risk to the inhalation cancer risk derived using USEPA methodologies. Results from this study indicate the ratio of the TBB inhalation to ingestion lifetime cancer risk is 8 to 1, and the TBB inhalation to USEPA-derived inhalation cancer risk is 58 to 1. Considering that the shower (inhalation) and drinking (ingestion) benzene water concentrations were the same, USEPA default exposure values alone do not provide a complete basis for risk assessment. TBB is a much more valuable indicator of risk. Total body burden calculated from pharmacokinetic modeling can be linearly adjusted to consider any inlet water concentration of benzene or shower duration. This same methodology can be applied to other chemicals of concern. © 1998 Published by Elsevier Science B.V. All rights reserved.

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1. Introduction

Investigations into human health risks have identified human activities as important factors when studying the impact of various contaminant emissions [1]. The relative

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importance of different activities as well as different exposure routes have been quantified. The Agency for Toxic Substances and Disease Registry (ATSDR) assumes lifetime inhalation exposure to VOCs to be comparable to that from ingestion. In addition, many scientists [2–5] have shown that inhaling volatile organic chemicals (VOCs), such as benzene-contaminated water during showering, results in larger lifetime exposures than ingesting or dermally absorbing the VOCs from similarly contaminated water. These studies base their assessments in terms of potential exposure and not the amount of a contaminant in the body at any given instant (total body burden, TBB). When evaluating potential risks, TBB is a much more valuable indicator of risk than exposure concentrations which are used to estimate or predict the TBB.

One VOC of particular interest at petroleum-contaminated sites is benzene. Groundwater has been contaminated with benzene nation-wide from various environmental sources [6] including: leaking underground storage tanks; chemical spills; landfills; and gasoline (filling) stations [7]. Benzene, because of its prevalence and toxicity, is the human health risk driver for volatile contaminant cleanup at petroleum-contaminated sites. Typically, cleanup levels are based on the USEPA Maximum Contaminant Level (MCL) for benzene, 5 $\mu g\, l^{-1}$, with little if any consideration of air pathway exposures.

2. Purpose

The purpose of this paper is to exemplify the importance of considering TBB in assessing risk, specifically when exposure results from inhalation. The following study compares benzene TBB after inhalation during a 6-min shower to benzene TBB after ingestion of 2 l of water. Calculations were made using the same benzene concentrations in both exposure scenarios. Cancer risks were also calculated for the inhalation pathway based on exposure concentration, the current method used to evaluate inhalation cancer risks. The results indicate that, when considering TBB, the inhalation lifetime risk for benzene is dramatically greater than the ingestion lifetime risk. Even greater disparities occur between the inhalation TBB cancer risk compared with the inhalation cancer risk based on exposure concentrations. Therefore, when studies neglect TBB in their assessments, risk levels from inhalation of benzene (and other VOCs) are greatly underestimated or may even be ignored. This study also shows that TBB can be scaled in a linear fashion to any benzene water concentration and any shower duration, making TBB easily quantified when calculating lifetime cancer risks.

3. Methods

To model TBB received via inhalation of benzene, Wallace [8,9] developed a three-compartment breath model representing intake air, mixed venous and arterial blood and body compartments (muscle and viscera, as well as adipose). This pharmacokinetic model assumes instantaneous equilibrium between the air and the blood. Metabolism is assumed to take place in the blood, which communicates directly with the body compartments. The concentration of benzene in the exhaled breath is representative of

TBB for benzene. Likewise, lung blood is representative of TBB since lung blood and exhaled air are directly proportional to one another by an equilibrium partition coefficient. This breath model is used together with a three-compartment model for a house represented by the shower, bathroom and remainder of the residence.

A 4th order Runge–Kutta numerical method is used to solve the following system of ordinary differential equations.

Indoor air (three-compartment house model):

$$\mathring{C}_s = K_s \times (C_o - C_s/H) - (q_{sr}/V_s) \times C_s + (q_{rs}/V_r) \times C_r, \tag{1}$$

$$\mathring{C}_r = -(q_{rs}/V_r) \times C_r - (q_{rh}/V_r) \times C_r + (q_{sr}/V_s) \times C_s + (q_{hr}/V_h) \times C_h, \tag{2}$$

$$\mathring{C}_h = -(q_{hr}/V_h) \times C_h - (q_{ho}/V_h) \times C_h + (q_{rh}/V_r) \times C_r. \tag{3}$$

Pharmacokinetic (three-compartment breath model):

$$\mathring{C}_1 = a_{11} \times C_1 + a_{12} \times C_2 + a_{13} \times C_3 + (V_{\text{alv}}/V_1) \times C_s, \tag{4}$$

$$\mathring{C}_2 = a_{21} \times C_1 + a_{22} \times C_2, \tag{5}$$

$$\mathring{C}_3 = a_{31} \times C_1 + a_{33} \times C_3. \tag{6}$$

The indoor air quality parameters [8] are: C_s = concentration of benzene in shower (μg l^{-1}); C_r = concentration of benzene in bathroom (μg l^{-1}); C_h = concentration of benzene in house (μg l^{-1}); K_s = 0.54 m^3 h^{-1} (shower flow rate of 10 LPM and shower temperature of 40°C); C_o = concentration of benzene in the inlet shower water (μg l^{-1}); H = 0.01 (dimensionless Henry's law constant at 40°C); q = air flow rate (m^3 h^{-1}); the first subscript denotes the originating room and the second the receiving room (s = shower 50 m^3 h^{-1}, r = bathroom 1 m^3 h^{-1}, h = house 1 m^3 h^{-1}, o = outdoors 1 m^3 h^{-1}); V_s = volume of shower (1 m^3); V_r = volume of bathroom (10 m^3); V_h = volume of residence (250 m^3).

The pharmacokinetic parameters [8,9] are: C_1 = concentration in blood (μg l^{-1}); C_2 = concentration in muscle and viscera (μg l^{-1}); C_3 = concentration in fat (μg l^{-1}); V_{alv} = alveolar ventilation rate (175 l h^{-1}); a = blood and body compartments; the first subscript denotes the originating compartment and the second the receiving compartment; subscript 1 denotes blood (5 l), subscript 2 denotes muscle and viscera (28 l) and subscript 3 denotes adipose (14 l); the calculated physiological parameters are: $a_{11} = -27.1$; $a_{12} = 7.27$; $a_{13} = 0.51$; $a_{21} = 2.73$; $a_{22} = -1.81$; $a_{31} = 2.38$; $a_{33} = -0.0238$.

4. Results

Fig. 1 is a composite of a histogram for shower duration [10] and the corresponding TBBs for each showering duration from 1 to 20 min. A unit inlet water concentration of 1 μg l^{-1} benzene was used in the model. All values on the x-axis have been normalized to a dimensionless value by dividing by 1 μg l^{-1}. Therefore, for any given benzene water concentration, the TBB can be calculated by multiplying the x-axis value by the concentration of interest.

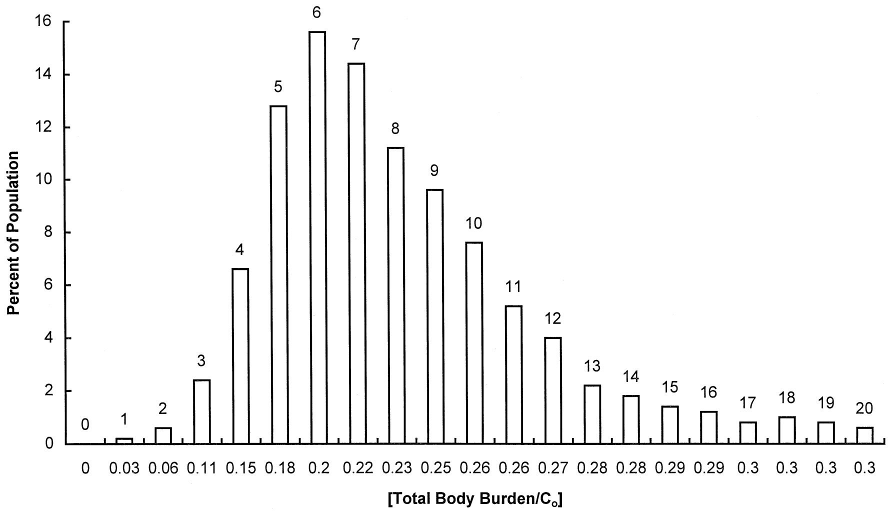

Fig. 1. TBB/C_o as a function of shower duration and normalized to 1 $\mu g l^{-1}$. Legend: Tops of bars are labeled 0 to 20 min for shower duration.

Consider the TBB incurred by a 6-min shower (which according to Fig. 1 is taken by sixteen percent of the sampled population) using water with a benzene level of 5 $\mu g l^{-1}$ (USEPA MCL). [1] TBB is calculated by choosing a showering time of interest, in this case 6 min, then multiplying the corresponding *x*-axis value of 0.2 by 5 $\mu g l^{-1}$ (the benzene MCL). This yields a TBB of 1 $\mu g l^{-1}$.

Once the TBB of benzene has been determined, a standard USEPA risk calculation can be done with Eq. (7) [11] for lifetime risk due to taking one 6-min shower per day at the MCL for benzene of 5 $\mu g l^{-1}$. [2]

TBB = (water concentration, $\mu g l^{-1}$) × (normalized TBB from histogram); Using the MCL for benzene of 5 $\mu g l^{-1}$ and a 6-min shower and referring to Fig. 1 yields:

$$\mathrm{TBB} = (5\ \mu g l^{-1}) \times (0.2) = 1\ \mu g l^{-1}$$

Inhalation cancer slope factor = $(8.3 \times 10^{-3}\ \mu g\ l^{-1})^{-1}$ [12].

For a 6 min shower in water contaminated with benzene at 5 $\mu g\ l^{-1}$,

$$\text{Lifetime Cancer Risk} = (\mathrm{LADD}) \times (\text{inhalation cancer slope factor}) \tag{7}$$

$$\mathrm{LADD} = (\mathrm{TBB} \times \mathrm{EF} \times \mathrm{ET} \times \mathrm{ED})/(\mathrm{AT}), \tag{8}$$

where: LADD is the lifetime daily dose; EF = 350 $d\,yr^{-1}$; ED = 30 yr at a residence;

[1] Because benzene can cause Leukemia, the USEPA established a Maximum Contaminant Level Goal (MCLG) of 0 $\mu g l^{-1}$ in drinking water. Since this goal may be technologically unattainable, a goal of 0.066 $\mu g l^{-1}$ is considered more reasonable.

[2] Note the histogram for showering times consists of whole numbers. When dealing with fractions, interpolation using this histogram is a simple matter and can be done manually or stochastically. TBBs ($\mu g l^{-1}$) can be estimated in a linear fashion from this histogram data based on the shower duration. This is possible because all the processes modeled for both the house and the body are first order in nature.

ET = fraction of day exposed in shower (6 min/1440 min); AT = averaging time (lifespan), 70 yr (for carcinogenesis); LADD = (0.001 mg l^{-1}) × (1000 l/m^3) × (6 min/1440 min) × (350 d yr^{-1}) × (30 yr)/(70 yr × 365 d yr^{-1}); LADD = 0.0017 mg/m^3; Lifetime cancer risk = (LADD) × (inhalation cancer slope factor); Lifetime cancer risk = (1.7 μg/m^3) × (8.3 × 10^{-6} μg/m^3)$^{-1}$; Lifetime cancer risk = 1.4 × 10^{-5}.

In comparison, the lifetime cancer risk for ingesting 2 l d^{-1} of water contaminated with benzene can be determined as follows:

$$\begin{aligned}&\text{Lifetime cancer risk} = \text{LADD} \times (\text{ingestion cancer slope factor})\\&\text{LADD} = (\text{CC} \times \text{CR} \times \text{EF} \times \text{ET} \times \text{ED})/(\text{AT} \times \text{BW})\end{aligned} \tag{9}$$

where: ingestion cancer slope factor = 2.9 × 10^{-2} (mg kg^{-1} d^{-1})$^{-1}$; CC = concentration of chemical of concern (mg l^{-1}); CR = consumption rate (2 l d^{-1}); BW = body weight (70 kg). For 5 μg l^{-1} benzene: LADD = (0.005 mg/l × 2 l/d × 350 d/yr × 30 yr)/(70 kg × 70 yr × 365 d yr^{-1}); LADD = 5.9 × 10^{-5} mg kg^{-1} d^{-1}; lifetime cancer risk = (5.9 × 10^{-5} mg kg^{-1} d^{-1}) × (2.9 × 10^{-2}(mg kg^{-1} d^{-1})$^{-1}$); lifetime cancer risk = 1.7 × 10^{-6} [13].

The ratio of the inhalation to ingestion lifetime risk for cancer in this example is 8 to 1. This ratio illustrates the importance of considering the inhalation route of exposure for homes using VOC-contaminated drinking water for showering. Perhaps even more significant is the difference with the inclusion of exposures to other vapor producing water devices (e.g. dishwasher, clothes washer, bathroom), which increases potential inhalation exposures another 68% (single-person dwelling: male occupant) to 114% (two-person dwelling: male and female occupants) [1].

The average shower duration shown in Fig. 1 is 8 min, the median is about 7 min and the 90th percentile shower duration is 12 min. The corresponding TBBs are: 0.23 μg l^{-1}, 0.22 μg l^{-1} and 0.27 μg l^{-1} and the corresponding lifetime cancer risks are: 2.2 × 10^{-4}, 2.3 × 10^{-4} and 2.6 × 10^{-4} at the MCL for benzene (5 μg l^{-1}). The equilibrium equation for partitioning from air to blood is eight; therefore, if the air concentration was constant the blood concentration (TBB) will approach eight times the air concentration.

The lifetime cancer risk from inhalation exposures using the current USEPA methodologies and the same values from the inhalation TBB yields the following: LADD = ((AC) × IR × EF × ET × ED)(CF)/(BW × AT); AC = air concentration (80 μg/m^3); IR = inhalation rate (20 m^3 d^{-1}) (EPA Region III); CF = conversion factor (1 μg × 10^3/1 mg); LADD = ((80 μg/m^3)) × (20 m^3 d^{-1} yr) × (350 d yr^{-1}) × (6 min/1440 min) × (30 yr))/((70 kg) × (25,550 d)); LADD = (3.9 × 10^{-2} mg kg^{-1} d^{-1}); Lifetime cancer risk = (LADD) × (inhalation cancer slope factor); TBB = (1.7 μg/m^3) × (8.3 × 10^{-6} μg/m^3)$^{-1}$ = 1.4 × 10^{-5}; Lifetime cancer risk = (3.9 × 10^{-5} mg kg^{-1} d^{-1}) × (8.3 × 10^{-3}(mg kg^{-1} d^{-1})$^{-1}$); Lifetime cancer risk = 2.4 × 10^{-7}.

The ratio of the inhalation TBB to inhalation exposure concentration lifetime risk for cancer in this example is 58 to 1. This ratio indicates that the air exposure concentration inhalation cancer risk calculated with USEPA methodologies greatly underestimates the inhalation cancer risk.

5. Discussion

Currently, USEPA Regions III and IX incorporate an inhalation component into their risk based concentration screening levels and preliminary remediation goals by calculating what a person processes by breathing. Although this is a step in the right direction, this screening approach does not take into account pharmacokinetic modeling, which is more representative of actual dose. Our study shows that when assessing risk from inhalation, it is important to consider TBB. In addition, when determining new or revising current MCLs the USEPA must consider exposures from both ingestion and inhalation.

The first-order, linear model presented here links shower duration with TBB of benzene. This information can be used by toxicologists and risk assessors to examine TBBs, or calculate lifetime cancer risks. This model should be generally applicable to other volatile chemicals given knowledge of their physiochemical and physiological properties.

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