

する必要があるだろう。しかし、本研究の結果から、新生児に特異的な毒性を示すことを示唆するデータが無い限りは、個人差を考慮した不確実係数 10 及び重要な情報の欠落を考慮した不確実係数 3~10 を用いることで、適切にリスクアセスメントが実施することができると考えられる。

D. 結論

(1) 水質基準・目標・要検討項目等に関する最新情報のフォローアップ: WHO の飲料水水質ガイドラインにおける最新の評価は、LOAEL の代わりにベンチマークドーズ (BMDL) を使用していること、動物実験の結果をヒトに外挿する際に PBPK 手法を用いて標的臓器等における化学物質濃度を補正していること、遺伝毒性発がん物質について BMDL を出発点とした直線外挿を行っていること、などが特徴的であった。食品安全委員会において清涼飲料水に係る化学物質の健康影響評価が行われている 9 物質のうち、1,1-ジクロロエチレン、ジクロロアセトニトリル及び抱水クロラールについては平成 15 年度改定時と比較して評価が大きく変わっていたものの、それ以外の 6 物質の評価法についてはほとんど違いがみられなかった。

(2) 内分泌攪乱物質や新たに健康影響等が懸念される物質の毒性情報収集: 有機スズ化合物については、生殖発生毒性および免疫毒性に関する研究は多く報告されているが、その他の一般毒性、特に長期曝露に関する情報はほとんどないことが明らかとなった。得られた情報からブチルあるいはフェニルの三および二置換体が同レベル曝露で影響を示すのに対して、モノ置換体の毒性は弱いことが示唆された。また、メチルおよびエチルなどの低級アルキル置換体は、生殖発生毒性および免疫毒性よりも神経毒性を示す傾向が高いことが示された。PBDE に関しては、毒性データは限られていたものの、多くの場合、肝重量の増加、T4 の減少、生殖発生影響が数 mg/kg 以上で認められていた。一方で、一部の同族体 (BDE-47 や BDE-99: Penta-BDE の主成分) については、より低用量での胎生/新生児期曝露による影響 (精子数減少や行動異常など) が認められていることが明らかとなった。HBCD と TBBPA については比較的多くの情報を得ることが出来た。HBCD については肝臓および甲状腺への影響が報告されており、最近報告された 28 日間反復投与試験では甲状腺重量の変化をもとに BMDL は 1.6

mg/kg/day とされている。一方、TBBPA の 28 日/90 日間反復投与試験では 1,000 mg/kg/day 投与によっても明確な有害影響は観察されていない。HBCD 及び TBBPA 共に、胎児毒性/催奇形性は認められていないが、最近、神経発達への影響を示唆する変化が報告されていた。

(3) 安全性評価手法に関する研究: 日本と WHO の水道水質基準値設定手法の比較においては、TDI と VSD の算出のための一般原理は同じであるが、適用されたエンドポイントが異なることが明らかになった。さらに、基準値の算出に用いられた飲水寄与率が異なることも明らかになった。化学物質に対する新生児の感受性に関する研究では、対象とした 18 物質のうち、およそ 2/3 の物質については、新生児ラットが若齢ラットよりも明らかに高い感受性 (新生児ラットで 2 倍から最大 8 倍の感受性) を示し、残りの物質については、若齢ラットと同等の感受性、もしくは新生児ラットの方が低い感受性 (0.1 から 2 倍未満) を示すことが明らかになった。

E. 健康危険管理情報

なし

F. 研究発表

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- G. 知的財産権の出願・登録状況 (予定を含む)
1. 特許取得 (該当なし)
 2. 実用新案登録 (該当なし)
 3. その他 (該当なし)

研究成果の刊行に関する一覧表

書籍

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研究成果の刊行物・別刷

Estimation of geographical variation of cancer risks in drinking water in Japan

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Abstract The cancer risks posed by ten substances in raw and purified water were estimated for each municipality in Japan to compare risks between raw and purified water, and inter-municipality. Water concentrations were estimated by use of statistical data. Assigning cancer unit risks to each substance and applying the assumption of additive toxicological effects to multiple carcinogens, total cancer risks of the waters were estimated. As a result, the geometric means of total cancer risks in raw and purified water were 1.16×10^{-5} and 2.18×10^{-5} , respectively. In raw water, the contribution ratio of arsenic to total cancer risk accounted for 97%. In purified water, that of four trihalomethanes (THMs) accounted for 54%. The increase of total cancer risks in purified water was due to THMs. In regard to the geographical variation, the relationship between population size and total cancer risks were investigated. The result was that there were higher cancer risks in the big cities with the population more than a million both in raw and purified water. One plausible reason for the higher risks in purified water in the big cities is a larger chlorination dose due to the huge water supply areas. The reason for the increase in raw water remained unclear.

Keywords Arsenic; cancer risk; drinking water; geographical variation; trihalomethane; water purification

Introduction

Drinking water quality issues, especially the issues on adverse health effects, have been one of the great concerns both of water works and water consumers. Although statistical data on drinking water quality have been provided by Japan Water Works Association (JWWA) for a long time, the data are merely a number of concentrations of substances, and thus it is very difficult for people to understand. Recently, Geographical Information System (GIS) has been widely applied as one of the new tools for visualization and spatial analyses. Integration of statistical water quality data and GIS may clarify the geographical characteristics of raw and purified water quality.

In this study, we focus on the carcinogenic substances in drinking water in Japan. Ten carcinogenic substances were selected for evaluation and the concentrations of these substances both in raw and purified water were estimated by the municipality unit. Applying the oral cancer unit risk for each substance and the assumption of additive toxicological effects to multiple carcinogens, total cancer risks of the waters were estimated by the municipality unit, and nationwide maps regarding the total cancer risks in raw and purified water were drawn with GIS. Furthermore, the characteristics and geographical variation of cancer risks were analyzed by use of drawn maps and statistical methods. The differences in substances contributing to the total cancer risks between raw and purified water, and the relationship between population size and total cancer risks were discussed.

Methods

Selection of target substances and assignment of their cancer unit risks

Chemical substances for the estimation of cancer risks were selected based on the following conditions. First, the substances that were in the Japanese Drinking Water Quality

Standard of 2001 were chosen. Although the new Standard was amended in 2004, statistical water quality data for 2004 were not yet available. Therefore, carcinogenic substances such as haloacetic acids and bromate, which were newly introduced in the Standard, were not included in this study. Second condition was that the substances should be carcinogenic or suspected to be carcinogenic. Third was that the substances should have oral unit risks as carcinogen in the Integrated Risk Information System (IRIS) by the United States Environmental Protection Agency (US-EPA). Consequently, ten substances were chosen for the analysis in this study. The names of the substances and oral unit risks assigned in this study, and Standard Values of Japanese Drinking Water Quality as of 2001 are shown in Table 1.

The term 'oral unit risk' is defined as the upper-bound excess lifetime cancer risk estimated to result from continuous exposure to an agent at a concentration of 1 mg/L in water (US-EPA, 2005) and expressed as the probability of developing tumors. The unit risks used in this study were mainly quoted from IRIS database (US-EPA, 2005). The unit risks of several substances were presented as several discrete values or a range of values. In this case, the geometric mean (*G*-mean) of the several unit risks or that of the maximum and the minimum values was used. The unit risk of chloroform is an exception. The oral unit risk of chloroform is not applicable in IRIS as of 2005 because EPA relies on a nonlinear dose-response approach and the use of margin-of-exposure analysis for cancer risk, for chloroform is not expected to produce rodent tumors via a mutagenic mode of action (US-EPA, 2005). Nonetheless, it was considered to be very useful to estimate and compare the extent of cancer risks of chloroform as one of trihalomethanes (THMs). Therefore, the unit risk of 1.8×10^{-4} (per mg/L) for chloroform, which had formerly been applied by IRIS, was used in this study. It should be noted that the quantitative cancer risk of chloroform might cause the overestimation of total cancer risk in this study.

Procedures to estimate the total cancer risks by the municipality unit

Concentrations of target substances in raw and purified water in each water purification plant. Statistics on water supply ("*Suidou Toukei*" in Japanese) were used as water quality and quantity database. The statistics have been edited by JWWA every year and consist of the data of water utilities which have more than 5000 design population served. Therefore, data of the smaller water utilities are not included in the statistics and were omitted in this study.

The statistics published in 2003 (JWWA, 2003), which describe the data of the fiscal year 2001, were mainly used in this study. The statistics include the data on

Table 1 Substances and oral unit risks assigned in this study, and Standard Values of Japanese Drinking Water Quality (2001)

Substances (CAS No.)	Oral unit risks assigned in this study (per mg/L)	Standard Values of Japanese Drinking Water Quality as of 2001 (mg/L)
1,2-Dichloroethane (107-06-2)	2.6×10^{-3}	0.004
1,3-Dichloropropene (542-75-6)	1.8×10^{-3}	0.002
Dichloromethane (75-09-2)	2.1×10^{-4}	0.02
Arsenic, inorganic (7440-38-2)	5×10^{-2}	0.01
Benzene (71-43-2)	8.4×10^{-4}	0.01
Carbon tetrachloride (56-23-5)	3.7×10^{-3}	0.002
Chloroform (67-66-3)	1.8×10^{-4}	0.06
Bromodichloromethane (75-27-4)	1.8×10^{-3}	0.03
Dibromochloromethane (124-48-1)	2.4×10^{-3}	0.1
Bromoform (75-25-2)	2.3×10^{-4}	0.09