Serum concentrations of polyfluoroalkyl compounds in the general US population: Data from the National Health and Nutrition Examination Survey (NHANES)

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Abstract

We measured the serum concentrations of several polyfluoroalkyl compounds (PFCs), including perfluorooctane sulfonate (PFOS) and perfluorooctanoate (PFOA), in participants 12 years of age and older of the U.S. National Health and Nutrition Examination Survey (NHANES). PFCs were extracted from serum using on-line solid-phase extraction coupled to isotope dilution-high performance liquid chromatography-tandem mass spectrometry; limits of detection were in the low parts-per-billion. Our data on 1,562 NHANES 1999–2000 participants provide the first estimation of concentrations of 11 PFCs in a representative sample of the civilian, non-institutionalized U.S. population in 1999-2000 when both PFOS and PFOA were being manufactured in the United States. We then used 54 pooled serum samples collected from 1,832 NHANES 2001–2002 participants to obtain estimates of mean concentrations of the same PFCs in selected demographic groups during the phase-out production in the United States of PFOS and related compounds in 2000-2002. We will discuss the usefulness of biomonitoring programs, using NHANES as example, to provide indisputable evidence of exposure and absorption of PFCs in humans and to assess temporal changes in internal dose when actions are taken that lead to changes in the environmental concentrations of these chemicals.

Introduction

Polyfluoroalkyl chemicals (PFCs) have been used extensively in numerous commercial applications including surfactants, lubricants, paper and textile coatings, polishes, food packaging, and fire-retarding foams. Perfluorooctane sulfonate (PFOS) and perfluorooctanoate (PFOA), two widely used PFCs, are persistent, bioaccumulative, and have been found around the world in humans and wildlife. Some PFCs have demonstrated developmental, reproductive, genotoxic, and carcinogenic toxicity in animal studies[1;2]. By contrast, in a small number of occupational studies, no clear association has been established between human exposure to PFCs and adverse health effects[3;4]. In addition, the sources, mechanisms and pathways of exposure to PFCs in humans are not well characterized. We measured the serum concentrations of 11 PFCs in by on-line solid-phase extraction coupled to isotope dilution-high performance liquid chromatography-tandem mass spectrometry in participants of several NHANES to assess exposure to PFOS, PFOA,

and other PFCs in the U.S. general population, and to determine if serum concentrations have changed as a result of changes in manufacturing practices, including the phase-out of PFOS and related materials based on perfluorooctanesulfonyl fluoride (POSF) in 2000-2002.

Materials and Methods

NHANES, conducted by the National Center for Health Statistics (NCHS) of the Centers for Disease Control and Prevention (CDC), is an ongoing complex, multistage probability survey designed to measure the health and nutrition status of the civilian, noninstitutionalized U.S. population. The surveys include household interviews, collection of medical histories, standardized physical examinations, and collection of biological specimens. Some of these specimens can be used to assess exposure to environmental chemicals[5]. Serum samples analyzed for PFCs were obtained from random one-third subsamples of people 12 years of age and older: 1,562 from NHANES 1999-2000[6] and 2,150 from NHANES 2001-2002[7]. For NHANES 2001-2002, the available amount of serum for analysis was insufficient and we used 1,832 individual serum samples to prepare 54 pooled samples each representing a combination of race/ethnicity, sex, and age. Informed written consent was obtained from all participants.

The serum concentrations of PFOS, PFOA, perfluorooctane sulfonamide (PFOSA), 2-(N-methyl-perfluorooctane sulfonamido) acetate (Me-PFOSA-AcOH), 2-(N-ethyl-perfluorooctane sulfonamido) acetate (Et-PFOSA-AcOH), perfluorohexane sulfonate (PFHxS), perfluoroheptanoate (PFHpA), perfluorononanoate (PFNA), perfluorodecanoate (PFDeA), perfluoroundecanoate (PFUA), and perfluorododecanoate (PFDoA) were measured using online solid phase extraction coupled to high performance liquid chromatography-tandem mass spectrometry, described in detail elsewhere[8]. Briefly, after dilution with 0.1 M formic acid, one aliquot of 100 μL of serum was injected into a commercial column switching system (Spark Holland, Plainsboro, NJ) allowing for concentration of the analytes on a HySphere HD C18 solid-phase extraction column ((7 μm, 10 mm × 1 mm; Spark Holland). This column was placed automatically in front of a Betasil C8 high-performance liquid chromatography column (3 mm × 50 mm, 5 μm; ThermoHypersil Keystone, Bellefonte, PA) for chromatographic separation of the analytes. Detection and quantification were done using negative-ion TurboIonSpray ionization-tandem mass spectrometry on a API 4000 mass spectrometer (Applied Biosystems, Foster City, CA). Three isotope-labeled internal standards were used for quantification: $^{18}O_2$-PFOSA, $^{18}O_2$-PFOS, and $^{13}C_2$-PFOA; the calibration standards were spiked into calf serum. The limits of the detection (LODs) were 0.1 ng/mL for PFHxS, PFOA, and PFNA; 0.2 ng/mL for PFOS, Me-PFOSA-

AcOH, Et-PFOSA-AcOH, PFDeA, PFUA, and PFDoA; 0.4 ng/mL for PFHpA; and 0.05 ng/mL for PFOSA. Low-concentration quality control materials (QCs) and high-concentration QCs, prepared from a calf serum pool, were analyzed with the unknown samples to insure accuracy and reliability of the data[8].

Statistical analyses were performed using the statistical software packages SAS and/or SUDAAN[6;7]. For concentrations below the LOD, a value equal to the LOD divided by the square root of 2 was used. The analyses were considered to be statistically significant when $p < 0.05$.

Results and Discussion

PFOS was found at the highest serum concentrations, followed by PFOA and PFHxS in both NHANES populations. PFOS, PFOA and several other PFCS were detected in more than 90% of the samples. We observed differences in concentrations based on race/ethnicity and sex. Specifically, males had higher concentrations of PFOS and PFOA than females, and Mexican American had the lowest PFOS and PFOA concentrations compared to non-Hispanic whites and non-Hispanic blacks. These sex and race/ethnicity differences may be related to differences in exposure and/or pharmacokinetics of PFCs. However, unlike other persistent organic pollutants (POPs), such as organochlorine compounds and despite the fact that PFCs have been used since the 1950s, we did not observe trends of increasing concentrations with age suggesting that PFCs do not behave like traditional POPs. Both the high prevalence of exposure to PFCs and the observed demographic differences highlight the need for additional research to identify sources of human exposure to PFCs and to study the environmental distribution of these chemicals.

In 2002, the 3M Company—the sole U.S. manufacturer of PFOS and the principal manufacturer worldwide—discontinued the production of PFOS and related POSF-based materials, including PFOA. PFOA and its salts are still being produced by other companies using a different manufacturing procedure. Therefore, the NHANES 1999–2000 PFCs data can serve as a nationally representative baseline of exposure, a baseline to which PFCs levels can be compared to evaluate the effectiveness of 3M's intervention. Preliminary evidence suggests that, as a result of the phase-out of POSF-based materials, the PFOS and PFOA concentrations in plasma samples collected in 2005 from 40 Red Cross blood donors in Minneapolis-St. Paul, Minnesota are lower than the serum concentrations in 100 (non-paired) samples collected in 2000 from the same donor population[9]. To confirm these findings and whether technological changes implemented by other companies have indeed contributed to a decline in PFC serum concentrations in the U.S. general population, a comparison between the NHANES 1999-2000 data and future NHANES is of interest. The NHANES 2001-2002 data, although based on pooled samples, do suggest that the

concentrations of PFOS and PFOA appear to be declining. The upcoming 2003–2004 NHANES should provide evidence of potential temporal changes in internal dose as a result of intervention that lead to changes in the environmental concentrations of these compounds.

Disclaimer

The use of trade names is for identification only and does not constitute endorsement by the U.S. Department of Health and Human Services or the CDC. The findings and conclusions in this report are those of the authors and do not necessarily represent the views of CDC.

References

1. Kennedy, G. L., Butenhoff, J. L., Olsen, G. W., O'Connor, J. C., Seacat, A. M., Perkins, R. G., Biegel, L. B., Murphy, S. R., Farrar, D. G. (2004) Crit Rev.Toxicol., 34, 351.

2. OECD. Hazard assessment of perfluorooctane sulfonate (PFOS) and its salts. [http://www.oecd.org/dataoecd/23/18/2382880.pdf], 1-362. 2002. Organisation for Economic Co-operation and Development (OECD).

3. Alexander, B. H., Olsen, G. W., Burris, J. M., Mandel, J. H., Mandel, J. S. (2003) Occup.Environ.Med., 60, 722.

4. Olsen, G. W., Burlew, M. M., Marshall, J. C., Burris, J. M., Mandel, J. H. (2004) J.Occup.Environ.Med., 46, 837.

5. CDC. Third National Report on Human Exposure to Environmental Chemicals. [http://www.cdc.gov/exposurereport/report.htm]. 2005. Atlanta, GA, Centers for Disease Control and Prevention; National Center for Environmental Health; Division of Laboratory Sciences.

6. Calafat, A. M., Kuklenyik, Z., Reidy, J. A., Caudill, S. P., Tully, J. S., Needham, L. L. (2007) Environ.Sci.Technol., 41, 2237.

7. Calafat, A. M., Kuklenyik, Z., Caudill, S. P., Reidy, J. A., Needham, L. L. (2006) Environ.Sci.Technol., 40, 2128.

8. Kuklenyik, Z., Needham, L. L., Calafat, A. M. (2005) Anal.Chem., 77, 6085.

9. Olsen, G. W., Mair, D. C., Reagen, W. K., Ellefson, M. E., Ehresman, D. J., Butenhoff, J. L., Zobel, L. R. (2007) Chemosphere, 68, 105.