Food and Chemical Toxicology 48 (2010) 3098–3108

Contents lists available at ScienceDirect

Food and Chemical Toxicology

journal homepage: www.elsevier.com/locate/foodchemtox

Dietary Acrylamide Exposure and Hemoglobin Adducts – National Health and Nutrition Examination Survey (2003–04)

N.L. Tran *, L.M. Barraj, M.M. Murphy, X. Bi

E^x^ponent®, Inc., Washington, DC 20036, United States

ARTICLE INFO

Article history:
Received 23 November 2009
Accepted 4 August 2010

Keywords:
Acrylamide
Glycidamide
Hemoglobin adducts
Dietary exposure
Blood cotinine

ABSTRACT

The objective of this study is to evaluate the relationship between dietary AA and hemoglobin adducts using the National Health and Nutrition Examination Survey (NHANES, 2003–04). Measured acrylamide (AA–Hb) and glycidamide (Gly–Hb) hemoglobin adducts for over 7000 participants >3 years, 24-h dietary recall, food frequency questionnaire (FFQ), lifestyle and demographic data, and anthropometric measurements are available from NHANES (2003–04). The 24-h dietary recall and FFQ data were combined with AA concentration data in food from the US FDA to estimate "usual" AA dietary exposure. The associations between dietary AA and AA–Hb and Gly–Hb were evaluated using linear regression models with smoking, age, gender, energy and macronutrient intake, body surface area, and activity level as covariates. Dietary AA positively correlates with AA–Hb and Gly–Hb ($p < 0.05$) but the correlation is small (*R*-Squared < 3.5%). Relative to the background adduct levels, the incremental increase in AA–Hb and Gly–Hb from average dietary AA is small (7% and 9% for AA–Hb and Gly–Hb, respectively). Non-dietary sources of exposure, measurement errors associated with the use of the FFQ, and uncertainty in the data on AA levels in foods are possible explanations for the observed lack of association between dietary AA and AA–Hb and Gly–Hb.

1. Background

Since the initial findings in 2002 by researchers at the Swedish National Food Administration and Stockholm University of the presence of acrylamide (AA) in a variety of fried and oven-baked foods and of its formation associated with high temperature cooking traditionally used for certain carbohydrate-rich foods, similar findings have been reported elsewhere, including the US (Al-Dmoor et al., 2004; Arisseto et al., 2007; Bekas et al., 2006; Cheng et al., 2006; Duxbury, 2004; Fohgelberg et al., 2005; FSA, 2006; Jackson and Al-Taher, 2005; Murkovic, 2004; Ono et al., 2003; Senyuva and Gokmen, 2005; Tareke et al., 2002; Tateo et al., 2007; Totani et al., 2007; Yoshida et al., 2005; Yuzo et al., 2006). As a potential human carcinogen and a known human neurotoxicant (Doerge et al., 2005), AA presence in foods may pose a public health concern.

The main objective of the current study is to evaluate the relationship between dietary AA exposure and measured hemoglobin adducts using the National Health and Nutrition Examination Survey data (NHANES, 2003–04). In the NHANES (2003–04), hemoglobin adducts of acrylamide (AA–Hb) and its primary metabolite glycidamide (Gly–Hb) were measured in blood samples collected from over 7000 NHANES participants age 3 years and older. Dietary intake information from 24-h dietary recalls and a food frequency questionnaire (FFQ), lifestyle data (exercise, smoking, and blood cotinine), demographic data (age, gender, ethnicity, and race) and anthropometric measurements (body weight, height) are also available.

2. Materials and methods

NHANES is a program of studies designed to assess the health and nutritional status of adults and children in the United States. In 1999, the survey became a continuous program in which a nationally representative sample of about 5000 persons is examined each year. The NHANES historically has been conducted as a series of surveys focusing on different population groups or health topics. The survey combines interviews and physical examinations. The NHANES interview includes demographic, socioeconomic, dietary, and health-related questions. The examination component of NHANES consists of medical, dental, and physiological measurements, as well as laboratory tests administered by medical personnel. Since data are collected at the individual participant level, linkage of these factors at the individual level and correlation analyses among these factors are feasible.

2.1. Food intake data

Responses to the FFQ and the 24-h dietary recall data collected in the NHANES (2003–04) were used to estimate long term usual food intake in the study analysis. The data files for the FFQ and the 24-h dietary recall were obtained from the CDC website (<http://www.cdc.gov/nchs/nhanes/nhanes2003–2004/exam03_04.htm>).

* Corresponding author. Address: Exponent Inc., 1150 Connecticut Ave. NW, Suite 1100, Washington, DC 20036, United States.
E-mail address: ntran@exponent.com (N.L. Tran).

0278-6915/$ - see front matter © 2010 Elsevier Ltd. All rights reserved.
doi:10.1016/j.fct.2010.08.003

The NHANES FFQ collected information on the frequency of consumption of various kinds of foods during the past 12 months. The questionnaire covered 152 categories of foods, and included sub-questions for selected foods by season, e.g., soup in the winter versus the rest of the year, or strawberries in season versus the rest of the year. The frequency questions also included questions about the proportion of the time certain foods (such as sugar-free soft drinks, whole grain foods, and light, lowfat, or fat-free varieties of foods) were eaten over the past 12 months. The responses to the FFQ were categorized into a total of 239 unique food categories; and the frequency of consumption for each food category for each respondent is available in the NHANES data files. The basis for the FFQ used in NHANES is the National Cancer Institute (NCI) diet history questionnaire, a food frequency instrument commonly used in nutritional epidemiology research, which has been validated against other FFQ instruments used in epidemiologic research (Subar et al., 2001). The NHANES FFQ has been validated in adults by Subar et al. (2006) with data from multiple 24-h recalls.

Portion size information was not collected with the FFQ. However, amounts of food consumed per eating occasion or day are available from the 24-h dietary recall interviews and individual portion size distributions were derived from that dataset and used in this study.

2.2. Acrylamide concentration data

The US Food and Drug Administration (FDA) analyzed numerous food samples in the time period of 2002–2006 to determine levels of acrylamide in these products. The food samples were collected as part of FDA's Total Diet Study (TDS) or as part the Survey on Acrylamide in Food: Individual Food Products (FDA, 2009). The TDS collects and analyzes samples of approximately 280 foods to determine levels of various contaminants and nutrients in those foods. TDS samples are analyzed as composites of three samples per composite, while the results from the FDA Acrylamide in Food survey were for individual food products.

The AA concentration data are publicly available. The number of concentration values assigned to each relevant FFQ food in this study varied depending on the number of foods available from FDA's TDS and the special acrylamide survey. Since FDA's survey focused on foods known to have higher AA, breads, cereals, coffee, fried chicken, fried potatoes, and potato chips were foods with the largest number of samples. In general the distributions of the AA concentrations were skewed with long right hand tail, i.e., with a few high observations. The mean and range of the concentration data used in this study are listed in Table 1.

2.3. Biomarker data

NHANES (2003–04) biomonitoring data for acrylamide were released in December 2008. Hemoglobin adducts of acrylamide (AA–Hb) and its primary metabolite glycidamide (Gly–Hb) were measured in red blood cells for more than 7000 NHANES participants age 3 years and older (AA–Hb and GLY–Hb measurements were available for 7101 and 7278 subjects, respectively). The hemoglobin adduct data were downloaded from the CDC website at <http://www.cdc.gov/nchs/nhanes/nhanes2003–2004/lab03_04.htm>. Serum cotinine levels are also available for 7792 NHANES (2003–04) survey participants age 3 and older and were downloaded from the same CDC website.

2.4. Other variables

Demographic, anthropometric, smoking, and exercise data for the NHANES (2003–04) subjects were downloaded from the following CDC websites:

- Demographic: <http://www.cdc.gov/nchs/nhanes/nhanes2003–2004/DEMO_C.htm>
- Anthropometric: <http://www.cdc.gov/nchs/nhanes/nhanes2003–2004/exam03_04.htm>
- Smoking: <http://www.cdc.gov/nchs/nhanes/nhanes2003–2004/quex03_04.htm>
- Exercise: <http://www.cdc.gov/nchs/nhanes/nhanes2003–2004/quex03_04.htm>
- Total energy and nutrient intakes: <http://www.cdc.gov/nchs/nhanes/nhanes2003–2004/exam03_04.htm>

2.5. Sample size

All NHANES respondents ages 2 and older who provided at least one 24-h dietary recall interview were eligible to complete the FFQ. A total of 6472 NHANES (2003–04) respondents participated in the FFQ. The net total of 5306 NHANES (2003–04) participants 3 years and older with both FFQ and blood data were included in this study analysis, of which 1019 are children age 3–12, 561 are males and 640 are females age 13–19 years, and 1408 are males and 1678 are females age 20+ years. It should be noted that AA–Hb or Gly–Hb measurements were missing for some individuals; hence the total number of subjects with FFQ, cotinine and AA–Hb data was 4799 and the total number of subjects with FFQ, cotinine and Gly–Hb data was 4892.

2.6. Dietary AA exposure

2.6.1. Identifying foods for inclusion in the study analysis

FDA acrylamide concentration data were reviewed and each food found to have a quantifiable level of acrylamide in at least one sample was mapped to the FFQ food category representative of that food. The purpose of the mapping is to identify the FFQ food categories that could be contributing sources of dietary acrylamide for inclusion in the exposure assessments. Of the 152 FFQ food categories, 44 corresponded to one or more acrylamide-containing foods in the FDA acrylamide dataset. The remaining 108 FFQ food categories did not correspond to acrylamide-containing foods. Table 1 lists the acrylamide-containing food categories, along with the name of FFQ sub-categories captured in the category. These 44 FFQ food categories were included in the intake and exposure analysis. Several foods with acrylamide values from the FDA dataset did not directly map to any specific FFQ category or were limited to a very small portion of a FFQ category, for example, dry soup mixes, chocolate syrup, some food mixtures, canned apricots and okra. These foods were excluded from the exposure assessment. These are minor food sources of AA and thus not expected to have an impact on the dietary AA estimates.

2.6.2. Estimating usual intake – Monte Carlo model

Using a Monte Carlo method, the NHANES FFQ and 24-h dietary recall data were combined with the AA concentration data to estimate longterm (usual) AA dietary exposure. The following approach was used to estimate the long term dietary AA exposure:

i For each food or food group corresponding to a FFQ food category, a distribution of amounts consumed per eating occasion based on the NHANES (2003–04) 24-h dietary recall database was derived using Exponent's Foods and Residue Evaluation Program (FARE™). FARE™ is proprietary research software that was developed to facilitate the mining and statistical analysis of the thousands of individual intake records in the NHANES database. The weighted distributions of amount per eating occasion (A_j) were derived for each food or food group mapped to FFQ foods for the following subpopulations: (1) children age 3–12 years, (2) males 13–19 years, (3) females 13–19 years, (4) males 20+ years, and (5) females 20+ years.

ii Distributions of the AA concentrations for each food or food group corresponding to a FFQ food category were created. No parametric distributions were fitted to the data. Since the data from FDA's survey of acrylamide in individual foods are for individual samples while the TDS data refer to composites, averages of similar foods (if available) were derived from the AA concentrations from FDA's survey to create distributions of AA values that are comparable to those extracted from FDA's TDS.

iii The following Monte Carlo procedure was applied to derive estimates of long-term daily dietary AA exposure. Specifically, Crystal Ball® was used to randomly sample individuals from the FFQ database and combine their frequency of consumption of AA-containing foods with a corresponding amount consumed per eating occasion (step i) randomly sampled from the mapped distribution of amount per eating occasion, and AA concentration randomly sampled from the corresponding AA levels in the food (step ii).
The samples were drawn independently from the two sets of distributions (amount per eating occasion, and AA concentrations in foods) using Latin Hypercube sampling, to increase the likelihood of sampling from the entire distribution. The within person correlations were maintained in the frequency of consumption. The following algorithm was applied:

- Select a participant from the FFQ distributions.
- Identify his/her frequency of consumption of AA FFQ food categories.
- For each FFQ category, randomly select an eating occasion amount from the corresponding amounts per eating occasion distribution.
- For each FFQ food category randomly select an AA concentration from the corresponding AA concentrations distribution.
- For each FFQ food consumed by the randomly selected participant, compute the corresponding AA exposure by multiplying the frequency of consumption, the randomly selected amount consumed by eating occasion, and the randomly select AA concentration.
- The long term total AA exposure for the randomly selected NHANES participant was derived by summing the calculated exposures for each FFQ food consumed by this participant.
- The process was repeated 57,880 times (10 times the number of subjects age 3+ years with valid FFQ data). This ensured that all subjects with FFQ data were selected at least once in the Monte Carlo procedure. In fact, the minimum number of times each subject was selected in the Monte Carlo was two, and the median, 10th and 90th percentiles for the number of times each subject was selected in the Monte Carlo were 10, 7, and 13, respectively, indicating that most subjects were selected with similar frequencies.
- For each participant an average exposure estimate was derived by averaging the exposure estimates derived from the various iterations in the Monte Carlo procedure described above.