Food and Chemical Toxicology 90 (2016) 151–159

Contents lists available at ScienceDirect

Food and Chemical Toxicology

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

Burden of disease of dietary exposure to acrylamide in Denmark

Lea Sletting Jakobsen [a, *], Kit Granby [b], Vibeke Kildegaard Knudsen [a], Maarten Nauta [a], Sara Monteiro Pires [a], Morten Poulsen [a]

[a] Division for Diet, Disease Prevention and Toxicology, The National Food Institute, Technical University of Denmark, Mørkhøj Bygade 19, 2860 Søborg, Denmark
[b] Division for Food Technology, The National Food Institute, Technical University of Denmark, Mørkhøj Bygade 19, 2860 Søborg, Denmark

ARTICLE INFO

Article history:
Received 13 August 2015
Received in revised form
14 January 2016
Accepted 26 January 2016
Available online 2 February 2016

Keywords:
Acrylamide
Cancer
DALY

ABSTRACT

Acrylamide (AA) is a process-contaminant that potentially increases the risk of developing cancer in humans. AA is formed during heat treatment of starchy foods and detected in a wide range of commonly consumed products. Increased focus on risk ranking and prioritization of major causes of disease makes it relevant to estimate the impact that exposure to chemical contaminants and other hazards in food have on health. In this study, we estimated the burden of disease (BoD) caused by dietary exposure to AA, using disability adjusted life years (DALY) as health metric.

We applied an exposure-based approach and proposed a model of three components: an exposure, health-outcome, and DALY-module. We estimated BoD using two approaches for estimating cancer risk based on toxicological data and two approaches for estimating DALY.

In Denmark, 1.8 healthy life years per 100.000 inhabitants are lost each year due to exposure to AA through foods, as estimated by the most conservative approach.

This result should be used to inform risk management decisions and for comparison with BoD of other food-borne hazards for prioritizing policies. However, our study shows that careful evaluation of methodological choices and assumptions used in BoD studies is necessary before use in policy making.

1. Introduction

Acrylamide (AA) is a food-process contaminant and classified as a 'probable human carcinogen' (IARC, 1994). Long-term carcinogenicity studies in rats and mice have shown that oral AA exposure may lead to tumors in multiple organs of the rodents (Johnson et al., 1986; Friedman et al., 1995; Beland et al., 2013; FDA, 2012). These findings strongly support mechanistic studies that have shown that AA is a genotoxic carcinogen by its metabolic activation to glycidamide (GA), which is reactive towards DNA and proteins (Fennell et al., 2005; Beland et al., 2013). AA is produced during high temperature processing (>120 °C) of commonly consumed starchy foods, and the relationship between dietary intake of AA and the risk of cancer in humans has been evaluated in several epidemiological studies. A borderline significant increase in risk of cancer of the kidneys (RR = 1.20, CI95: 1.00–1.45), endometrium (RR = 1.23 (1.00–1.51)), and ovaries (RR = 1.39 (0.97–2.00)) was identified in a recent meta-analysis (Pelucchi et al., 2015). Additionally, a significantly increased risk of estrogen receptor-positive breast cancer and mortality has been identified in a study using biomarkers for AA exposure (Olsen et al., 2012; Thonning Olesen et al., 2008). On this basis, EFSA reconfirmed that 'AA in food potentially increases the risk of developing cancer for consumers of all age groups' (EFSA, 2015), and therefore it is of relevance to investigate the contribution of dietary AA to the disease burden of cancer.

Burden of disease (BoD) is the impact that a disease has on society in terms of mortality, morbidity and disability. Several measures have been developed to estimate BoD; one of these is the Disability Adjusted Life Year (DALY), which integrates disease incidence, severity, duration, and mortality (Murray and Lopez, 2013). Estimation of BoD using DALYs is a useful tool to compare the health impact of various diseases, and evaluate the contribution of the risk factor(s) to the disease burden. BoD studies have been conducted for environmental risk factors (e.g. Hanninen et al., 2014), nutritional factors (e.g. Lim et al., 2013), and foodborne pathogens (e.g. Havelaar et al., 2012; Kretzschmar et al., 2012).

For risk ranking purposes and inclusion in risk-benefit

* Corresponding author.
E-mail addresses: leaja@food.dtu.dk (L.S. Jakobsen), morp@food.dtu.dk (M. Poulsen).

http://dx.doi.org/10.1016/j.fct.2016.01.021
0278-6915/

assessments, it is of interest to estimate the burden of disease attributed to exposure to chemicals through foods, using DALY as a health metric. The risk due to exposure to the chemical needs to be quantified and expressed as an annual incidence of the given health effect caused by the chemical. The risk quantification can be based on toxicological data, epidemiological data or both, depending on data availability for the chemical.

The aims of this study were to estimate the burden of cancer due to dietary exposure to AA in Denmark in terms of DALYs, and to estimate the contribution of different foods to this disease burden. We applied an exposure-based approach based on toxicological data, and evaluated the impact of different models to quantify the human cancer risk, as well as the impact of different approaches to calculate DALY.

2. Method and materials

To estimate the disease burden, we built a model consisting of three components: an exposure-, health outcome- and DALY module (Fig. 1). In the exposure module we estimated the lifetime mean daily exposure to AA of the Danish population. This estimate was integrated with the health-outcome module, in which the probability of occurrence of the selected health outcomes following exposure to AA was estimated based on dose–response relationships from animal studies. In the third module, we used the probability of occurrence of the health ouctomes, estimates of life expectancy, disease duration and disability weights to calculate the BoD in terms of DALYs. A more detailed description of the model follows.

2.1. Exposure assessment module

We defined exposure as the mean daily intake over a lifetime of μg AA per kg body weight, y, calculated by:

$$y = \frac{\sum_{i=1}^{N_{indi}} \sum_{j=1}^{N_{food}} \frac{I_{ij} C_j}{bw_i}}{N_{indi}} \quad (1)$$

where N_{indi} is the total number of individuals in the model, N_{food} is the total number of food types in the model, I_{ij} is the mean intake over seven days by individual *i* of food *j* in g/day, C_j is the mean concentration of AA in food *j* in μg/kg, and bw_i is the bodyweight of individual *i* in kg.

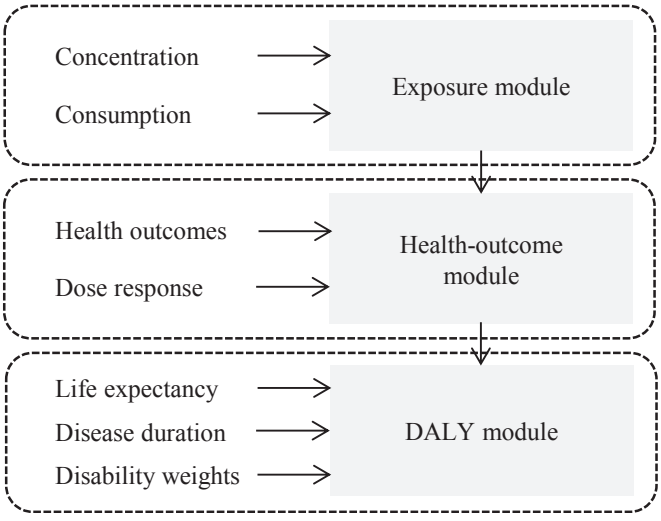

Fig. 1. Framework of model used to estimate the burden of disease of dietary exposure to acrylamide.

2.1.1. Concentration data

Concentrations of AA in various food types have been investigated in Denmark since 2003. Data for the analysis was obtained from Danish surveys on specific food types and from the general monitoring program (Petersen et al., 2013).[1] We used all available concentration data from 2003 to 2013, as no substantial change over time in concentrations in the investigated foods was observed. The food types, mean concentrations and standard deviations are shown in Table 1.

2.1.2. Consumption data

The consumption data were obtained from the Danish National Survey of Diet and Physical Activity, a national-wide, cross-sectional survey in a representative sample of the Danish population (Biltoft-Jensen et al., 2009). Diet is assessed by seven day pre-coded food records, and intake of foods and nutrients estimated by use of the Danish food composition tables (www.foodcomp.dk) and the software system GIES developed at DTU Food. Data applied in this study were collected in 2005–2008 from 2700 individuals. To adjust for potential skewness in the study population, weighting factors constructed on the basis of age, gender and education were applied.

2.2. Health-outcome module

2.2.1. Choice of health effects

The pivotal effects in humans following exposure to AA are neurotoxicity and carcinogenicity (Beland et al., 2013; Burek et al., 1980; Friedman et al., 1995; Johnson et al., 1986). In this study we selected cancer as the health effect to be accounted for in the model, as neurotoxicity is assumed to be caused by higher levels of exposure experienced for example in occupational settings rather than through diet (EFSA, 2015). The cancer types with a (borderline) statistically significant association with AA estimated by Pelucchi et al. (2015), and cancer types identified using biomarkers in exposure assessment of AA by Thonning Olesen et al. (2008) and Olsen et al. (2012) were selected. The following four health outcomes were included in the model: kidney cancer, ovarian cancer, endometrial cancer and breast cancer. In parallel, we accounted for total cancer in the model, recognizing that AA is a multi-site carcinogen (Beland et al., 2013; EFSA, 2015; US EPA, 2010) and assuming that the carcinogenic potency of AA is similarly in all tissues.

2.2.2. Dose-response modeling

We applied two different dose–response models to estimate the slope factor (SF). SF is the slope of a straight line drawn from a dose on the dose–response curve in the observable tumor range (the point of departure (PoD)) to the origin (0,0) in order to estimate effects in the low dose range. SF expresses the increase in the risk of cancer per daily unit of exposure to the carcinogen throughout lifetime (US EPA, 2005). We applied; 1) a model proposed by the US EPA in the toxicological review of AA (US EPA, 2010), and 2) a model proposed by Dybing and Sanner (2003). Both models use extrapolation from the same PoD, but the approach and order of inter- and intra-species extrapolation steps differ. These differences are detailed in Fig. 2.

The data used for the interspecies extrapolation also differ between the models. US EPA used toxicokinetic data based on

[1] Also including the 2011-13 monitoring data, not published in Petersen et al. (2013).