Environmental Research 120 (2013) 43–54

Contents lists available at SciVerse ScienceDirect

Environmental Research

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

Fish consumption, omega-3 fatty acids, and environmental contaminants in relation to low-grade inflammation and early atherosclerosis ☆

A.W. Turunen [a,*], A. Jula [b], A.L. Suominen [a,c], S. Männistö [d], J. Marniemi [b], H. Kiviranta [a], P. Tiittanen [a], H. Karanko [b], L. Moilanen [e], M.S. Nieminen [f], Y.A. Kesäniemi [g,h], M. Kähönen [i,j], P.K. Verkasalo [k]

[a] Department of Environmental Health, National Institute for Health and Welfare, Neulaniementie 4, P.O. Box 95, FI-70210 Kuopio, Finland
[b] Department of Chronic Disease Prevention, National Institute for Health and Welfare, Peltolantie 3, FI-20720 Turku, Finland
[c] Institute of Dentistry, University of Eastern Finland, P.O. Box 1627, FI-70211 Kuopio, Finland
[d] Department of Chronic Disease Prevention, National Institute for Health and Welfare, P.O. Box 30, FI-00271 Helsinki, Finland
[e] Department of Medicine, Kuopio University Hospital, P.O. Box 1777, FI-70211 Kuopio, Finland
[f] Department of Medicine, Helsinki University Hospital, P.O. Box 340, FI-00029 HUS, Helsinki, Finland
[g] Institute of Clinical Medicine, Department of Internal Medicine and Biocenter Oulu, University of Oulu, P.O. Box 5000, FI-90014, Oulu, Finland
[h] Clinical Research Center, Oulu University Hospital, Oulu, Finland
[i] Department of Clinical Physiology, Tampere University Hospital, P.O. Box 2000, FI-33521 Tampere, Finland
[j] University of Tampere, Tampere, Finland
[k] Department of Adult Psychiatry, Kuopio University Hospital, P.O. Box 1777, FI-70211 Kuopio, Finland

ARTICLE INFO

Article history:
Received 20 January 2012
Received in revised form
20 September 2012
Accepted 24 September 2012
Available online 22 October 2012

Keywords:
Fish
Omega-3
Environmental contaminants
Inflammation
Atherosclerosis

ABSTRACT

Background: Fish consumption and omega-3 polyunsaturated fatty acid (PUFA) intake are shown to protect from cardiovascular diseases (CVD). However, most fish contain environmental contaminants such as dibenzo-*p*-dioxins and dibenzofurans (PCDD/Fs), polychlorinated biphenyls (PCBs), and methylmercury (MeHg) that may have adverse effects on cardiovascular health.
Objective: Our aim was to elucidate the associations of fish consumption, omega-3 PUFAs, environmental contaminants with low-grade inflammation, early atherosclerosis, and traditional CVD risk factors.
Methods: The Health 2000 survey participants ($n=1173$) represented the general Finnish population and the Fishermen study participants ($n=255$) represented a population with high fish consumption and high exposure to environmental contaminants. Model-adjusted geometric means and tests for linear trend were calculated for CVD risk factors by tertiles of fish consumption and serum omega-3 PUFAs, and additionally in the Fishermen study only, by tertiles of serum PCDD/F+PCB, and blood MeHg.
Results: Serum triglyceride decreased across omega-3 PUFA tertiles in both sexes and studies. Insulin resistance, C-reactive protein, tumour necrosis factor α, and interleukin 6 decreased across omega-3 PUFA tertiles among the Health 2000 survey participants. Among the Fishermen study men, insulin resistance and arterial stiffness indicated by β-stiffness index tended to increase and the RR estimate for carotid artery plaque tended to decrease across tertiles of PCDD/F+PCB and MeHg.
Conclusion: Previously established hypotriglyceridemic and anti-inflammatory effects of omega-3 PUFAs were seen also in this study. The hypothesised favourable effect on insulin sensitivity and arterial elasticity was suggested to be counteracted by high exposure to environmental contaminants but the effect on plaque prevalence appeared not to be harmful.

1. Introduction

Many of the traditional risk factors for cardiovascular diseases (CVD) and diabetes, such as hypertension, dyslipidemia, and insulin resistance, are suspected to be favourably affected by high fish consumption and high intake of fish-derived long-chain omega-3 polyunsaturated fatty acids (PUFAs) (Calder and Yaqoob, 2009; Carpentier et al., 2006; Riediger et al., 2009). Further, omega-3 PUFAs have been observed to decrease the production of pro-inflammatory eicosanoids and cytokines and thus, fish consumption is believed to protect from diseases involving inflammatory processes (Calder, 2006; Wall et al., 2010). Fish consumption and omega-3 PUFA intake have also been suggested to slow the progression of atherosclerosis (Massaro et al., 2008) and to reduce arterial stiffness (Hall, 2009).

In contrast, most fish contain bioaccumulative environmental contaminants that have endocrine-disrupting potency and may

☆ *Funding*: The present work was supported by the Academy of Finland (project nos. 77008, 205324, 206950, 124286), the Finnish Cancer Organisations, the Yrjö Jahnsson Foundation, and the Juho Vainio Foundation.
* Corresponding author. Fax: +358 29 524 6497.
E-mail address: anu.turunen@thl.fi (A.W. Turunen).

0013-9351/$ - see front matter © 2012 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.envres.2012.09.007

have an adverse effect on cardiovascular health (Bushkin-Bedient and Carpenter, 2010). For example, high exposure to 2,3,7, 8-tetrachlorodibenzo-*p*-dioxin (TCDD), the most toxic congener of polychlorinated dibenzo-*p*-dioxins and dibenzofurans (PCDD/Fs), is hypothesised to increase the risk of circulatory diseases and diabetes (Consonni et al., 2008). In addition, PCDD/Fs, polychlorinated biphenyls (PCBs), and methylmercury (MeHg) are suspected to have a capacity to increase both blood pressure and oxidative stress, alter lipid, glucose and insulin metabolism, and promote inflammatory processes (Everett et al., 2011; Hennig et al., 2007; Mozaffarian, 2009). Especially exposure to PCBs has lately been linked with obesity, dyslipidemia, insulin resistance (Lee et al., 2011) and the risk of diabetes (Airaksinen et al., 2011).

Although the benefits of fish consumption and omega-3 PUFAs have been extensively studied, some controversy still remains (Hooper et al., 2006; Salas-Salvado et al., 2011) and one explanation for conflicting findings might be competing effects of environmental contaminants in fish (He, 2009). More importantly, the benefits of fish consumption and omega-3 PUFA intake have rarely been studied in populations with high exposure to environmental contaminants. Our aim was to study the associations of habitual fish consumption and serum concentrations of fish-derived omega-3 PUFAs and environmental contaminants with chronic low-grade systemic inflammation, early signs of atherosclerosis, and traditional CVD risk factors taking into account the overall effect of beneficial and hazardous compounds in fish. We conducted the analyses in a sub-sample of the general Finnish population and among professional Baltic Sea area fishermen and their family members. The latter is a unique population with high fish consumption and high exposure to environmental contaminants.

2. Methods

2.1. Study populations

The nationally representative Health 2000 health examination survey (the Health 2000 survey) was conducted in 2001–2002 (Heistaro, 2008). A total of 1526 volunteers, aged 45–74 years, and living near the five university hospitals (Helsinki, Turku, Tampere, Kuopio, and Oulu) participated in a cardiovascular and diabetes sub-study and of those, 532 men and 641 women had complete dietary, health interview, and basic health examination data for the present work. Further, of those, 406 men and 499 women had also ultrasound data for the analyses of vascular structure and function.

The Nutrition, environment and health study (the Fishermen study) on professional Baltic Sea area fishermen, their wives, and other family members was conducted in 2004–2005 (Turunen et al., 2008). A total of 309 volunteers, aged 22–74 years, and living near Helsinki and Turku study centres participated in a health examination study and of those, 123 men and 132 women had complete dietary, health questionnaire, and basic health examination data for the present work. Further, of those, 84 men and 90 women had also ultrasound data for the analyses of vascular structure and function.

Both studies were coordinated by the National Institute for Health and Welfare (THL) in Finland. The studies were conducted according to similar study protocols and the guidelines laid down in the Declaration of Helsinki and Uniform Requirements for manuscripts submitted to Biomedical journals. The study protocols were approved by the ethical committee of the Hospital District of Helsinki and Uusimaa, and a written informed consent was obtained from all participants.

2.2. Dietary data

In both studies, diet was assessed by the same calibrated (i.e., determined to have relative validity) self-administered 128-item food frequency questionnaire (FFQ) designed to cover the whole diet and the use of dietary supplements (such as fish oil capsules) over the past 12 months (Männistö et al., 1996; Paalanen et al., 2006). Consumption of fish and other foods and the intakes of alcohol and salt (g/day) were calculated with the national Fineli® Finnish Food Composition Database. Dietary data has been described in detail elsewhere (Turunen et al., 2010).

2.3. Laboratory analyses

Blood samples were drawn from antecubital vein after 10–12 h of fasting. Serum concentrations of fatty acids were analysed using a gas chromatograph and flame ionisation detector (Jula et al., 2005). The sum of eicosapentaenoic acid (EPA), docosapentaenoic acid (DPA), and docosahexaenoic acid (DHA) (namely omega-3 PUFAs) was calculated as a proportion from all serum fatty acids (% FAs).

Serum total cholesterol and triglyceride concentrations were analysed by spectrophotometric enzymatic method, high-density lipoprotein (HDL, mmol/l) cholesterol by a direct method, glucose (mmol/l) by hexokinase method, and insulin (mU/l) by microparticle enzyme immunoassay. Homeostasis model assessment (HOMA) indexes, namely insulin resistance index (HOMA-IR) and pancreatic β-cell function (HOMA-%B), were calculated using formulas listed in Table A1.

Serum concentrations of highly sensitive C-reactive protein (CRP, mg/l), tumour necrosis factor α (TNF-α, ng/l), and interleukin 6 (IL-6, ng/l) were analysed using a solid-phase enzyme-labelled chemiluminescent immunometric assay in the Health 2000 survey. In the Fishermen study, CRP was analysed immunoturbidimetrically. Participants with CRP < 10 mg/l were included in the study.

In the Fishermen study only, serum concentrations of 17 PCDD/F and 37 PCB congeners were analysed gravimetrically from serum fat using a high resolution mass spectrometer equipped with a gas chromatograph. The method has been described in detail elsewhere (Kiviranta et al., 2002). PCDD/Fs and PCBs were expressed as toxic equivalent quantity (TEq) recommended by the World Health Organization (WHO). The sum of PCDD/F-TEq and PCB-TEq (PCDD/F+PCB-TEq, pg/g fat) was calculated. Blood MeHg concentration (ng/ml) was analysed from whole blood using an isotope dilution-gas chromatograph/mass spectrometer (Airaksinen et al., 2010). Blood samples to analyse environmental contaminants were not available in the Health 2000 survey.

2.4. Vascular measurements

Intima media thickness (IMT, mm) and arterial diameter change according to pulse pressure (ADC, mm) were measured from the right common carotid artery (CCA) at the level of the carotid bifurcation by high-resolution B-mode ultrasound. The method has been described in detail elsewhere (Niiranen et al., 2007; Sipila et al., 2011). The presence of formed atherosclerotic plaques in the carotid artery, defined as a focal raised lesion of > 1.5 mm in size in at least one of the images of the carotid bulb, was determined. Measures for arterial stiffness, namely carotid artery compliance (CAC, %/10 mmHg), Young's elastic modulus (YEM, kPa), and β-stiffness index (SI), were calculated based on ADC using formulas listed in Table A1. Participants with all six arterial diameter measurements (approximately 90% of those who had participated in vascular measurements) were included in the analyses concerning ultrasonographic variables.

2.5. Body composition, blood pressure and other basic health characteristics

Body mass index (BMI) was calculated using measured weight and height. Blood pressure was measured three times from the right brachial artery by an electronic sphygmomanometer (OMRON HEM 722C/OMRON M4, Omron Corporation, Japan) in sitting position after a 10 min rest. For the calculations of the vascular markers, blood pressure was measured again three times in supine position directly before the ultrasound examination. Data on smoking, physical activity, and the use of insulin, oral glucose lowering drugs, lipid modifying drugs (such as statins), and blood pressure lowering drugs were obtained from a structured interview and a self-administered health questionnaire in the Health 2000 survey and from the self-administered health questionnaire in the Fishermen study.

2.6. Statistical analyses

For the primary analyses (Tables 2–5), the participants were categorised into tertiles according to their non-transformed total fish consumption and serum omega-3 PUFAs, and additionally in the Fishermen study only, according to their serum PCDD/F+PCB-TEq and blood MeHg. Due to skewed variable distributions, all continuous variables except for age and blood pressure were transformed according to natural logarithm. After log transformations, the normality of the residuals was satisfactory. Each log-transformed risk factor or marker was treated as a response variable at a time, and their model-adjusted geometric means were calculated by the above mentioned tertiles using GLM procedure in the Statistical Analysis Systems (SAS) and tested for linear trend. Since the geometric means for the tertiles were not equally spaced, the coefficients for linear contrasts were produced by SAS/IML software. Adjusted risk ratio (RR) for the presence of atherosclerotic plaque in the carotid artery wall was calculated by the above mentioned tertiles using a Poisson regression model with robust error variance and GENMOD procedure in SAS, and tested for linear trend.