Nutrition, Metabolism & Cardiovascular Diseases (2018) xx, 1–8

Available online at www.sciencedirect.com

Nutrition, Metabolism & Cardiovascular Diseases

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

Associations between persistent organic pollutants and metabolic syndrome in morbidly obese individuals

S. Dusanov [a,*], J. Ruzzin [b], H. Kiviranta [c], T.O. Klemsdal [a], L. Retterstøl [d], P. Rantakokko [c], R. Airaksinen [c], S. Djurovic [e,f], S. Tonstad [a]

[a] Section for Preventive Cardiology, Department of Endocrinology, Morbid Obesity and Preventive Medicine, Oslo University Hospital, P.b. 4956 Nydalen, N-0424, Oslo, Norway
[b] Department of Biology, University of Bergen, Bergen, Norway
[c] National Institute for Health and Welfare, THL, Department of Health Security, P.O. Box 95, FI-70701, Kuopio, Finland
[d] Department of Medical Genetics, Oslo University Hospital, Oslo, Norway
[e] Department of Medical Genetics, Oslo University Hospital, Bergen, Norway
[f] KG Jebsen Centre for Psychosis Research, Department of Clinical Science, University of Bergen, Bergen, Norway

Received 15 January 2018; received in revised form 5 March 2018; accepted 6 March 2018
Handling editor: A. Siani
Available online ■ ■ ■

KEYWORDS
Metabolic syndrome;
POPs;
Morbid obesity;
Insulin resistance

Abstract *Background and aims:* Persons with "metabolically healthy" obesity may develop cardiometabolic complications at a lower rate than equally obese persons with evident metabolic syndrome. Even morbidly obese individuals vary in risk profile. Persistent organic pollutants (POPs) are widespread environmental chemicals that impair metabolic homeostasis. We explored whether prevalence of metabolic syndrome in morbidly obese individuals is associated with serum concentrations of POPs.

Methods and results: A cross-sectional study among 161 men and 270 women with BMI >35 kg/m^2 and comorbidity, or >40 kg/m^2. Circulating concentrations of 15 POPs were stratified by number of metabolic syndrome components. In multiple logistic regression analysis odds ratios between top quartile POPs and metabolic risk factors versus POPs below the top quartile were calculated adjusting for age, gender, body mass index, smoking status, alcohol consumption and cholesterol concentrations. Age-adjusted concentrations of *trans*-nonachlor and dioxin-like and non-dioxin-like polychlorinated biphenyls (PCBs) increased with number of metabolic syndrome components in both genders ($p < 0.001$), while the organochlorine pesticides HCB, β-HCH and p,p'DDE increased only in women ($p < 0.008$). Organochlorine pesticides in the top quartile were associated with metabolic syndrome as were dioxin-like and non-dioxin-like PCBs (OR 2.3 [95% CI 1.3–4.0]; OR 2.5 [95% CI 1.3–4.8] and 2.0 [95% CI 1.1–3.8], respectively). Organochlorine pesticides were associated with HDL cholesterol and glucose (OR = 2.0 [95% CI = 1.1–3.4]; 2.4 [95% CI = 1.4–4.0], respectively). Dioxin-like PCBs were associated with diastolic blood pressure, glucose and homeostatic model assessment-insulin resistance index (OR = 2.0 [95% CI = 1.1–3.6], 2.1 [95% CI = 1.2–3.6] and 2.1 [95% CI = 1.0–4.3], respectively).

Conclusion: In subjects with morbid obesity, metabolic syndrome was related to circulating levels of organochlorine pesticides and PCBs suggesting that these compounds aggravate clinically relevant complications of obesity.

* Corresponding author.
E-mail address: sasdus@ous-hf.no (S. Dusanov).

https://doi.org/10.1016/j.numecd.2018.03.004
0939-4753/

Please cite this article in press as: Dusanov S, et al., Associations between persistent organic pollutants and metabolic syndrome in morbidly obese individuals, Nutrition, Metabolism & Cardiovascular Diseases (2018), https://doi.org/10.1016/j.numecd.2018.03.004

Introduction

Obesity represents one of the most widespread public health and clinical challenges worldwide [1], and is commonly associated with a cluster of cardiometabolic risk factors [2]. Notably, obesity is not always associated with metabolic syndrome, even among persons characterized as morbidly obese (BMI of $\geq$40 kg/m^2 or $\geq$ 35 and with obesity related health conditions). Obese persons that do not meet criteria for metabolic syndrome have been characterized as "metabolically healthy obese" [3]. While these individuals are at risk for type 2 diabetes and cardiovascular events, they may be at lower risk than persons with metabolic syndrome, at the same level of obesity, at least in the short term [4–6]. Why some obese persons develop cardiometabolic risks earlier or more markedly than others may be related to lifestyle or polygenic variability but remains poorly understood.

During the last years, emerging evidence has linked environmental pollutants, particularly persistent organic pollutants (POPs), to obesity and related health problems [7]. Among POPs, organochlorine pesticides and polychlorinated biphenyls (PCBs) are lipophilic chemicals that accumulate in living organisms, acting as endocrine and metabolic disruptors [8]. Though the manufacture and usage of many of these compounds have been regulated, the prior environmental burden may influence current body levels and result in hazardous health conditions.

Results of observational studies have shown that serum concentrations of POPs are related to risk of type 2 diabetes [7,8]. Furthermore, in persons without diabetes, organochlorine pesticides and PCBs have been associated with insulin resistance, dyslipidemia and metabolic syndrome in the United States [9–12]. These relationships have been confirmed in studies that analyzed adipose depots of POPs [13,14]. Even in normal weight individuals POP concentrations appear to associate with unhealthy metabolic phenotypes [15]. Interestingly, the burden of POPs may be more strongly related to some metabolic risks than others [11–16] and may correlate with degree of atherosclerosis [17]. Accumulated POPs may differ according to population characteristics, including ethnic and socioeconomic variables [18].

In persons with already established obesity, some data have shown associations between POPs and metabolic risks. In obese postmenopausal women the metabolically healthy obese phenotype was associated with lower concentrations of POPs compared to metabolically abnormal phenotypes [19]. In patients that underwent bariatric surgery, POPs concentrations in adipose tissue were linked to metabolic syndrome [13].

Patients with morbid obesity bear the largest burden of excess body fat. However, even in this high-risk group, metabolic risks may vary therefore requiring a range of clinical approaches to treatment [20]. The current study examined whether circulating concentrations of POPs were associated with metabolic syndrome in a sample of consecutive men and women with morbid obesity referred for treatment.

Methods

Patients referred to the Preventive Cardiology Clinic at Oslo University Hospital, Oslo, Norway between April 2005 and December 2010 were asked to participate, and included provided that they gave written informed consent. The study conformed to the Helsinki Declaration and was evaluated by the Ethics committee for region 1 in Norway.

Participants with BMI $\geq$35 kg/m^2 with accompanying obesity-related comorbidity (including hypertension, sleep apnea, dyspnea, polycystic ovarian syndrome, asthma, hypercholesterolemia, gout, musculoskeletal symptoms, gall bladder symptoms, esophageal reflux, pulmonary or deep vein embolism, intermittent claudication, angina pectoris and depression) or BMI $\geq$40 kg/m^2 regardless of comorbidity were included in the present study (n = 431). Subjects with type 2 diabetes were excluded as the focus of the present study was on cardiometabolic risks.

Participants completed a health questionnaire and underwent anthropometric measurements. Waist circumference was measured at midpoint between the inferior costal margin and the highest point of the iliac crest, and hip circumference was measured at the widest point around the hips. Height was recorded to the nearest cm. Patients were weighed to the nearest 1.0 kg using a calibrated mobile electronic scale (Seca 720, Medical Scales and Measuring Systems, Birmingham, UK) and BMI was calculated. Blood pressure was measured using an automatic blood pressure monitor (52000 Series Vital Signs Monitor, Welch Ally, New York, USA) following a 5-min rest.

Classification of metabolic syndrome was performed according to the harmonized definition [2] and included $\geq$3 of the following: waist circumference $\geq$102 cm for men and $\geq$88 cm for women; blood pressure $\geq$130/85 mmHg or drug-treated hypertension; triglycerides $\geq$1.7 mmol/l; HDL-cholesterol $\leq$1.0 mmol/l for men or $\leq$1.3 mmol/l for women; and fasting glucose $\geq$5.6 mmol/l. Subjects were stratified by number of these components.

Laboratory analyses

Participants fasted overnight for $\geq$10 h, before providing blood samples between 0800 h and 1100 h. Analyses of blood samples were performed at Oslo University Hospital (Clinical Chemistry Laboratory at Ullevål and Endocrine Laboratory at Aker). Total cholesterol, HDL-cholesterol, triglycerides, glucose, and high-sensitivity C-reactive protein (CRP) concentrations were measured on an automated analyzer Cobas Integra 800 (Roche Diagnostics, Mannheim, Germany). Insulin was determined by non-competitive immunofluorometric assay, using an AutoDelfia 1235 Automatic Immunoassay System (H1855-21291) (Perkin Elmer Inc.) in 209 subjects with BMI $\geq$40 kg/m^2. The Homeostasis Model Assessment insulin resistance index (HOMA-IR) to estimate insulin resistance was calculated in subjects with insulin measurements [21].

Please cite this article in press as: Dusanov S, et al., Associations between persistent organic pollutants and metabolic syndrome in morbidly obese individuals, Nutrition, Metabolism & Cardiovascular Diseases (2018), https://doi.org/10.1016/j.numecd.2018.03.004