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Consumption of seafood and its estimated heavy metals are associated with lipid profile and oxidative lipid damage on healthy adults from a Spanish Mediterranean area: A cross-sectional study

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ABSTRACT

The association between the consumption of seafood and its benefits on cardiovascular (CVD) risk can be challenged by its heavy metal (HM) content. This study aimed to explore the association of seafood consumption and its estimated HM contents with the lipid profile and lipid oxidation biomarkers in adults from a Spanish Mediterranean area who do not present risk factors for CVD.

In this cross-sectional study, the clinical history, three-day dietary record, lipid profile (LDLc, HDLc, APOB/A, and triglyceride levels), plasma oxidised LDL (oxLDL) and 8-isoprostane levels of 81 adults without risk factors for CVD [43% men, with a mean age of 43.6 years (95%CI: 40.1–47.1)] were assessed. The HM [arsenic (As), cadmium (Cd), mercury (Hg), and lead (Pb)] contents of seafood were estimated according to data from analyses of marine species in the same Mediterranean area. Moderate adherence to the Mediterranean diet (score: 4.6 of 9) with a mean seafood consumption of 74.9 g/day (95%CI: 59.9–89.9), including 22.7 g of shellfish per day (95%CI: 13.5–31.9), was observed. The estimated HM contents were lower than the provisional tolerable weekly intakes (PTWIs): 21.12 μg/kg/week As, 0.57 μg/kg/week InAs, 0.15 μg/kg/week Cd, 1.11 μg/kg/week Hg and 0.28 μg/kg/week Pb.

After adjusting by confounder variables, an increase in shellfish consumption was associated with increases in the levels of LDLc ($P=0.013$), non-HDLc ($P=0.015$), APOB/A ($P=0.02$) and plasma oxLDL ($P=0.002$). Moreover, an increase in the estimated As and Hg levels in shellfish was associated with an increase in LDLc ($P=0.015$ and $P=0.018$, respectively), non-HDLc ($P<0.008$ and $P<0.008$, respectively), APOB/A ratio ($P=0.008$ and $P=0.009$, respectively), and oxLDL ($P\leq0.001$ and $P\leq0.001$, respectively) levels.

In conclusion, in adults without risk factors for CVD, increasing shellfish consumption, even by a moderate amount, could favour a pro-atherogenic lipid profile and a higher level of oxidised LDL. These associations are likely influenced by the estimated exposure to As and Hg from shellfish despite these values are lower than the PTWIs.

Abbreviations: APO, apolipoprotein; As, arsenic; BMI, body mass index; BP, blood pressure; Cd, cadmium; CVD, cardiovascular disease; InAs, inorganic-As; LDLc, low-density lipoprotein; LRM, Linear regression model; MD, Mediterranean diet; HDLc, high-density lipoprotein; Hg, mercury; oxLDL, oxidised LDL; PA, physical activity; Pb, lead; PUFAs, polyunsaturated fatty acids; SENC, Spanish Scientific Society of Community Nutrition; TDS, Total Diet Study; TG, triglycerides; WC, waist circumference

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1. Introduction

The beneficial effects of regular seafood, in particular, fish consumption on cardiovascular disease (CVD) have been demonstrated (Abeywardena, 2011; Piepoli et al., 2016; Catapano et al., 2016). Nevertheless, little information is available regarding the effects of shellfish consumption on CVD.

Seafood contributes to the diet, providing proteins with high biological value, fatty acids, including long-chain omega 3 polyunsaturated fatty acids (PUFAs), certain vitamins, as vitamins A and D, and several minerals, such as iodine, selenium, and calcium (Catapano et al., 2016). As a result, international scientific associations, such as the American Heart Association (AHA, 2006), and the 2016 European Guidelines for the Management of Dyslipidaemias from the European Society of Cardiology (ESC) and the European Atherosclerosis Society (EAS) recommend that for the prevention of CVD, older children, adolescents, and adults should consume seafood (fish and shellfish) at least twice per week (i.e., two servings of 130–150 g per week, preferably lean and oily fish) and have a moderate intake of shellfish (Catapano et al., 2016; EFSA, 2014). In Spain, the Ministry of Health and the Scientific Societies of Nutrition recommend three to four servings of seafood per week but do not specify the type of seafood (Dapcich et al., 2004; AECOSAN, 2015). These nutritional recommendations focus on lowering the levels of low-density lipoprotein cholesterol (LDLc), which is the main risk factor for CVD (AHA, 2006; Piepoli et al., 2016), and other lipid biomarkers, such as triglycerides (TG) and apolipoprotein B-100 (APO B-100), whereas enhancing high-density lipoprotein cholesterol (HDLc) and apolipoprotein A-1 (APO A-1) is encouraged (AHA, 2006; Piepoli et al., 2016).

However, the actual seafood recommendations are controversial due the levels of heavy metal (HM) contaminants found in seafood. Seafood consumption is the major dietary source of exposure to arsenic (As), inorganic-As (InAs), cadmium (Cd), mercury (Hg), and lead (Pb), which have no established biological functions and are considered non-essential metals (Chang et al., 1996; Domingo, 2016).

The potential toxicity of HMs and their adverse effects on human health, including CVD, have been well described, and these adverse effects are observed even at relatively low HM levels (Martorell et al., 2011; Sharma et al., 2014; Domingo, 2016). A high intake of Hg from non-fatty freshwater fish and the consequent accumulation of Hg in the body are associated with an excess risk of acute myocardial infarction, which could be due to the promotion of lipid peroxidation by Hg, as observed in Eastern Finnish men (Salonen et al., 1995). In contrast, some results support the conclusion that children who consume fish have a significantly more atheroprotective lipid profile accompanied by higher levels of blood Hg compared with those observed in children who do not consume fish (Gump et al., 2012). Thus, elucidating the relative risks of CVD adverse effects, linked to seafood consumption due to its content in HM is a challenge (Domingo, 2016).

Based on the proposed mechanism of action of HMs, exposure to As, Hg, Cd and Pb can potentially induce the production of highly reactive chemical entities, such as free radicals, which are able to cause lipid peroxidation, DNA damage, and oxidation of the sulfhydryl groups of proteins, leading to several diseases, such as CVD (Valko et al., 2005; Flora et al., 2008; Carocci et al., 2014). In this context, blood oxidised LDL (oxLDL) is the recognised gold-standard for lipid oxidation damage and is used as a biomarker of CVD (EFSA, 2011).

Thus, additional information regarding the effects of seafood consumption and the consequently unavoidable intake of HMs on CVD is needed. Therefore, studying lipid peroxidation and lipid profiles as risk factors of CVD in adults who lead a healthy lifestyle and do not present any known risk factors of CVD is necessary to avoid any interferences due to treatments for illnesses involved in CVD.

As a first approach, this study aimed to explore the association of seafood consumption and its estimated HM contents with the lipid profile and levels of lipid oxidation biomarkers in adults from a Spanish Mediterranean area who do not present risk factors for CVD.

2. Materials and methods

2.1. Study design and subjects

This cross-sectional study of healthy subjects was conducted in the Hospital Universitari Sant Joan de Reus (Catalonia, Spain) from March to July 2008 and from February to July 2009. The sample of eligible subjects was established with the following inclusion criteria: men and women aged 18–75 years having signed the informed consent and not meeting any exclusion criteria. The exclusion criteria were the following: systolic blood pressure $\geq$140 mmHg; diastolic blood pressure $\geq$90 mmHg; body mass index (BMI) $\geq$30 kg/m^2; pathological physical examination; LDLc level > 4.88 mmol/L (189 mg/dL); triglyceride level $\geq$4 mmol/L (350 mg/dL; the upper limit for correctly determining LDLc by the Friedewald formula); smoking; intake of antioxidant supplement, acetylsalicylic acid or any other drug with known antioxidative properties or vitamins; chronic alcoholism; hypolipidemic and/or antihypertensive treatment prior to trial initiation and stopped at least two months before starting the study; diabetes mellitus (fasting blood glucose > 126 mg/dL; measurements were repeated for confirmation); renal disease (plasma creatinine levels $\geq$1.4 mg/dL for women and $\geq$1.5 mg/dL for men); acute and chronic infectious diseases (hepatitis B and C and human immunodeficiency virus); malignancies, severe liver insufficiency, chronic respiratory insufficiency and associated endocrine diseases; other conditions with special nutritional requirements; participation in a clinical trial in the three months prior to the study; current participation in a clinical trial; inability to continue participating in the study; history of a gastrointestinal disease that can impair the absorption of nutrients; depression syndrome or self-injuring ideation; high plasma C-reactive protein and ESR concentrations; and administration of immunisation during the last two months. Table 1 shows the baseline characteristics of the participants.

The subjects were recruited from databases established by our research group that include a large number of subjects without CVD risk factors who had previously participated in some of our studies. The response rate of the contacted candidates was of 95%. A physician assessed the participants' eligibility or exclusion through a screening visit and their biochemical test results.

The eligible volunteers were called to come in the following week for their inclusion visit and were asked to provide a three-day dietary record (two working days and one weekend day) at their next visit. In their inclusion visit, after fasting for at least 8 h, a blood sample was collected. The three-day dietary record was revised by a nutritionist.

The clinical research ethics committee of Hospital Universitari Sant Joan de Reus approved the study protocol (08-01-31/proj1).

2.2. Anthropometric measurements

The body weight and height were obtained while the participants were wearing lightweight clothing and no shoes. These data were collected by trained study personnel using a calibrated scale and a well-mounted stadiometer, respectively. The waist circumference (WC) was measured midway between the lowest rib and the iliac crest using an anthropometric tape. The anthropometric measurements were taken according to the anthropometric standardisation reference manual.

2.3. Physical activity

The physical activity (PA) was monitored using the validated Spanish version of the Minnesota Leisure Time Physical Activity Questionnaire (Elosua et al., 1994), and metabolic equivalents (METs) were calculated according to Tornos (Sobejano-Tormos et al., 2009). The energy expenditure for physical activity (EEPA, MET·min/week)