Nutrition, Metabolism & Cardiovascular Diseases (2014) **24**, 1310–1316

Available online at www.sciencedirect.com

Nutrition, Metabolism & Cardiovascular Diseases

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

Fish and omega-3 fatty acid intake in relation to circulating fibroblast growth factor 23 levels in renal transplant recipients

L.C. Baia [a,b,1], E. Van den Berg [a,1], M.G. Vervloet [c], I.P. Heilberg [b], G. Navis [a], S.J.L. Bakker [a], J.M. Geleijnse [d], D. Kromhout [d], S.S. Soedamah-Muthu [d], M.H. De Borst [a,*], on behalf of the NIGRAM consortium

[a] Department of Nephrology, University Medical Center Groningen and University of Groningen, The Netherlands
[b] Department of Nephrology, Federal University of São Paulo, São Paulo, Brazil
[c] Department of Nephrology, VU University Medical Center Amsterdam, The Netherlands
[d] Division of Human Nutrition, Wageningen University, The Netherlands

Received 13 February 2014; received in revised form 16 May 2014; accepted 15 June 2014
Available online 23 June 2014

KEYWORDS
Omega-3 fatty acids;
Fibroblast growth factor;
Cardiovascular;
Kidney transplantation

Abstract *Background and aims:* A high circulating fibroblast growth factor 23 (FGF23) level is an independent risk factor for cardiovascular mortality in renal transplant recipients and the general population. N-3 fatty acids eicosapentaenoic (EPA) and docosahexaenoic acid (DHA) may contribute to cardiovascular risk reduction. We investigated whether fish and EPA-DHA intake are related to FGF23 levels in renal transplant recipients.
Methods and results: We performed a cross-sectional analysis in 619 stable renal transplant recipients (mean age 53 years, 57% male, estimated glomerular filtration rate [eGFR] 53 ± 20 mL/min/1.73 m^2). Dietary intake was assessed by a 177-item food frequency questionnaire. Serum intact FGF23 was measured by ELISA. We examined differences in FGF23 levels across categories of fish and EPA-DHA intake using analysis of variance models adjusted for age, sex, dietary and lifestyle factors and key determinants of FGF23. Patients consumed on average 15 g of fish and 139 mg EPA-DHA/day. Median FGF23 was 62 pg/mL (IQR 43–98 pg/mL). Higher dietary EPA-DHA and fish intake were associated with lower serum FGF23 levels. Subgroup analyses revealed that particularly in patients with reduced renal function (eGFR <60 mL/min/1.73 m^2), adjusted FGF23 levels (114, 79, 75 pg/mL, $P = 0.0001$) were inversely associated with tertiles of EPA-DHA intake. Similarly, we observed an inverse association between fish consumption and serum FGF23 levels in adjusted analyses.
Conclusion: A higher intake of fish and dietary *n*-3 fatty acids (EPA-DHA) is related to lower circulating FGF23 levels in renal transplant recipients. Further research is needed to assess the causality of this association and the clinical implications.
© 2014 Elsevier B.V. All rights reserved.

Introduction

Chronic kidney disease (CKD) is a worldwide health burden, affecting about 15% of the Western adult population. For most patients with end-stage renal disease, kidney transplantation is the preferred treatment. Although short-term graft and patient survival have improved

Abbreviations: CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; FGF23, fibroblast growth factor 23; PTH, parathyroid hormone.

* Corresponding author. University of Groningen, University Medical Center Groningen, Department of Nephrology, PO Box 30.001, 9700 RB Groningen, The Netherlands. Tel.: +31 50 3616161; fax: +31 50 3619310.
E-mail address: m.h.de.borst@umcg.nl (M.H. De Borst).
[1] Contributed equally.

http://dx.doi.org/10.1016/j.numecd.2014.06.006
0939-4753/© 2014 Elsevier B.V. All rights reserved.

impressively over the past decades, cardiovascular disease limits long-term patient survival [1]. Both the incidence and prevalence of cardiovascular disease are several times higher in renal transplant recipients than in the general population [2].

In patients with impaired renal function, deregulated phosphorus metabolism characterized by elevated circulating levels of the phosphaturic hormone fibroblast growth factor 23 (FGF23) plays a specific role in the pathophysiology of cardiovascular disease. In response to – particularly inflammatory – renal injury, the renal expression of Klotho, a mandatory cofactor for the specific FGF23 receptor, is lost [3] which may contribute to increased circulating FGF23 levels [4]. Besides being an indicator of impaired renal function and disturbed phosphorus metabolism, high circulating FGF23 levels may also directly contribute to the development of left ventricular hypertrophy [5]. Many epidemiologic studies have identified a high FGF23 level as an independent risk factor of cardiovascular disease and all-cause mortality in the general population [6], across stages of CKD[7], and in renal transplant recipients [8,9]. Consequently, strategies to reduce FGF23 levels may have clinical impact.

Patients with impaired renal function have lower serum levels of the n-3 fatty acids eicosapentaenoic (EPA) and docosahexaenoic acid (DHA), mainly consumed through fish, which may be linked to a higher cardiovascular disease risk in these patients [10]. Randomized controlled trials in patients with chronic kidney disease (CKD) showed a decrease in serum inflammatory markers after EPA-DHA supplementation [11]. Given the role of FGF23 as a cardiovascular risk factor in renal patients and the potential cardioprotective and anti-inflammatory effects of *n*-3 fatty acids, we investigated whether intake of fish and EPA-DHA are related to serum FGF23 levels in a well-defined cohort of 619 renal transplant recipients.

Methods

Study population

We conducted a cross-sectional analysis in a large, single center renal transplant recipient cohort. We invited all renal transplant recipients ($\geq$18 years) with a functioning graft for at least one year, who visited our outpatient clinic between November 2008 and March 2011. Renal patients had all been transplanted in the University Medical Center Groningen. They had sufficient knowledge of the Dutch language and no history of drug or alcohol addiction. Of 817 initially invited patients, 707 (87%) signed written informed consent to participate in this study. After exclusion of patients with missing data on dietary n-3 fatty acids (n = 82), missing data on eGFR (n = 2) and FGF23 concentrations (n = 4), data from 619 patients were available for analyses. The Institutional Review Board on human experimentation approved the study protocol (METc 2008/186), which was in adherence to the Declaration of Helsinki. The routine regimen included no specific dietary counseling, except for discouraging excess sodium intake and encouraging losing weight in overweight individuals. Renal transplant recipients were on standard antihypertensive and immunosuppressive therapy, which was as previously described [12]. Data on current medication including vitamin D treatment (cholecalciferol, alfacalcidol or paricalcitol) was extracted from the medical records.

Dietary assessment

All patients adhered to their regular dietary habits during examination. Dietary intake was assessed using a semi quantitative food frequency questionnaire (FFQ) which has been validated as described previously [13]. The FFQ inquired about intake of 177 food items during the last month. For each item, the frequency was recorded in times per day, week, or month, and seasonal variations were taken into account. The number of servings was expressed in natural units (for example, slice of bread or apple) or household measures (for example, cup or spoon). The questionnaire was self-administered and filled out at home. At the day of the visit to the outpatient clinic, all FFQs were checked for completeness by a trained researcher and inconsistent answers were verified with the patients. Total energy and nutrient intake per day was calculated using Dutch Food Composition Tables [14]. Additionally, all participants were instructed to collect a 24-h urine sample according to a strict protocol. Sodium intake was estimated from 24-h urine sodium excretion and the accuracy of FFQ for protein intake estimation was inferred by correlating protein intake with the protein equivalent of nitrogen appearance (PNA) [15].

Clinical and biochemical parameters

Information on patient's health status and medical history was obtained from patient records. Patients received state-of-the art treatment (Table 1), and data on current medication was extracted from the medical records. Body weight and height were measured while participants wore indoor clothing without shoes. Body Mass Index (BMI) was calculated as weight divided by height squared (kg/m^2). Blood pressure (BP) was measured as described previously [16]. Hypertension was defined as BP $\geq$140/90 mmHg or use of antihypertensive medication. Diabetes mellitus was considered present when serum glucose was above 7 mmol/l (126 mg/dl) or when the patient used antidiabetic medication.

Blood was drawn after an 8–12 h overnight fasting period in the morning after completion of the 24 h urine collection. Urinary and plasma concentrations of sodium, chloride, potassium, calcium, phosphate and urea were measured using routine clinical laboratory methods as were plasma hsCRP, total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides and albumin. Intact parathyroid hormone (PTH) was measured in EDTA plasma using radioimmunoassay. Serum creatinine level was determined using a modified version of the Jaffé method (MEGA

Download English Version:

https://daneshyari.com/en/article/5996531

Download Persian Version:

https://daneshyari.com/article/5996531

Daneshyari.com