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Short communication

Optimal dietary calcium intake in HIV treated patients: No femoral osteoporosis but higher cardiovascular risk☆

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SUMMARY

Background & aims: We performed a cross-sectional study on adult HIV-infected patients, on HAART, without calcium or vitamin D supplementation to evaluate if the cardiovascular risk or the presence of osteoporosis may be predictive factors of an optimal daily calcium intake (DCI>1000 mg/day).
Methods: Patients underwent a dual-energy X-ray absorptiometry, measured biochemical parameters and compiled a validated questionnaire for the assessment of DCI. Osteoporosis (OP) was defined according to the WHO classification at either the vertebral spine or femoral neck. Cardiovascular risk was assessed by the 10-year Framingham cardiovascular risk score.
Results: 200 HIV-infected patients evaluated: 171 (86%) males with a median age of 48.1 (42.3–53.8) years and 10.6 (4.3–13.6) years of HAART exposure.
DCI was 889 (589–1308) mg/day and 79 (40%) patients had an optimal DCI. Framingham risk>20% was found in 13 (6.7%) patients and femoral OP was diagnosed in 12 (6%) pts.
By multivariate analysis, optimal DCI was more likely in patients with a Framingham risk>20% [OR = 5.547, 95% CI:1.337, $p = 0.025$] and less likely in patients with femoral osteoporosis [OR = 0.159, 95% CI: 0.018–0.790, $p = 0.047$].
Conclusions: We found that an optimal dietary calcium intake was more likely in patients with high cardiovascular risk and no femoral osteoporosis.

1. Introduction

Due to the success of combination antiretroviral therapy (cART), patients with HIV infection live longer and are exposed to ageing-related complications such as cardiovascular diseases (CVD) and bone mineral disorders.

Previous studies, conducted in the general population, have associated calcium supplements which are widely used in the prevention or treatment of osteoporosis, with a possible increase in the risk of adverse cardiovascular outcomes.[1] One cohort study identified no adverse effects associated with dietary calcium intake, although a near doubling risk of myocardial infarction (MI) was found in calcium supplements users.[2]

Limited data on dietary calcium intake are available among HIV-infected subjects. Although one study has recently identified a protective effect of calcium intake on the osteoporosis among HIV-infected subjects,[3] it remains unclear whether such advantage might enhance the cardiovascular risk. Thus, the aim of our study was to evaluate if the cardiovascular risk or the presence of osteoporosis may be predictive factors of an optimal daily calcium intake (DCI).

2. Materials and methods

We conducted a cross-sectional study on alive HIV$^+$ patients, aged>18 years, on HAART, without calcium or vitamin D supplementation, attending the Infectious Diseases Department of the San Raffaele Scientific Institute between May–June 2011. Patients, evaluated on the same day, underwent a dual-energy X-ray absorptiometry (DEXA), measured biochemical parameters and compiled a validated questionnaire for the assessment of DCI.[4] Briefly, the questionnaire is composed of 15 food items: selection of the items

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was based on the data of the Italian Institute of nutrition relative to the food composition of the Italian diet, frequency of use and relative importance as a calcium food source; additional subgroup items were added for high calcium content food such as milk and derivatives. Servings were listed in three quantitative groups identified as small, medium, large and with grams of food. Subjects were asked to indicate the relative weekly frequency of use of each item. The calcium content estimate was obtained by food tables (attached to the questionnaire) quantifying the calcium content of each food according to the serving and weekly frequency. The daily calcium intake was obtained dividing the weekly calcium intake by 7.

Optimal DCI was defined as a DCI>1000 mg/day (recommended threshold in adults according to the IOM[5]). Osteopenia and Osteoporosis (OP) were defined according to the WHO classification at either the vertebral spine or femoral neck: osteoporosis was defined by T-scores<−2.5 for subjects older than 50 years of age or by z-score<−2.5 for subjects younger than 50 years of age; osteopenia was defined by T-scoresranging between >−2.5/−1.0 for subjects older than 50 years of age or by z-score ranging between >−2.5/−1.0 for subjects younger than 50 years of age Cardiovascular risk was assessed by the 10-year Framingham cardiovascular risk score and used in the analysis as a categorical variable according to the threshold of 20% (an arbitrary cut-off value often used in the clinical setting and in the clinical studies to identify patients with a high 10-year risk of cardiovascular events).

2.1. Statistical analysis

To analyze whether the demographic and clinical characteristics of the subjects included in this study were similar, the chi-square test or the Wilcoxon rank sum tests were applied when dealing with categorical or continuous variables, respectively.

At multivariate analysis, logistic regression was applied to determine predictive factors of a DCI>1000 mg/day. Characteristics with a p-value <0.20 at the univariate logistic regression models were included into two multivariate models (Model1 considered among the covariates the diagnosis of osteoporosis at femoral neck and alternatively Model 2 considered the diagnosis of osteoporosis at vertebral spine). Odds ratios (OR) and the corresponding 95% confidence intervals (95% CI) were estimated and reported for each variable included in the model.

A two-sided p value <0.05 was considered statistically significant. All statistical analyses were performed with SAS software, version 9.2 (SAS Institute, Cary, North Carolina, United States).

3. Results

Two hundred HIV-infected patients were included: 171 (86%) were males; age was 48.1 (42.3–53.8) years; they were infected with HIV since 14.5 (7.1–19.5) years, had 10.6 (4.3–13.6) years of HAART.

DCI was 889 (589–1308) mg/day and 79 (40%) patients had an optimal DCI. As shown in Table 1, no significant differences were observed between the demographic, clinical, immuno-virological and metabolic characteristics between subjects with or without an optimal DCI.

Framingham risk >20% was found in 13 (6.7%) patients; 8/13 (61.5%) subjects had a DCI>1000 mg/day as compared to 71/187 (38.0%) of patients with a CVD risk<20% ($p = 0.141$). Subjects with a high CVD risk were older (median: 61 vs 47 years, $p < 0.0001$), had a slightly higher body mass index (median 25.6 vs 23.5, $p = 0.086$), had higher lipid values (median total cholesterol: 207 vs 188 mg/dL, $p = 0.068$; median LDL-cholesterol: 153 vs 120, $p = 0.004$; median triglycerides: 148 vs 120, $p = 0.056$), systolic and diastolic blood pressure (median systolic: 149 vs 120 mmHg, $p = 0.0001$; median diastolic: 84 vs 77 mmHg, $p = 0.028$) and fasting glucose values (median: 100 vs 87, $p = 0.0003$) as compared to those with a CVD risk<20%.

Osteopenia was diagnosed in 96 (48%) patients: 18 (9%) subjects had a diagnosis only at vertebral spine, 37 (18.5%) patients only at

Table 1
Patients' characteristics according to dietary calcium intake at the time of study evaluation.

Characteristic[a]	Overall ($N = 200$)	DCI ≤1000 mg/day ($N = 121$)	DCI >1000 mg/day ($N = 79$)	P-value
Age (years)	48.1 (42.3–53.8)	48 (42.7–53.8)	48.2 (42.2–53.9)	0.496[d]
Males	171 (86%)	104 (86%)	67 (85%)	0.840[c]
Smokers	94 (47%)	55 (46%)	39 (49%)	0.563[c]
Overweight (Body mass index ≥25 kg/m^2)	62 (31%)	35 (29%)	27 (34%)	0.365[c]
Years since first HIV positive test	14.5 (7.1–19.5)	13.9 (6.1–19.4)	16.4 (7.1–20.2)	0.413[d]
Years of exposure to HAART	10.6 (4.3–13.6)	9.7 (4.1–13.5)	11.6 (4.8–13.6)	0.782[d]
Nadir Cd4+ (cells/μL)	229 (102–329)	233 (100–328)	216 (108–329)	0.579[d]
Positive HCVAb	30 (15%)	19 (16%)	11 (14%)	0.475[c]
Type of antiretroviral regimen				0.754[c]
NRTI-based	4 (2%)	3 (3%)	1 (1%)	
NNRTI-based	27 (15%)	18 (16%)	9 (13%)	
PI-based	79 (43%)	45 (41%)	34 (47%)	
Other[b]	74 (40%)	45 (41%)	29 (40%)	
Use of tenofovir	89 (45%)	52 (43%)	37 (47%)	0.663[c]
CD4+ (cells/μL)	540 (384–777)	542 (376–801)	531 (406–751)	0.946[d]
CD4+ <500 cells/μL	85 (45%)	52 (45%)	33 (43%)	0.882[c]
HIV-RNA <50 copies/mL	164 (86%)	99 (86%)	65 (86%)	0.999[c]
Total cholesterol (mg/dL)	188 (164–218)	189 (164–217)	186 (164–218)	0.904[d]
HDL-cholesterol (mg/dL)	44 (36–54)	46 (36–55)	42 (36–50)	0.311[d]
LDL-cholesterol (mg/dL)	123 (103–151)	125 (99–152)	121 (107–151)	0.760[d]
Triglycerides (mg/dL)	124 (89–194)	120 (89–178)	129 (87–203)	0.395[d]
Fasting glucose (mg/dL)	88 (80–97)	88 (79–97)	87 (80–97)	0.630[d]
Systolic blood pressure (mmHg)	121 (112–133)	122 (113–132)	120 (111–133)	0.886[d]
Diastolic blood pressure (mmHg)	79 (70–87)	77 (70–85)	79 (71–89)	0.144[d]
25 (OH) Vitamin D (ng/mL)	19.8 (13.8–27.2)	20 (13.2–27.2)	19 (15.2–27.3)	0.726[d]

Abbreviations: DCI, dietary calcium intake; NRTI, Nucleoside Reverse Transcriptase Inhibitors; NNRTI, Non-nucleoside Reverse Transcriptase Inhibitors; PI, Protease Inhibitors.
[a] Median (first quartile- third quartile) or frequency (%) used to describe results of continuous or categorical variables, respectively.
[b] Other included the following drugs: maraviroc, raltegravir, etravirine.
[c] By chis-quare or Fisher exact test, as appropriate.
[d] By Wilcoxon rank sum test.