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Omega-3 Fatty Acid Supplementation in HIV+ Patients: A Randomized Clinical Trial

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BACKGROUND

- Osteopenia and Osteoporosis are common co-morbidities in HIV-infected patients [1].
- Residual systemic inflammation is thought to be a contributor to these disorders [2].
- Inflammatory cytokines increase osteoclast activity, decrease osteoblast activity and reduce calcitriol concentration [3].
- Protease inhibitors (PI) and Tenofovir (TDF) are the ARV drugs with the greatest impact on BMD, promoting the loss of bone density [4,5].
- Omega-3-Polyunsaturated fatty acid (O3) is a recommended treatment for hypertriglyceridemia, a highly prevalent metabolic disorder in HIV-infected population[6].
- O3 has shown to positively impact on BMD markers in non-HIV subjects, probably related to its anti-inflammatory effects [7].

OBJECTIVE

Primary Objective:

-To evaluate the effects of O3 on bone mineral density in a group of HIV-infected patients with hipertriglyceridemia.

-**Secondary Objectives**:

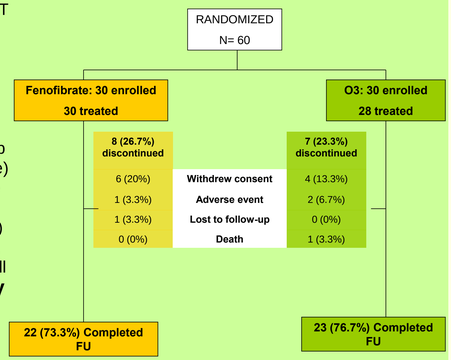
-To evaluate the effects of O3 on bone turnover parameters.

-To evaluate the effects of O3 on 1,25(OH)2D3 concentration.

PATIENTS AND METHODS

Eligibility criteria: HIV-1 infected, >40 years on stable ART (≥6 months) and plasma HIV viral laod <50c/mL (≥3 months) with plasma levels of triglycerides ≥2.2 mmol/dl were included. Subjects receiving glucocorticoids or anticoagulant therapy were not eligible.

Design: randomized, open label, comparative pilot clinical trial. 60 patients were randomized 1:1 into 2 groups. They were stratified by sex, age and ART (NNRTI vs PI). O3 group received 2 gr (460mg of EPA and 540mg of DHA per capsule) of O3 per day. Control group received 145 mg of fenofibrate per day. At baseline, month 12 and month 24 bone mineral density (BMD) (DXA Hologic QDR4500) measured in hip (PF) and lumbar spine (LS). PTH, calcitonin, C-telopeptide (CTX), Osteocalcin (BGLAP) and 1,25-(OH)2D3 were measured in all visits. **Primary outcome** was changes on BMD, **secondary outcomes** were changes in bone turnover markers and triglycerides. All markers were compared between the groups, as were changes in these parameters from baseline.



RESULTS

Baseline characteristics

	Omega-3 Group (n=28)	Fenofibrate Group (n=30)	P-value
	Mean (SD)	Mean (SD)	
Male %	85.7	86.7	1[4]
Age	52.8 (8.8)	48.9 (5.4)	0.05[1]
BMI (kg/m2)	26.6 (3.5)	25.8 (3.2)	0.389[1]
HIV viral load (copies)	40.4 (7.1)	44.1 (28.3)	0.563[2]
CD 4 T cell count	739.5 (251.1)	650 (263.3)	0.207[1]
LS BMD (g/cm2)	0.92 (0.14)	0.99 (0.13)	0.076[1]
PF BMD(g/cm2)	0.96 (0.15)	0.96 (0.14)	0.922[1]
Calcium (mmol/L)	2.4 (0.1)	2.4 (0.1)	0.302[2]
PTH (pmol/L)	7.8 (5.3)	6.7 (4.2)	0.212[2]
Calcitonin (ng/L)	4.4 (3.1)	5.6 (8)	0.472[2]
CTX (µg/L)	0.5 (0.4)	0.6 (0.3)	0.273[2]
BGLAP (µg/L)	27.2 (29.1)	19.8 (8.9)	0.497[2]
25-(OH)D3	50.14 (26.1)	60.7 (23.2)	0.135[1]
% Patients with vitamin D insufficiency*	52.2	37	0.283[3]
1,25-(OH)2D3 (pmol/L)	132.4 (34)	122.5 (50)	0.384[1]
Tiglycerides (mmol/L)	3.8 (1.7)	3.41 (0.94)	0.749[2]

1: T-test paired samples; 2: Mann-Whitney U-test; 3: Chi-square 4: Fisher Test

* 25-(OH)D3 <50 is considered vitamin D insufficiency.

Changes from Baseline to week 96

Changes from baseline to week 96	Fenofibrate		Omega-3		P-value
	N	Mean (SD)	N	Mean (SD)	
Lumbar Spine BMD (g/cm2)	22	-0.04 (0.19)	24	0.02 (0.07)	0.090[2]
Lumbar Spine BMD (%)	22	-3.07 (16.85)	24	2.94 (6.63)	0.079[2]
Proximal Femur BMD (g/cm2)	22	-0.08 (0.07)	23	-0.12 (0.08)	0.046[1]
Proximal Femur DMO (%)	22	-8.18 (7.72)	23	-12.51 (7.89)	0.070[1]
1,25-(OH)2D3	20	-6.22 (44.52)	22	-34.16 (41.53)	0.042[1]
Calcitonin	12	-2.71 (10.39)	14	0.07 (1.17)	0.795[2]
CTX	20	0,006 (0,32)	22	-0,031 (0,45)	0.97[2]
PTH	19	-1,41 (2,78)	22	0,23 (4,32)	0.229[1]
BGLAP	20	-2,98 (8,8)	22	-7,29 (16,56)	0.457[2]
Serum TG	20	-1.16 (1.21)	23	-0.76 (2.72)	0.706[2]

1: T-test paired samples; 2: Mann-Whitney U-test

ART and BMD

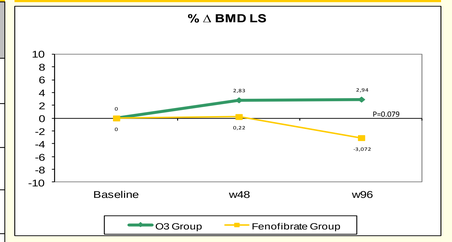
	TDF	No TDF	P-value[1]
Δ % DXA LS BMD w48	0.623	2.176	0.398
Δ % DXA PF BMD w48	-9.268	-7.833	0.691
Δ % DXA LS BMD w96	-2.318	2.253	0.242
Δ % DXA PFBMD w96	-11.098	-10.098	0.686
	PI	No PI	P-value[1]
Δ % DXA LS BMD w48	1.080	1.876	0.666
Δ % DXA PF BMD w48	-8.806	-8.134	0.852
Δ % DXA LS BMD w96	1.264	-1.187	0.533
Δ % DXA PFBMD w96	-9.586	-11.610	0.411

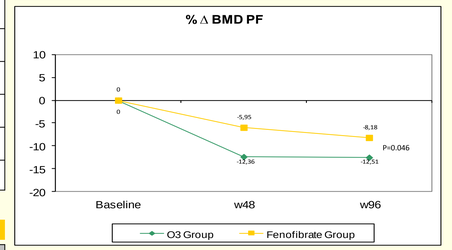
Baseline CD4 T cell count and BMD

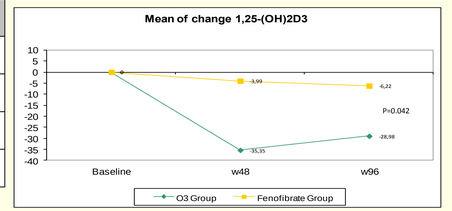
	CD4 T cell <500	CD4 T cell ≥500	P-value[1]
Δ % DXA LS BMD w48	1.703	0.999	0.738
Δ % DXA PF BMD w48	-5.604	-9.867	0.302
Δ % DXA LS BMD w96	-3.137	0.854	0.378
Δ % DXA PFBMD w96	-12.561	-10.178	0.396

1:T-test for independent measurements adjusted for multiple comparisons by Bonferroni

Results







CONCLUSIONS

1. Omega-3 fatty acid supplementation resulted in no beneficial effect on BMD or bone turnover markers.
2. A marked decrease in BMD (PF) was observed in both groups, mainly in those allocated to the O3 group.
3. A 25-(OH)D3 insufficiency not supplemented could lead to a further reduction in 1,25(OH)2D3. These changes may have contributed to the significant loss in BMD.
4. Baseline CD4 T cell count and PI- or TDF-containing regimens did not influence BMD changes.
5. Larger studies are required to confirm these findings and investigate their clinical significance.

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