

# EFFECT OF OMEGA-3 FATTY ACID ON VITAMIN D ACTIVATION IN HEMODIALYSIS PATIENTS

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## Introduction & Aims

◆ Extra-renal sources of 1, 25-dihydroxyvitamin D can be increased to normal serum 1, 25-dihydroxyvitamin D levels in chronic kidney disease patients after administration of high dose 25-hydroxyvitamin D.  
[G Jean et al, NDT 2009; 24: 3799–3805]

◆ Recent study observed that 1, 25-dihydroxyvitamin D concentrations were significantly increased after 3 months of omega-3 fatty acid (FA) supplementation compared to baseline levels without 25-hydroxyvitamin D administration in dialysis patients.  
[WS An et al, J Ren Nutr 2012; 32: 495–502]

◆ We hypothesized that omega-3 FA and 25-hydroxyvitamin D supplementations may increase 1, 25-dihydroxyvitamin D concentrations much more compare to 25-hydroxyvitamin D supplementation only in hemodialysis patients with insufficient or deficient 25-hydroxyvitamin D levels.

### Objective

- Primary
  - To investigate the change of 25-hydroxyvitamin D and 1,25-dihydroxyvitamin D concentrations at baseline, 6 weeks, and 12 weeks after administration of Omega-3 FA and cholecalciferol
- Secondary
  - To evaluate the change of erythrocyte membrane FA contents at baseline and 12 weeks after administration of Omega-3 FA and cholecalciferol

## Methods

### Study design

- Randomized, double-blind, placebo-controlled study (NCT01596842)
- Single Dong-A University Dialysis Center

### Subjects

- Patients who were treated with HD duration ≥6 months and 25-hydroxyvitamin D < 30 ng/mL
- ✓ **Omega-3 FA supplementation group** → treatment with omega-3 FA with a dose of 2.4 g/day for 12 weeks (n = 10)
- ✓ **Placebo group** → treatment with olive oil for 12 weeks (n = 7)
- Cholecalciferol supplementation
- ✓ Baseline 25-hydroxyvitamin D levels <15 ng/mL → 50,000 IU/week for 12 weeks
- ✓ Baseline 25-hydroxyvitamin D levels 16-30 ng/mL → 10,000 IU/week for 12 weeks

### Inclusion criteria

- Male or female patients aged 20 to 80 years
- Patients treated with PD for 6 or more months due to ESRD

### Withdrawal criteria

- Who needs operation or has bleeding, 2 or more weeks of hospitalization
- Who did not or failed to take a dose of omega-3 for 2 weeks or more, or wants to stop taking

### Measurements

- 25-hydroxyvitamin D levels and 1,25-dihydroxyvitamin D levels at baseline, 6 weeks, and 12 weeks
- Erythrocyte membrane FA contents by gas chromatography at baseline, 12 weeks
- We performed a diet survey and checked routine laboratory data

## Results

◆ Two patients were withdrawn during this trial because of vaginal bleeding and general weakness. Finally, 15 HD patients (cholecalciferol with olive oil, 7 patients vs. cholecalciferol with omega-3 FA, 8 patients) finished this trial.

◆ The 25-hydroxyvitamin D levels were significantly increased at 6 weeks and 12 weeks compared to baseline levels in both groups (p < 0.001 and p < 0.001, respectively; Figure 1).

◆ The 1, 25-dihydroxyvitamin D levels were increased in cholecalciferol with omega-3 FA supplemented group (17.7 ± 8.2 vs. 25.1 ± 12.3 pg/mL) compared to baseline levels, but were not changed in cholecalciferol with olive oil supplemented group (24.1 ± 11.1 vs. 23.2 ± 7.2 pg/mL; Figure 2). However, there is no significant change in both groups.

◆ The calcium, phosphorus and intact parathyroid hormone levels were not changed compared to baseline levels at 12 weeks in both groups.

◆ Erythrocyte membrane oleic acid and monounsaturated FA contents were significantly decreased and omega-3 index was significantly increased in cholecalciferol with omega-3 FA supplemented group.

Table 1. Baseline characteristics

	Cholecalciferol with Olive oil (n=7)	Cholecalciferol with Omega-3 FA (n=8)	P value
Age, years	64.4±8.5	60.0±7.3	0.298
25(OH)D (ng/mL)	10.2±1.9	10.2±4.0	0.992
1,25(OH)2D (ng/mL)	24.1±11.1	17.7±8.2	0.221
Hemoglobin (g/dL)	10.1±1.0	10.7±1.2	0.201
Calcium (mg/dL)	8.7±0.7	9.5±1.1	0.131
Phosphorus (mg/dL)	5.0±1.7	4.6±1.7	0.649
PTH (pg/mL)	560.8±236.5	325.9±338.7	0.149

Table 2. Levels of clinical parameters

	Cholecalciferol with Olive oil			Cholecalciferol with Omega-3 FA		
	Baseline	12weeks	P value	Baseline	12weeks	P value
Hemoglobin (g/dL)	10.1±1.0	10.3±0.7	0.689	10.8±1.2	10.7±1.1	0.806
<b>25(OH)D (ng/mL)</b>	<b>10.2±1.9</b>	<b>48.9±5.8</b>	<b>&lt;0.001</b>	<b>10.2±4.0</b>	<b>44.4±10.8</b>	<b>&lt;0.001</b>
1,25(OH)2D (ng/mL)	24.1±11.1	23.2±7.2	0.867	17.7±8.2	25.1±12.3	0.204
Calcium (mg/dL)	8.7±0.7	9.3±0.8	0.059	9.5±1.1	9.3±1.2	0.132
Phosphorus (mg/dL)	5.0±1.7	5.4±1.9	0.673	4.6±1.7	5.1±1.4	0.499
PTH (pg/mL)	560.8±236.5	381.5±215.6	0.075	325.9±338.7	289.2±273.0	0.566
Saturated FA	47.0±8.6	40.4±0.5	0.092	45.1±9.8	41.4±1.2	0.300
<b>Monounsaturated FA</b>	<b>17.8±1.9</b>	<b>16.1±0.9</b>	<b>0.033</b>	<b>17.5±1.5</b>	<b>15.9±1.0</b>	<b>0.022</b>
<b>Oleic acid</b>	<b>16.0±1.6</b>	<b>14.6±0.8</b>	<b>0.064</b>	<b>15.8±1.5</b>	<b>14.5±1.0</b>	<b>0.022</b>
Polyunsaturated FA	34.0±10.3	42.5±0.7	0.079	36.2±11.1	41.7±1.5	0.196
<b>Omega-3 FA</b>	<b>10.8±5.7</b>	<b>14.3±2.3</b>	<b>0.058</b>	<b>10.4±4.5</b>	<b>17.1±2.7</b>	<b>0.005</b>
EPA	1.6±0.9	2.0±0.9	0.120	1.3±0.5	3.9±1.4	<0.001
DPA	2.0±1.1	3.0±0.2	0.041	2.3±1.1	3.7±0.6	0.006
DHA	6.9±3.9	9.2±1.5	0.075	6.6±2.9	9.3±1.2	0.053
<b>Omega3 index</b>	<b>8.4±4.7</b>	<b>11.2±2.1</b>	<b>0.058</b>	<b>7.8±3.4</b>	<b>13.2±2.2</b>	<b>0.004</b>
Omega-6 FA	23.3±5.0	28.2±2.8	0.115	25.8±7.0	24.6±2.3	0.615
Arachidonic acid	10.0±4.0	14.1±1.2	0.053	11.2±4.6	11.3±1.8	0.973
<b>Omega6:Omega3</b>	<b>2.7±1.3</b>	<b>2.1±0.6</b>	<b>0.080</b>	<b>2.8±1.1</b>	<b>1.5±0.4</b>	<b>0.008</b>
Total Trans-FA	0.9±0.2	0.9±0.1	0.865	0.9±0.2	0.9±0.1	0.660

Figure 1 Levels of 25-hydroxyvitamin D according to time

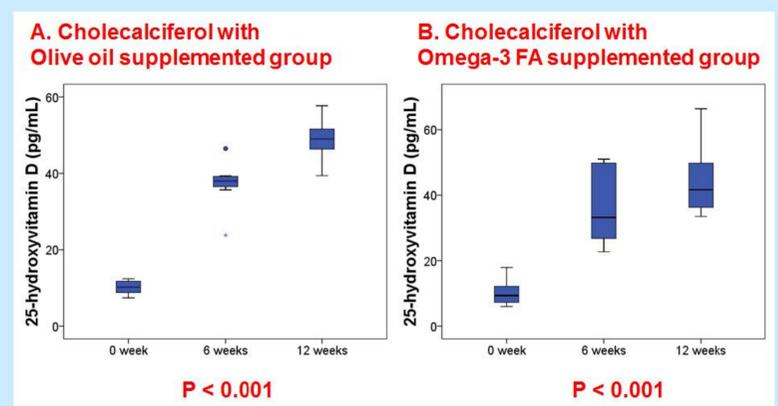
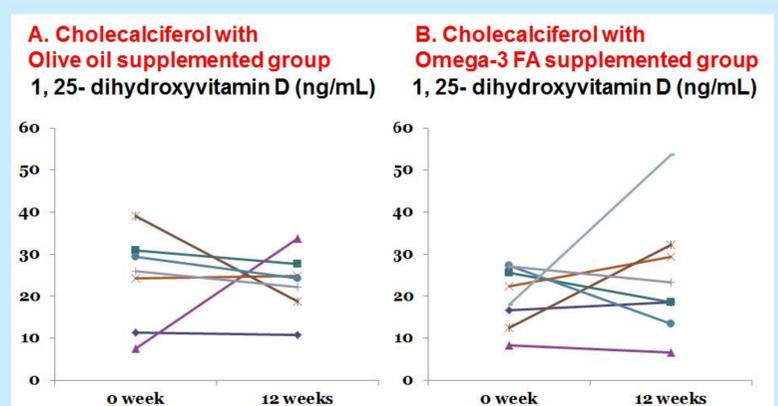


Figure 2 Levels of 1,25-dihydroxyvitamin D according to time



## Conclusions

◆ Cholecalciferol supplementation definitely increased 25-hydroxyvitamin D levels without increasing calcium and phosphorus levels in hemodialysis patients with insufficient or deficient 25-hydroxyvitamin D levels.

◆ Omega-3 FA supplementation may be related with activation of vitamin D although increased 25-hydroxyvitamin D levels caused by cholecalciferol supplementation was not related with activation of vitamin D in hemodialysis patients. Further large prospective studies are necessary for elucidate the effect of omega-3 fatty acids on vitamin D activation.

