FP 808; May the 29th 2015, 52nd ERA-EDTA Congress in ExCel London

INHIBITORY EFFECT OF EICOSAPENTAENOIC ACID ON PLAQUE PROGESSION IN HIGH AGED HEMODIALYSIS PATIENTS.

Inhibitory effect of Eicosapentaenoic acid on plaque progression in high aged hemodialysis patients.

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Background and aim

In hemodialysis (HD) patient, advanced age, diabetes mellitus, hypertension, dyslipidemia, inflammation, malnutrition, oxidative stress, vascular calcification play a role in the development of accelerated atherosclerosis [1, 2]. And carotid intima-media thickness (IMT) can be used as a surrogate marker of atherosclerosis in these patients. On the other hand Eicosapentaenoic acid (EPA) is prevalent in fish oil and their vascular protective effects are consider to be mediated by anti-inflammatory mechanisms [3]. But due to dietary limitation, HD patients might not able to intake sufficient amount of EPA by daily meal including fish (Figure 1). The aim of this study is to determine efficacy of pure EPA medication on carotid plaques of ESRD patients.

Figure 1. If Japanese healthy adult intake recommended amount of EPA and/or DHA by dietary fish only・・・

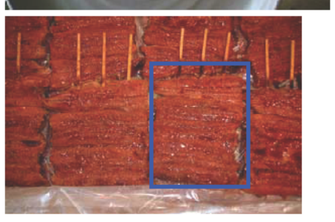
Sea breams 90g
(Protein 20.8g)
↓
1/2 piece

Yellowtail (fish) 80g
(Protein 17.2g)
↓
1 piece

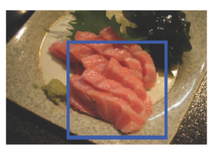
Salmon 220g
(Protein 50g)
↓
4 pieces **Photo×2 dishes**

Pacific saury 120g
(Protein 30g)
↓
2 fish **Photo×2 dishes**

Sardine 120g
(Protein 31g)
↓
3 fish **Photo×3 dishes**



Eel(grilled)
50g
(Protein 23g)
↓
1 Skewer



fattytuna (from the belly section)
66g
(Protein 13.2g)
↓
Sashimi 5〜6 pieces

Thunnus orientalis(Tuna)
2,100g
(Protein 560g)
↓
Sashimi 160 pieces
Photo×20 dishes

Bonito 800g
(Protein 206g)
↓
Sashimi 60 pieces
Photo×4 dishes

Methods

Forty-three HD patients, whose EPA/ arachidonic acid (AA) ratio under 0.50 was included in this study. Using B-mode ultrasonography, we measured IMT and plaque occurrence in the carotid arteries in these patients. Plaque was determined as IMT thickness over 1mm. Biochemical parameters were determined in all participants according to standard laboratory procedure, systolic and diastolic blood pressure was measured. Proximal internal carotid artery (ICA) = S1, carotid bulb = S2, distal common carotid artery (CCA) = S3 and proximal CCA = S4. The plaque index (PI) was calculated by summing all the plaque thickness measurements in both carotid arteries of S1, S2, S3 and S4 [4]. Summated bilateral Max IMT (BMax) was also calculated. Plaque with calcification was also determined. Ethyl icosapentate (1800mg/ day) was started 32 patients who desired to intake. Plaque was determined 2 years later by ultrasonography.

Table.1 Data of Patients

	All n = 43	Calcified Plaque (+) n=28	Calcified Plaque (-) n = 15	
Age (year)	70.6 ± 1.5	72.8 ± 1.8	66.5 ± 2.6	p=0.0497
Hemodyalisis Duration (year)	5.2 ± 0.8	4.2 ± 0.7	7.0 ± 1.9	n.s.
Sex (Female / Male)	(17 / 26)	(8 / 20)	(9 / 6)	n.s.
Diabetes (With / Without)	(20 / 23)	(15 / 13)	(5 / 10)	n.s.
Calcium(mg/dl)	8.9 ± 0.1	8.6 ± 0.1	9.4 ± 0.2	p=0.0027
Phosphate (mg/dl)	4.9 ± 0.2	5.0 ± 0.2	4.9 ± 0.4	n.s.
Intact PTH (pg/ml)	157 ± 28	159 ± 29	155 ± 59	n.s.
Systolic blood pressure (mmHg)	160 ± 9	166 ± 13	149 ± 5	n.s.
Diastolic blood pressure (mmHg)	76 ± 2	75 ± 2	77 ± 3	n.s.
Plaque index	4.42 ± 0.67	6.13 ± 0.78	0.99 ± 0.61	p<0.0001
Bilateral IMT Max	2.79 ± 0.18	3.35 ± 0.18	1.66 ± 0.13	p<0.0001
EPA/ AA	0.37 ± 0.02	0.36 ± 0.02	0.39 ± 0.06	n.s.
EPA medication (Yes / No)	(28 / 15)	(19 / 9)	(9 / 6)	n.s.
EPA/ AA 6M after medication start	1.21 ± 0.11	1.21 ± 0.14	1.21 ± 0.18	n.s.
	n=31※	n=18	n=13	
Plaque index 2 years after	5.30 ± 0.90	7.50 ± 1.07	2.25 ± 1.13	p=0.0020
(progress / improve / no change)	(18 / 6 / 7)	(13 / 5 / 0)	(5 / 1 / 7)	
Bilateral IMT Max 2 years after	2.99 ± 0.25	3.60 ± 0.31	2.18 ± 0.28	p=0.0022
(progress / improve)	(21 / 9)	(10 / 7)	(11 / 2)	
EPA medication (Yes / No)	(18 / 13)	(9 / 9)	(9 / 4)	

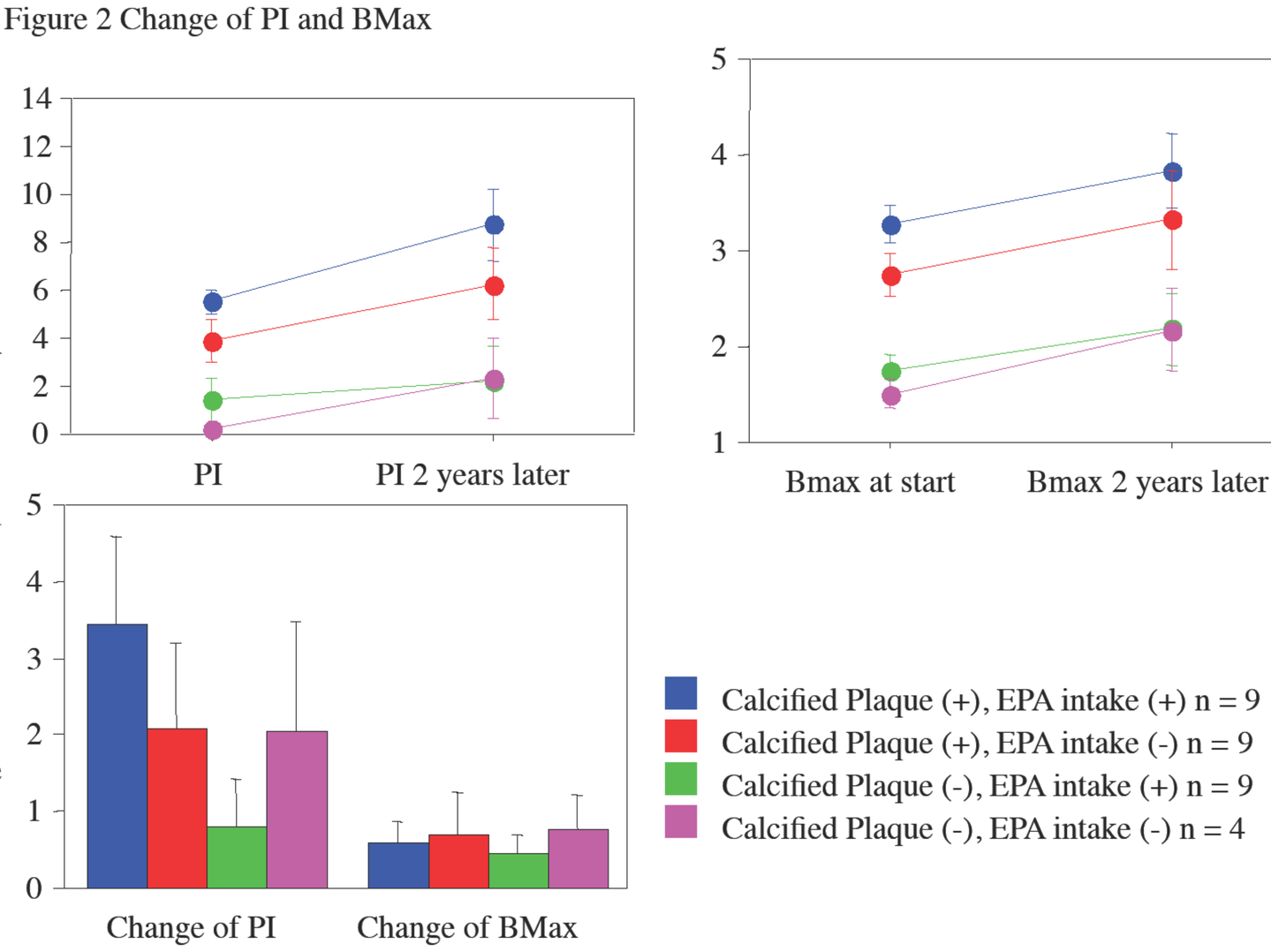
mean ± S.E.

※; Eight patients had died, 1 move to other clinic, 3 had not done 2nd echocardiogram

Result

Plaques were obtained from 33 patients (mean age 72.6 years [51.7–92.5]; calcified type plaque was found in 28 patients, non calcified type plaque in 5 patients). Patients with plaque were older than whom without plaque (72.6 years vs. 63.9 years; $P < 0.05$). Four patients were discontinued therapy because of adverse effect (skin trouble 3 and nausea 1). Six month later EPA/AA ratio was elevated in the group who continued ethyl icosapentate (0.36 to 1.54, $P < 0.05$). Thirty-one patients could exam follow-up CCA ultrasonography 2 years later. Life prognosis were bad in patients with calcified plaque(Table. 1). Patients without calcified type plaque at initial exam, change of PI and BMax were relative smaller in mean in ethyl icosapentate intake group (n.s.) (Figure 2).

Figure 2 Change of PI and BMax



Conclusion

1) Bilateral calcified plaque was found in relatively elder patients. 2) PI was higher in patients with calcified type plaque. 3) Patients with calcified plaque were relatively poor life prognosis. 4) In high aged ESRD patients undergoing HD therapy, EPA efficacy of retroaction of CCAs plaque is not confined.

Reference
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DOI: 10.3252/pso.eu.52era.2015