MP 568 The effect of lanthanum carbonate on calciprotein particles in hemodialysis patients

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Introduction & Objectives

○Fetuin-A is a serum protein that inhibits precipitation of calcium phosphate (CaPi) in the extra-osseous tissues. Fetuin-A can absorb numerous CaPi nuclei to prevent their growth into large precipitates.

○CaPi-laden fetuin-A molecules aggregate to become nanoparticles called calciprotein particles (CPP), which are dispersed as colloidal particles in the serum and eventually phagocytosed by reticuloendothelial cells.

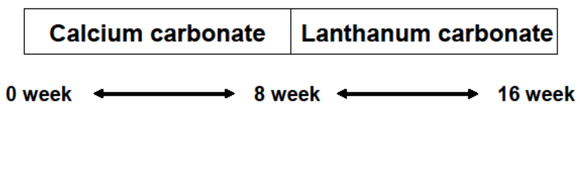
○Previous studies have shown that the serum CPP levels are increased with CKD progression and associated with chronic inflammation, vascular stiffness, and vascular calcification.

○Because CPPs have the ability to induce innate immune response, CPPs may function as a ‘’pathogen” causing poor prognosis in CKD.

○We tested whether the serum CPP levels would be reduced by treatment with calcium carbonate (CC) or lanthanum carbonate (LC) in hemodialysis (HD) patients.

Methods

【Selection criteria】
Patients with hyperphosphatemia treated by CC, age older than 20 years.
【Exclusion criteria】
Patients who have been already treated by LC, treated by parathyroidectomy or percutaneous ethanol injection therapy into parathyroid, undergoing Peritoneal Dialysis, the presence of serious digestive disturbance or liver dysfunction, pregnant or lactating.



	0 week	8 week	16 week
CPP	●	●	●
Ca, P, i-PTH	●	●	●
FGF23, Klotho	●	●	●
Fetuin-A	●	●	●
ACI	●		

※ACI：Aortic calcification Index

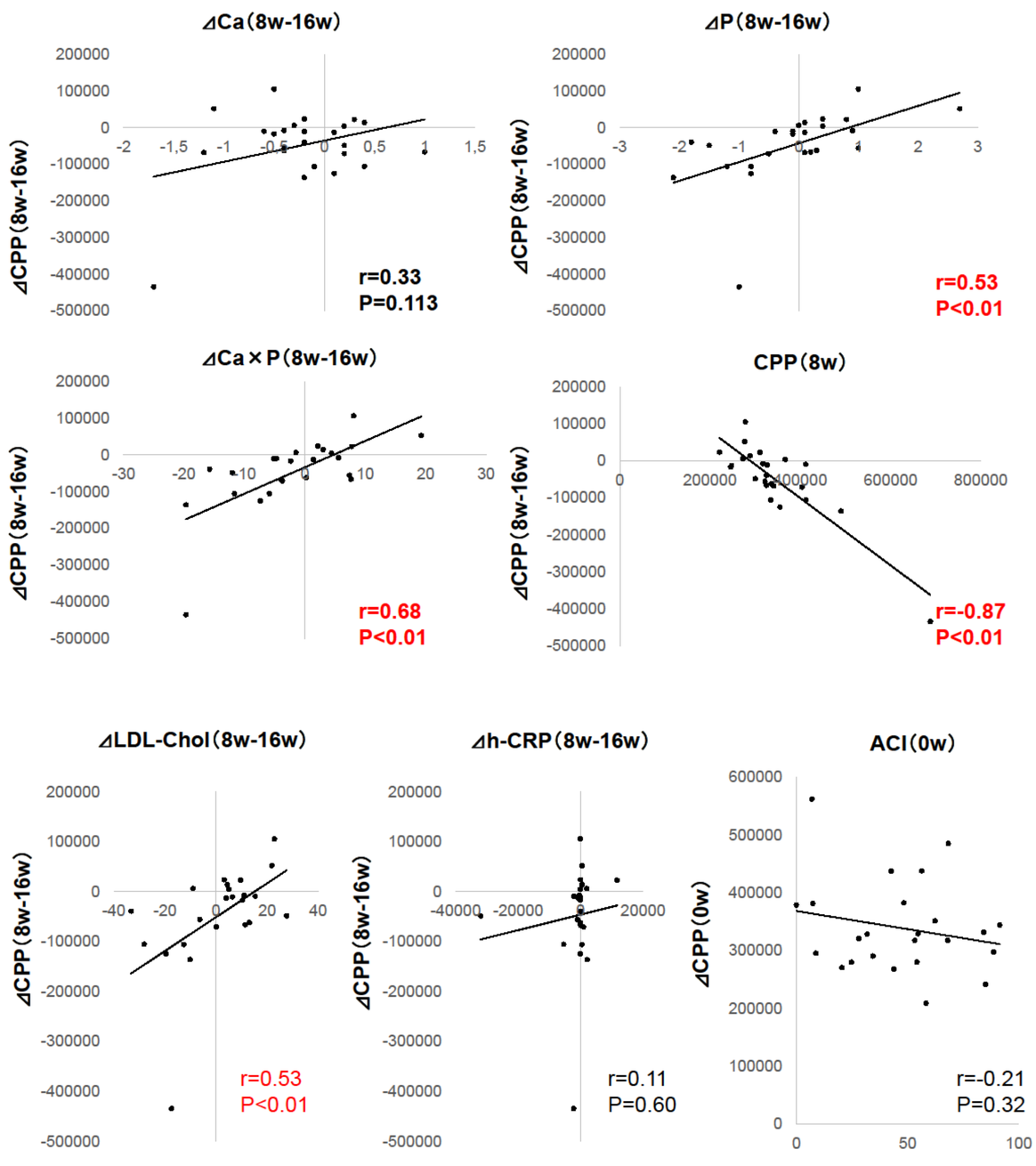
【Primary end point】The change of CPP
【Secondary endpoint】The change of Ca, P, intact-PTH (i-PTH), Fetuin-A, FGF23, α-Klotho (soluble Klotho)

Result

Patients data	n=24
Age (year)	68 ±12
Sex (%male)	12 (50)
BMI (kg/m^2)	21.2 ± 2.3
SBP (mmHg)	144 ± 23
DBP (mmHg)	76 ± 13
Period of hemodialysis (month)	7 ± 6
Kt/v	1.74 ± 0.34
ACI (%)	46.8 ± 27.1
GNRI	98.0 ± 5.8
Serum albumin (g/l)	3.9 ± 0.2
LDL cholesterol (mmol/l)	84.9 ± 25.5
Serum Ca (mg/dl)	9.1 ± 0.7
Serum P (mg/dl)	5.2 ± 1.3
Ca × PO_4 product	47.0 ± 11.6
i-PTH (pg/ml)	117.8 ± 129.6
FGF23 (Log) (pg/ml)	3.1 ± 0.6
α-Klotho (pg/ml)	484.6 ± 160.0
Fetuin-A (μg/ml)	223.5 ± 34.4
hs-CRP (mg/l)	1.3 ± 2.3

Patients data	0W	8W	16W	P
Serum albumin (g/l)	3.9 ± 0.2	3.8 ± 0.3	3.8 ± 0.3	0.30
LDL cholesterol (mmol/ l)	84.9 ± 25.5	85.6 ± 27.6	86.9 ± 23.1	0.71
Serum Ca (mg/dl)	9.1 ± 0.7	9.1 ± 0.8	8.9 ± 0.6	0.08
Serum P (mg/dl)	5.2 ± 1.3	5.0 ± 1.1	4.9 ± 1.0	0.66
Ca × PO_4 product	47.0 ± 11.6	45.5 ± 10.1	43.5 ± 8.3	0.33
iPTH (pg/ml)	117.8 ± 129.6	108.8 ± 95.0	145.7 ± 86.4	<0.01
FGF23 (Log) (pg/ml)	3.1 ± 0.6	3.1 ± 0.5	3.1 ± 0.5	0.41
α-Klotho (pg/ml)	484.6 ± 160.0	489.7 ± 180.1	461.6 ± 153.0	0.25
Fetuin-A (μg/ml)	223.5 ± 34.4	220.7 ± 35.3	214.3 ± 31.4	0.16
hs-CRP (mg/ l)	1.3 ± 2.3	3.1 ± 7.3	2.1 ± 5.0	0.47
CPP	339455 ± 79029.1	341825 ± 94543.36	294281 ± 50321.99	<0.05

Paired T test, P value : 8w vs 16w



Discussion

○Calcium-phosphate crystals are more important to cause vascular calcification than phosphate.

Ewence AE et al. Cirsulation research 2008

○CPP may stimulate pro-inflammatory and pro-apoptotic cascades in macrophages.

Smith ER et al. PloS one 2013

○CPP cause transition of vascular smooth muscle cells to osteoblast-like cells.

Sage AP et al. Kidney international 2011

○Serum CPP levels increased with CKD progression and vascular stiffness and calcification are positively correlated with serum CPP levels.

Hamano T et al. Journal of the American Society of Nephrology 2010

○The decrease in serum CPP levels after switching CC to LC suggests that calcium absorbed from the intestine may contribute to CPP in the blood.

Conclusion

○The serum CPP levels were decreased by switching the phosphate binder from calcium carbonate to lanthanum carbonate in HD patients.

○These results may explain why non-calcium-containing binders are associated with better clinical outcomes than calcium-containing binders.

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Matters requiring disclosure of COI with regard to our presentation are as follows

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