

# Can long time/high dose hemodialysis, LTD decrease in serum interleukin-6, IL-6, tumor necrotic factor- $\alpha$ , TNF- $\alpha$ and fibroblast growth factor-23, FGF-23?

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## INTRODUCTION AND AIMS

Many studies reported that long time/high dose hemodialysis, LTD improves mortality, blood pressure control, anemia, quality of life, QOL of hemodialysis patients [1-4]. Although routine laboratory data of LTD patients were monitored, any other specific data were not enough reported. High concentrations of the phosphate-regulating hormone-like substance, fibroblast growth factor 23, FGF-23 has been recently recognized as an independent risk factor for disease progression, cardiovascular disease, and death for chronic kidney disease, CKD and hemodialysis patients [5-7]. In this study, we measured FGF-23, cytokines such as serum IL-6 and TNF- $\alpha$ , including routine laboratory data in order to reveal the efficacy of LTD.

## PATIENTS CHARACTERISTICS

	SD, HDP < 54	LTD, HDP $\geq$ 54
Patients, cases	129 (53 females, 76 males)	77 (27 females, 50 males)
Diabetic nephropathy, cases	28, 21.7%	18, 23.3%
Age, years	66.8 $\pm$ 12.8	61.1 $\pm$ 11.4
Dialysis Duration, years	9.4 $\pm$ 8.7	11.5 $\pm$ 7.6
Frequency, times/week	3.0 $\pm$ 0.1	3.6 $\pm$ 0.6
Dialysis Time, hours/session	13.5 $\pm$ 1.3	19.4 $\pm$ 3.3
HDP	40.9 $\pm$ 4.1	68.4 $\pm$ 14.5

SD: Standard Hemodialysis Patients, LTD: Long Time/High Dose Hemodialysis Patients  
HDP = (Dialysis Time) x (Frequency, times/week)<sup>2</sup>, an index of dialysis adequacy[8]

## RESULTS

serum concentration	SD patients	LTD patients	p
Hemoglobin, g/dl	10.8 $\pm$ 1.0	11.1 $\pm$ 1.1	0.097
Albumin, g/dl	3.9 $\pm$ 0.3	4.0 $\pm$ 0.3	0.219
Calcium, mg/dl	8.9 $\pm$ 0.6	8.9 $\pm$ 0.6	0.902
i-Phosphate, mg/dl	<b>4.9 <math>\pm</math> 1.3</b>	<b>4.4 <math>\pm</math> 1.0</b>	<b>&lt; 0.01</b>
$\beta_2$ -MG, mg/l	<b>27.1 <math>\pm</math> 5.6</b>	<b>24.4 <math>\pm</math> 3.3</b>	<b>&lt; 0.01</b>
i-PTH, pg/ml	149 $\pm$ 138	143 $\pm$ 156	0.76
IL-6, pg/ml	<b>6.99 <math>\pm</math> 6.78</b>	<b>4.99 <math>\pm</math> 4.06</b>	<b>&lt; 0.05</b>
TNF- $\alpha$ , pg/ml	5.6 $\pm$ 34.3	3.8 $\pm$ 16.3	0.666
FGF-23, mg/dl	<b>1,182 <math>\pm</math> 905</b>	<b>789 <math>\pm</math> 771</b>	<b>&lt; 0.01</b>

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## METHODS

1. Subjects were 206 hemodialysis patients, who accepted the consent of our study in documents.
2. They were well-controlled out-patients in our clinics and divided in two groups, whose hemodialysis product, HDP was higher or lower than 54 (ex. 6 hours/session and 3 times weekly).
3. The blood sample was obtained directly through an arteriovenous fistula before hemodialysis on the day of the longest interval between consecutive dialysis sessions.
4. Measurements
  - Hemoglobin was measured by an automated cell counter, Sysmex XE-2100 (Sysmex Corp., Kobe, Japan).
  - Albumin, Calcium, inorganic phosphate, i-Phosphate concentrations were measured using Automated Clinical Chemistry Analyzer JCA-BM2250 (JOEL Ltd., Akishima, Tokyo).
  - $\beta_2$ -MG was measured using latex enhanced immunoturbidimetric assay kit 'EIKEN' $\beta_2$ -M-II (Eiken Chemical Co. Ltd. Tokyo, Japan) and Automated Clinical Chemistry Analyzer JCA-BM9130 (JOEL Ltd., Akishima, Tokyo).
  - Intact parathyroid hormone, i-PTH; Elecsys<sup>®</sup> PTH and automated immunoanalyzer Modular Analytics (Roche Diagnostics, Mannheim, Germany).
  - IL-6 & TNF- $\alpha$ ; PeliKine<sup>™</sup> human IL-6 ELISA kit & PeliKine Compact<sup>™</sup> human TNF- $\alpha$  ELISA kit (Sanquin Blood Supply, Amsterdam, The Netherland) and FGF-23; FGF-23 ELISA Kit (KAINOS Laboratories, Inc., Tokyo, Japan). Wellwash & Multiscan FC (Thermo Fisher Scientific Inc., Waltham, MA, USA) were used for measurements.
5. Statistical analysis

All data and results are expressed as mean  $\pm$  s.d.

Statistical analysis was done using unpaired Student's test.

A p value <0.05 was considered statistically significant.

## DISCUSSION & CONCLUSION

1. Serum FGF-23 in two groups was lower than those, which were reported, because our Standard Hemodialysis, SD patients had also enough doses of hemodialysis and lower serum i-phosphate.
2. What's more, serum FGF-23 in Long Time/High Dose Hemodialysis, LTD patients was significantly lower than that in SD patients. As many studies were reported, LTD removed more phosphate and lower serum i-phosphate decreased FGF-23.
3. As serum  $\beta_2$ -MG and IL-6 in LTD patients were significantly lower than those in SD patients, lower  $\beta_2$ -MG might be caused by not only more removal but less production.
4. In conclusion, long time/high dose hemodialysis, LTD might bring better outcome to hemodialysis patients.

