

# Evaluation of intradialytic phosphate binding ability of new phosphate binder ferric citrate hydrate

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## BACKGROUNDS

- Efficacy of phosphate (IP) binders has been evaluated by the difference of predialytic IP concentration between before and after administration.
- However, it is not direct evaluation, because the predialytic concentration is influenced by hemodialysis (HD) conditions and patient's body size.
- The efficacy should be evaluated directly by IP binding ability or reduction amount of IP absorption.
- New IP binder ferric citrate hydrate (FCH) became recently clinically available in Japan.

## AIM

- The aim of this study is to evaluate directly the efficacy of IP binders by estimation of reduction amount of IP absorption. In this study, we used FCH as the IP binder.

## METHODS

Fourteen patients with hyperphosphatemia undergoing maintenance HD in our three HD centers were enrolled in this study.

We started FCH administration at daily dose of 1500mg to these patients.

Efficacy of FCH was evaluated by (1) reduction of predialytic serum IP concentration and (2) reduction of estimated amount of IP absorption.

Blood sampling and estimation of the amount of intradialytic IP removal (Rp) were performed twice each before and after start of administration. In IP mass balance, the amount of absorption and removal are considered to be equal. Estimated Rp (eRp) was calculated with the following formula as previously reported (NDT vol27, suppl.2, ii492 (SAP546), 2012),

$$eRp = 33.06 Qb(1 - (3Ht_0 + 2Ht_T)/500) ((1 - 0.125T) + 1.75(UN_T/UN_0)^{1/T}) Pa_0 + (1.726T - 2.174) Pa_T + 0.0689UF(Pa_0 + Pa_T)$$

Where eRp (mg/HD), Ht<sub>0</sub>=haematocrit at start of HD (%), Ht<sub>T</sub>= that at end of HD (%), T=HD duration (Hrs), UN<sub>T</sub>=urea nitrogen concentration at end of HD, UN<sub>0</sub>= that at start of HD (mg/dl), Pa<sub>0</sub>= IP at start of HD, Qb= blood flow rate (dl/min), Pa<sub>T</sub>= IP at end of HD (mg/dl), UF= amount of ultra-filtration (dl/HD).

Estimated weekly Rp (eRpw) was calculated with the following formula as previously reported (NDT vol28 suppl.1, i460 (MP543), 2013),  $eRpw = 2.793eRp_1$ , where eRp<sub>1</sub>= eRp at the first HD of the week. eRpw was considered to be equal to weekly amount of IP absorption. Thus, daily amount of IP absorption was calculated as eRpw /7.

## RESULTS

- (1) Alteration of predialytic IP were shown in figure 1. FCH reduced IP concentration by  $1.5 \pm 1.4$  mg/dl. The result of serum IP reduction by 1.5 mg/dl was consistent with the result of a clinical trial of FCH (Am J Nephrol, 2012;36(5):478-87).
- (2) Alteration of estimated amount of IP were shown in Figure 2. FCH reduced amount of IP absorption by  $78.2 \pm 73.2$  mg/day. This result was consistent with amount of reduction of daily urinary IP excretion by FCH administration in renal failure patients without HD (Clin J Am Soc Nephrol, 2014, 9(3), 543-52).
- (3) Relationship between reduction of serum IP concentration and that of IP absorption was shown in figure 3. They did not significantly correlated.

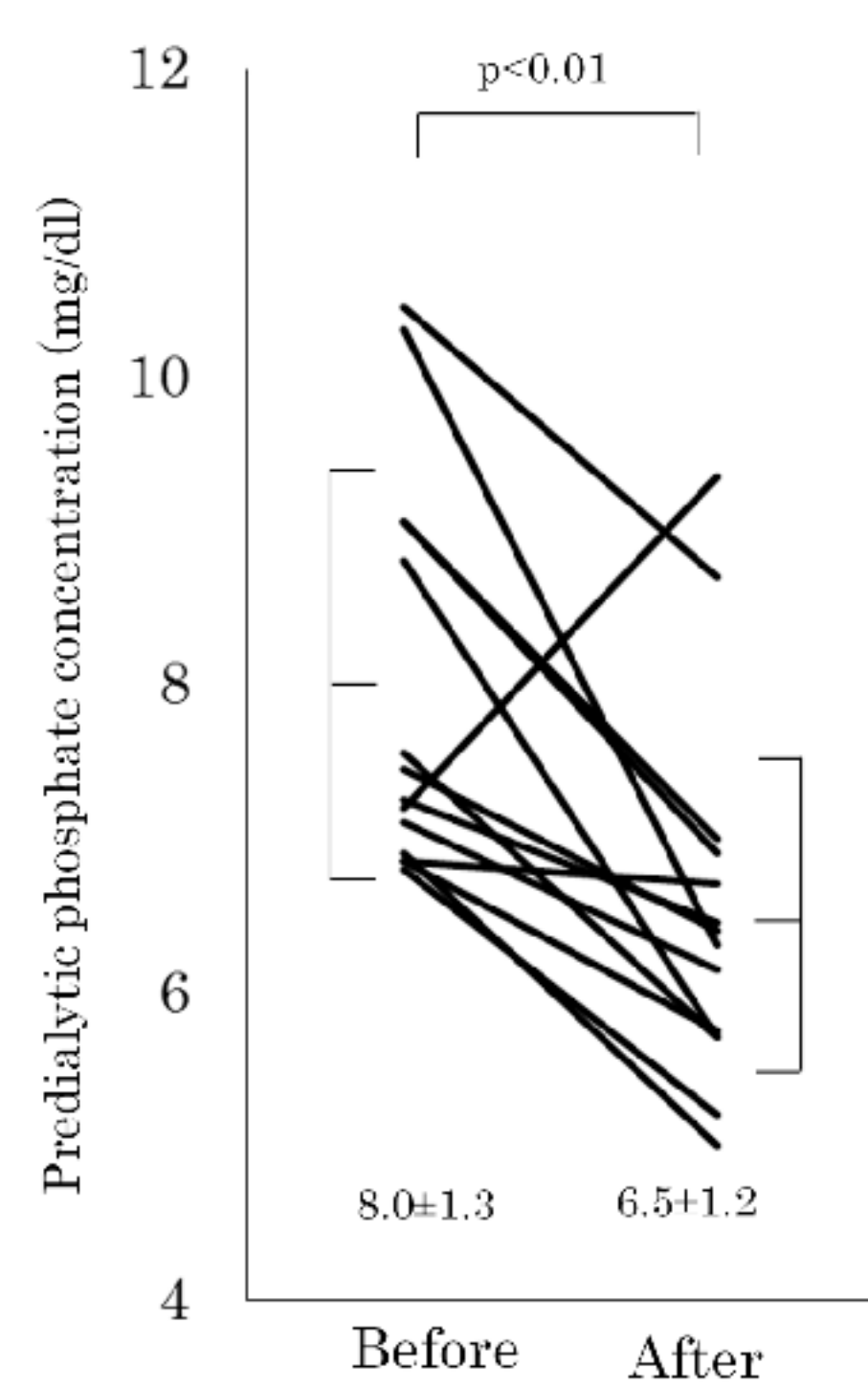


Figure 1

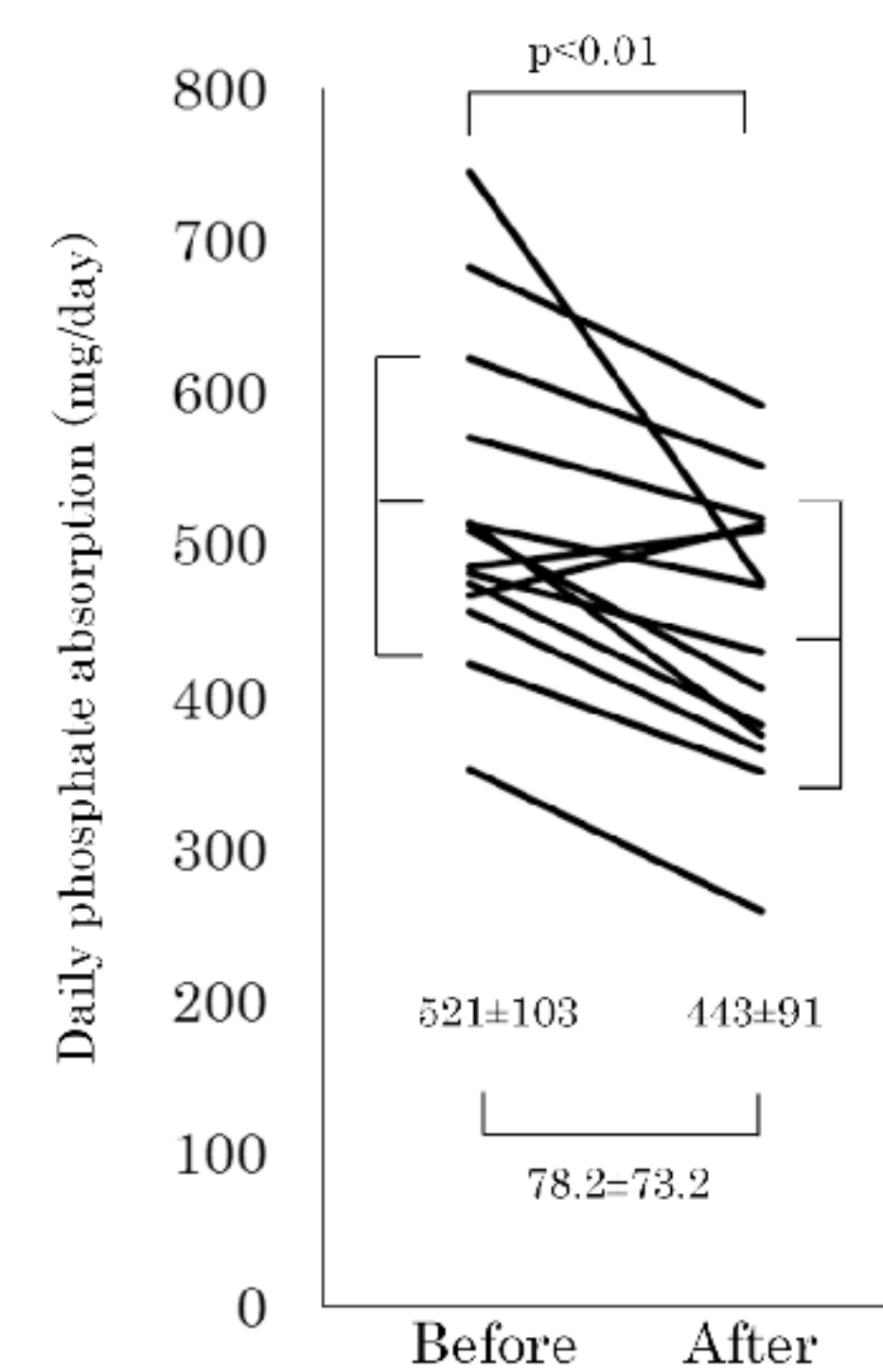


Figure 2

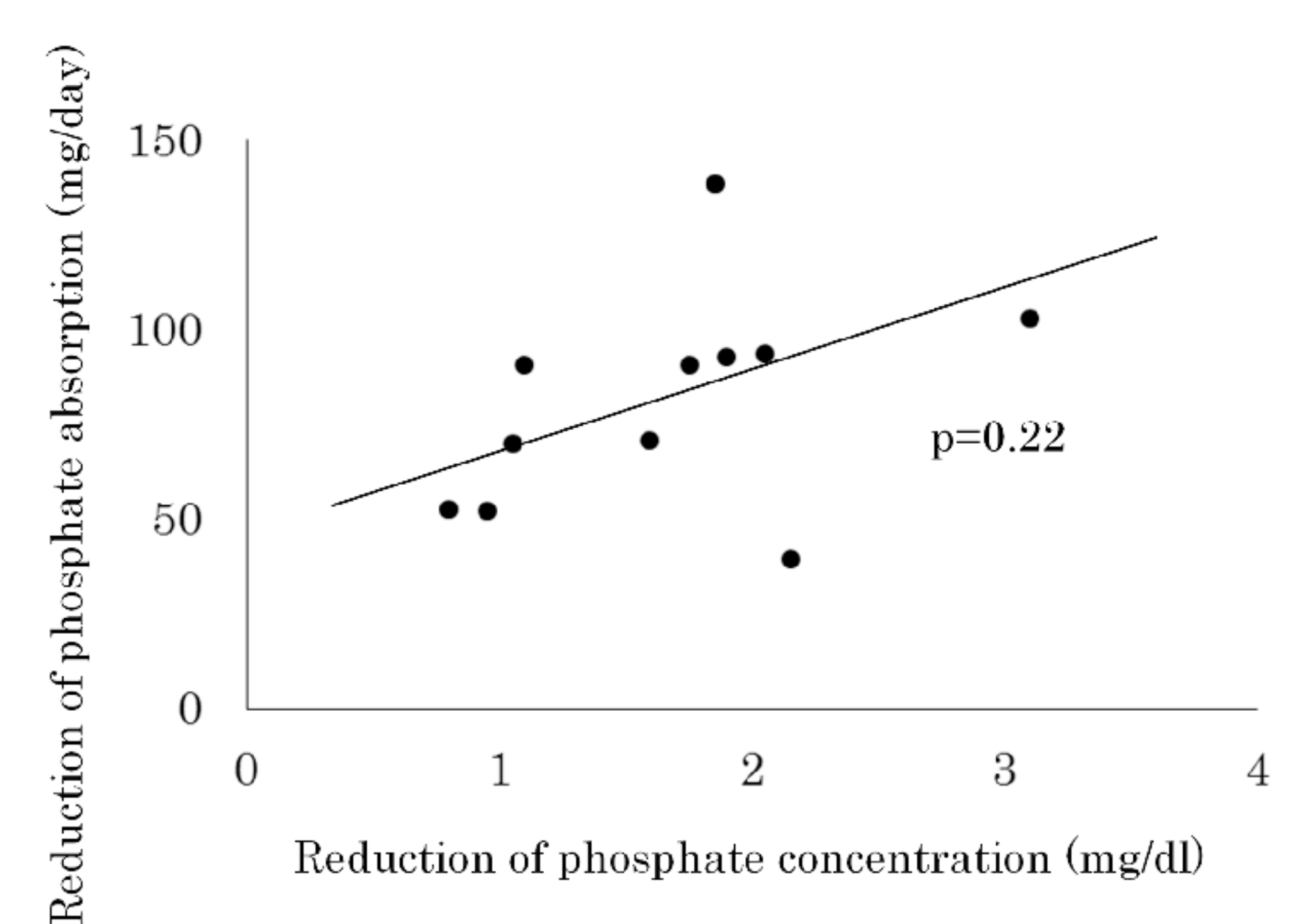


Figure 3

## CONCLUSIONS

- We were able to evaluate directly the efficacy of FCH by estimating reduced amount of IP absorption.
- Reduction of serum IP concentration did not correlate with reduction of IP absorption.

## DISCUSSIONS

Why does not reduction of serum IP concentration correlate with that of IP absorption? Each HD patient has a particular removal efficiency of IP. The efficiency is determined by body fluid volume, HD conditions and etc. Difference of efficiency causes differences of the amount of IP absorption in patients with same serum IP level. For example, the daily amount of IP absorption in patients with 7.0mg/dl of IP is approximately 400 - 600mg. If the absorption is reduced by the same amount, impact on serum IP concentration is considered to be greater in patient with 400mg removal than in patient with 600mg. That is why reduction of serum IP concentration did not correlate with that of IP absorption. Estimation of alteration of daily amount of IP absorption evaluated more directly the efficacy of FCH. The same procedure is considered to be able to apply to evaluation for efficacy of other IP binders or diet therapy.

