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Benefits of Combination Phosphate Binders on Hemoglobin Stability and Cardiovascular Outcomes through Optimal Phosphorus Control

EUNJI YANG[1], Jong Hyun Jhee[2]
[1]Department of Internal Medicine-Nephrology, CHA ILSAN MEDIACL CENTER, CHA UNIVERSITY, Korea, Republic of
[2]Department of Internal Medicine-Nephrology, Gangnam Severance Hospital, Korea, Republic of

Objectives : Hyperphosphatemia in hemodialysis patients results from impaired phosphate excretion, increasing CKD-MBD, vascular calcification, and mortality risks through elevated FGF-23 and PTH. High phosphate promotes inflammation and hepcidin production, affecting anemia. Single phosphate binders are often insufficient, requiring combinations. This study evaluated combined binders' effects on phosphate control and analyzed impacts on anemia and cardiovascular outcomes in hemodialysis patients.
Methods : This retrospective study included adult patients (≥18 years) from Korean Organ Replacement and Dialysis Registry System undergoing maintenance hemodialysis (2015-2024). Participants were grouped as single-agent(singlePB), combination(comboPB), or non-users(noPB) based on phosphate binder use. Using inverse probability treatment weighting, we analyzed mean value changes during observation. Primary endpoint assessed serum phosphorus changes, while secondary endpoint analyzed relationships between phosphorus management and cardiovascular events.
Results : A total of 6815 patients were included(noPB, 1750; singlePB, 4761; comboPB, 304). Mean age was 73.0 ± 12.8 years in no PB, 69.2 ± 12.9 in single PB, and 64.7 ± 13.4 in combo PB groups, with male proportions of 60.4%, 62.2%, and 65.1%. Dialysis vintage was 108.7 ± 72.2, 143.4 ± 80.2, 153.4 ± 91.1 months, and phosphorus/hemoglobin was 4.4 ± 1.5/10.2 ± 1.3, 5.0 ± 1.6/10.5 ± 1.2, 6.0 ± 1.6/10.6 ± 1.1. In adjusted linear mixed model, combination phosphate binders showed greater phosphorus reduction than single binders (β = −0.003 per month, p = 0.012). Patients with phosphorus control had higher hemoglobin stability (76.5% vs. 70.5%, P<0.001) and increased odds of stability (OR 1.38, 95% CI 1.28–1.49, P<0.001). Combination therapy was associated with lower cardiovascular mortality during severe hyperphosphatemia (HR, 0.07; 95% CI, 0.01–0.57; p=0.013).
Conclusions : Combination phosphate binder therapy reduced serum phosphate more than monotherapy in hemodialysis patients. Phosphate management improved anemia control and reduced cardiovascular mortality risk in hyperphosphatemia patients, suggesting combination therapy may improve outcomes.

Figure 1_KSNabstract.jpg

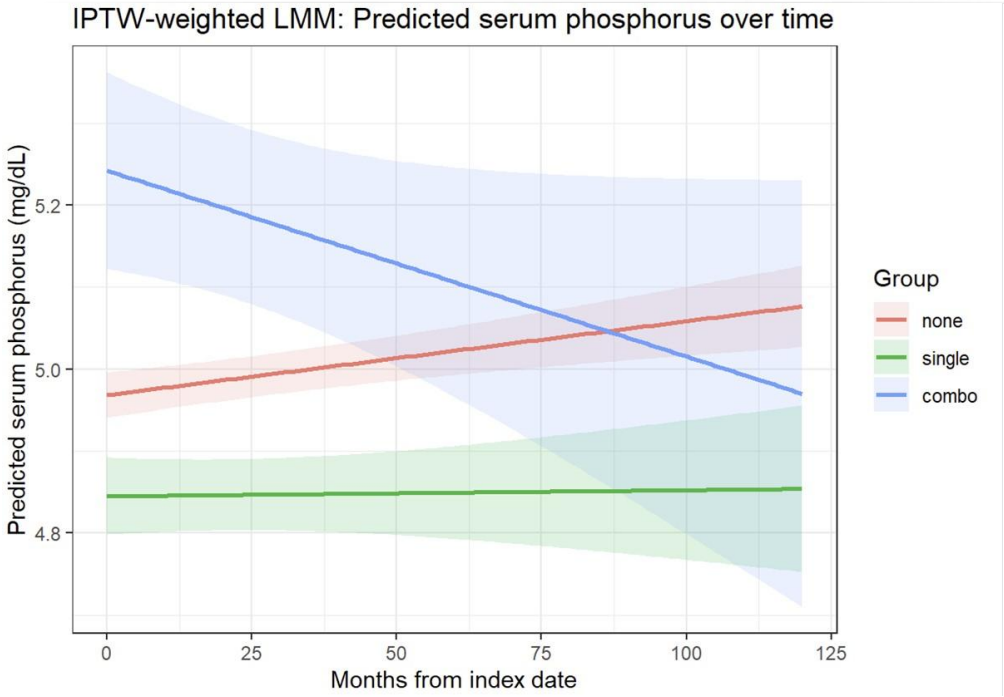

Figure 1_KSNabstract.jpg

Variable	Hazard Ratio (HR)	95% CI	P value
Combo vs single binder without severe hyperphosphatemia	2.4	1.09 – 5.27	0.029
Severe hyperphosphatemia in single binder	1.06	0.75 – 1.50	0.733
Modification of binder effect in severe hyperphosphatemia (interaction)	0.07	0.01 – 0.57	0.013
Derived HR for combo vs single in severe hyperphosphatemia	0.17	-	-

** Severe hyperphosphatemia (P ≥6 mg/dL).
** Derived HR was calculated from the interaction model: exp[β(pb_groupcombo) + β(interaction)].