Effect of Velphoro on Serum Phosphate and Albumin in Peritoneal Dialysis Patients
Luis M. Perez, Zhixing You, Jessica B. Kendrick, Isaac Teitelbaum. University of Colorado, Denver, CO.

Background: Hyperphosphatemia is common in patients on peritoneal dialysis (PD). Restricting phosphorus in the diet often leads to a decrease in protein intake, which may result in hypoalbuminemia. Hypoalbuminemia is associated with an increased risk of morbidity and mortality in PD patients. In observational studies, sucroferric oxyhydroxide (SO), an iron-based phosphate binder, was associated with improved phosphate control and higher serum albumin in hemodialysis patients. Whether SO improves phosphate control and nutritional status in PD patients is unknown.

Methods: We performed a prospective, open-label, 6-month pilot study of 17 adult PD patients from the Denver Metro Area. Patients had to use automated peritoneal dialysis for at least 3 months, have a serum albumin ≥ 3.8 g/dL, and have serum phosphate ≥ 5.5 mg/dL or ≥5.5 mg/dL on a binder other than SO. Patients currently on phosphate binders underwent a 2-week washout period. Participants were started on SO at a dose of 1 tablet daily with meals. Serum phosphate was checked monthly and the dose of SO was titrated to a goal serum phosphorus of < 5.5 mg/dL. The primary outcome was change in serum phosphate and serum albumin over 6 months.

Results: The mean (SD) age and dialysis vintage was 55 ± 13 years and 3.8 ± 2.7 years, respectively. The majority of patients were male (65%), white (82.4%) and non-Hispanic (64.7%). 88% of patients were on a phosphate binder at baseline and the majority were on sevelamer (73%). Twelve patients completed the study. Two patients withdrew due to side effects (diarrhea), 1 patient changed to hemodialysis and 2 patients died (unrelated to the study). Mild diarrhea and change in stool color were the most frequently reported side effects. Results are shown in Table 1. Serum phosphate decreased significantly from baseline but there was no significant change in serum albumin. Phosphate binder pill burden significantly decreased.

Conclusions: Serum phosphate decreased significantly with fewer phosphate binder pills/day after switching to SO. There was no change in serum albumin.

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The Impact of Peritoneal and Urine Protein Losses on Nutritional Status in Peritoneal Dialysis Patients
Cátia R. Figueiredo, Marisa Roldão, Hernâni M. Gonçalves, Francisco Ferrer, Flora Sofia. Centro Hospitalar do Medio Tejo EPE Unidade de Torres Novas, Torres Novas, Portugal.

Background: The etiology of malnutrition in peritoneal dialysis (PD) patients is multifactorial, but the peritoneal protein losses (PPL) and proteinuria may be important contributing factors. We aimed to evaluate if the total protein losses (into urine and dialysate) in PD patients have an impact on their nutritional status.

Methods: A retrospective observational study of PD patients over the first year in PD. Demographic, clinical, and analytical data were collected at baseline (time of PD initiation), 6 and 12 months later. Nutritional status was assessed using normalized protein catabolic rate (nPCR), body mass index (BMI), lean body mass (LBMI), and body fat mass (BFM). The total amount of 24h urine and dialysate protein losses (ProtUrine) and delta (Δ) values (difference between the end of follow-up period and baseline) of continuous variables were also calculated.

Results: Twenty patients were enrolled (55±8.10 years; 65% male). Except for serum albumin (sAlb), which changed significantly from the baseline to the end of the follow-up period (p=0.001), there were no differences in protein loss into dialysate (ProtDial), proteinuria (ProtUrine), nPCR, BMI, LBMI, and BFM over time. In the 3 time points there was a significant positive correlation between ProtUrine and nPCR (r = 0.563, p = 0.01; r = 0.584, p = 0.031; r = 0.611, p = 0.004, respectively). At the end of the follow-up period, we verified a negative correlation between sAlb and ProtDial (r = 0.613, p < 0.001). There was no correlation between ProtDial and nutritional parameters status, however, there was a positive correlation between ΔProtUrine and ΔBMI (r = 0.492; p = 0.028). Regarding ΔProtUrine, we verified a negative correlation with ΔLBMI (r = 0.664; p = 0.026) and, although not significant, a positive correlation with ΔBFM (r = 0.573; p = 0.066).

Conclusions: The PPL has already been linked to malnutrition in PD patients. However, we found that the total amount of protein losses daily (into urine and dialysate), and not each one individually, seems to influence the nutritional status of PD patients. Besides, proteinuria appeared to have a greater impact on nutritional changes than peritoneal losses. However, more studies with larger samples are needed to clarify this association.

MMP-7 Affects Peritoneal Ultrafiltration Associated with Elevated Aquaporin-1 Expression via MAPK/ERK Pathway in Peritoneal Mesothelial Cells
Yue Yin,1,2 Feng Zhang,1 Xiwen Xiao,1 Daming Zuo,2 Jun Ai,1 Southern Medical University Nanfang Hospital, Guangzhou, China; 2Southern Medical University, Guangzhou, China.

Background: Peritoneal membrane dysfunction and the resulting ultrafiltration failure are the major disadvantages of long-term peritoneal dialysis (PD). It becomes increasingly clear that mesothelial cells play a vital role in the pathophysiological changes of the peritoneal membrane. Matrix metalloproteinases (MMPs) function in the extracellular environment of cells and mediate extracellular matrix turnover during peritoneal membrane homeostasis. Aquaporin-1 (AQP-1), one of the water-specific channel proteins distributed in the endothelium lining the peritoneal capillaries, facilitates the osmotic transport of water across the capillary endothelium, thereby playing an essential role in ultrafiltration during PD.

Methods: Human peritoneal mesothelial cell (HPMCs)/line (HMrSV5) strain was continuously cultured in vitro and stimulated with MMP-7. Western Blot, RNA isolation, real time PCR and immunofluorescence assay were used to detect the expression of MMP-7, AQP-1 and mitogen-activated protein kinases (MAPKs) phosphorylation in HMrSV5 cells, to verify that MMP-7 affects peritoneal ultrafiltration associated with elevated aquaporin-1 expression via MAPK/ERK pathway in peritoneal mesothelial cells.

Results: We showed that dialysate MMP-7 levels markedly increased in the patients with PD, and the elevated MMP-7 level was negatively associated with peritoneal ultrafiltration volume. Interestingly, MMP-7 could regulate the cell osmotic pressure and volume of human peritoneal mesothelial cells. Moreover, we provided the evidence that MMP-7 activated mitogen-activated protein kinases (MAPKs) extracellular signal-regulated kinase 1/2 (ERK) pathway and subsequently promoted the expression of aquaporin-1 (AQP-1) resulting in the change of cell osmotic pressure. Using a specific inhibitor of ERK pathway abrogated the MMP-7-mediated AQP-1 upregulation and cellular homeostasis.

Conclusions: In summary, all the findings indicate that MMP-7 could modulate the activity of peritoneal cavity during PD, and dialysate MMP-7 might be a noninvasive biomarker and an alternative therapeutic target for PD patients with ultrafiltration failure.

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