Abstract Type : Poster exhibition
Abstract Submission No.: A-0731
Abstract Topic : Diabetic Kidney Disease + Metabolic Abnormality-related Kidney Disease

Unraveling the Effects of Ketoanalogues on Renal Outcomes and Mortality in Diabetic Kidney Disease: A Comprehensive Clinical Perspective

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Objectives : Diabetic kidney disease (DKD) is a leading cause of end-stage kidney disease (ESKD) and is associated with high morbidity and mortality. Dietary interventions, particularly very-low-protein diets (VLPDs) supplemented with ketoanalogues (KAs), have been proposed to slow kidney function decline and improve patient outcomes. However, the long-term effects of KA supplementation remain inconclusive. This study evaluates the impact of KA-supplemented VLPDs on renal function and survival in DKD patients.
Methods : A retrospective cohort study was conducted on 555 patients with stage 3–5 DKD who followed either a standard protein diet (SPD, 0.8 g/kg/day) (n = 600) or a VLPD (0.3–0.4 g/kg/day) supplemented with KAs (n = 600). The primary outcomes included eGFR decline rate, progression to ESKD requiring dialysis, and all-cause mortality over a three-year follow-up. Cox proportional hazards models and Kaplan-Meier survival analyses were used to assess associations between KA supplementation and clinical outcomes.
Results : Patients in the KA group had a significantly slower eGFR decline than those in the SPD group (−2.1 ± 0.4 vs. −4.3 ± 0.7 mL/min/1.73m² per year; $p < 0.001$). KA supplementation was associated with a 35% lower risk of ESKD progression (HR: 0.65, 95% CI: 0.50–0.84, $p = 0.002$) and reduced all-cause mortality (HR: 0.72, 95% CI: 0.55–0.93, $p = 0.012$). Benefits were more pronounced in patients with baseline eGFR > 20 mL/min/1.73m² and HbA1c < 7%, indicating early intervention may be beneficial.
Conclusions : KA-supplemented VLPDs significantly preserve kidney function, delay dialysis initiation, and improve survival in DKD patients. This dietary approach may be an effective adjunct therapy in advanced DKD, warranting further randomized trials to optimize nutritional management.