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Outcomes of Educational Initiatives for Advanced CKD
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Background: Timing of kidney replacement therapy (KRT) and transplant referral in chronic kidney disease (CKD) G4 and G5 is a difficult topic. The COVID-19 pandemic has disrupted nearly all aspects of healthcare, including the process of KRT plan. This study examined if the addition of a Transition Coordinator (TC) improved KRT transition plan despite the pandemic.

Methods: Retrospective descriptive study examining patients at single academic practice with eGFR <20 that completed CKD educational program (CKDEP). Control Group: 5/1/19-1/31/20 with virtual or in-person CKDEP, no TC. Intervention Group (IG): 5/1/20-1/31/21 with virtual or in-person CKDEP with addition of TC. TC called patient monthly to assess barriers to KRT planning, assist with scheduling, and communicate with Nephrologist. “Success” was defined as having a KRT plan. Failure was defined as either urgent start dialysis via dialysis catheter (DC) or patients without KRT plan.

Results: CG had n = 15 while IG had n = 47. Both groups were evenly distributed with age, average eGFR (15). The CG had slightly higher rates of urgent starts and patients without KRT plan compared to IG (Table 1). Patients were referred for Vascular access +/- Transplant 20% (3) in CG and 23% in IG. PD +/- Transplant was chosen in 6.7% (1) of CG and 36% (17) of IG. Success and Failure rates were similar in both groups (Table 2).

Conclusions: Despite the pandemic, there was no overall change in rate of failure (urgent start or lack of KRT plan), however, individual decreases in these groups were noted. This could indicate that TC may improve outcomes when the pandemic is controlled. Increased interest in PD was noted which could indicate greater understanding via follow up provided by TC.

Table 1
Table 2

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Chronic Hematuria Increases Chronic Kidney Injury and Epithelial Mesenchymal Transition in 5/6 Nephrectomy Rats
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Background: Chronic kidney disease (CKD) is a common outcome of many kidney diseases. Interstitial fibrosis and tubular atrophy (IFTA) is a histologic hallmark of CKD. Hematuria is a common symptom in many human kidney diseases. Free hemoglobin may affect tubular epithelial cells by generating reactive oxygen species (ROS). Epithelial mesenchymal transition (EMT) of the tubular epithelial cells has been shown to play an important role in the IFTA development. The aim of this study was to determine the effects of chronic hematuria on the CKD progression in 5/6 nephrectomy (5/6NE) rats.

Methods: 5/6NE rats were treated with oral warfarin (0.5 mg/kg/day) or vehicle (control). Animals were monitored for 26 weeks, prothrombin time (PT), serum creatinine (SCr) and hematuria were measured weekly. Stainings for iron, trichrome and EMT markers were performed on the remnant kidneys, ROS were detected in the kidneys by protein carbonyl assay at the end of the study.

Results: Warfarin treatment resulted in a PT increase 1.5-2.5 times from control, increase in hematuria and serum creatinine. Histologically, warfarin-treated animals had more iron-positive tubular epithelial cells and increased IFTA as compared to control (42.9±17% vs 18.3±2.6%), Fig 1. ROS were increased in the kidney in warfarin-treated rats. The number of tubules that show evidence of EMT was significantly higher in warfarin-treated 5/6NE as compared to control 5/6NE rats.

Conclusions: Chronic hematuria results in increased iron-positive tubular epithelial cells, EMT and more prominent IFTA in CKD rats. Our data suggests an important role of chronic hematuria in the progression of CKD.

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Figure 1. Histologic findings in 5/6NE rats with and without warfarin treatment.

A, B, C - 5/6NE rats non-treated with warfarin
D, E, F - 5/6 NE rats treated with warfarin
A, D - H&E stain, B, E - Iron (Prussian Blue) stain, C, F - Trichrome stain.

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Inhibition of Old Astrocyte Specifically Induced Substance (OASIS) in Myofibroblasts Suppressed Kidney Fibrosis
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Background: Although kidney fibrosis is a critical event for the onset of renal failure, molecular mechanisms are not fully understood. Previously, we found that Old astrocyte specifically induced substance (OASIS), a transcription factor, exacerbated kidney fibrosis in part by increased bone marrow stromal cell antigen 2 (B2u), using conventional knockout mice; however, the cell specificity of OASIS function in kidney fibrosis remains to be elucidated. In this study, we focused on the role of OASIS in myofibroblasts to elucidate novel mechanisms of kidney fibrosis.

Methods: OASIS expression in human kidneys was examined by immunohistochemistry with anti-OASIS and α-SMA antibodies. Cultured myofibroblasts were treated with AEBSF, an inhibitor of OASIS activation. In addition, C57BL/6 mice were intraperitoneally injected with AEBSF for 9 consecutive days starting 2 days before unilateral ureteral obstruction (UUO) surgery. To examine the effects of OASIS in myofibroblasts on kidney fibrosis, myofibroblast-specific OASIS knockout (cKO) mice were subjected to UUO. Day 7 after UUO, kidney fibrosis was examined by Sirius Red staining, hydroxyproline assay and immunofluorescence analysis. Isolated murine myofibroblasts were treated with TGF-β1 for 24 hours and chromosomes from cells, EMT and more prominent IFTA in CKD rats. Our data suggests an important role of chronic hematuria in the progression of CKD.

Funding: NIDDK Support

Table 1

Table 2

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Salvianolic Acid C Activates PPAR Signaling Pathway and Ameliorates Renal Fibrosis in Obstructive Kidneys
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Background: Salvianolic acid C (SAC) is a component of Danshen, a widely used herbal medicine for the treatment of renal cardiovascular diseases. Renal interstitial fibrosis is a common pathway of all kinds of chronic kidney diseases progressing to the end stage of renal diseases. We aimed to study the effect of SAC on renal fibrosis and explore its underlying mechanisms.

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Underline represents presenting author.