level. There is insufficient evidence about the effect of vitamin D on mediators of angiogenesis in general in patients with CKD. We investigated the effect of cholecalciferol supplementation on serum angio-poietin-2 levels in non-diabetic patients with CKD stage 3-4.

**Methods:** In this secondary analysis of our previously published randomized, double-blinded, placebo-controlled trial,[https://jasn.asnjournals.org/content/28/10/3100](https://jasn.asnjournals.org/content/28/10/3100), stable patients of either sex, aged 18-70 years, with non-diabetic CKD stage 3-4 and vitamin D deficiency (serum 25-hydroxyvitamin D ≤20 ng/ml) were randomized to receive either two directly observed oral doses of cholecalciferol (300,000 IU) or matching placebo at baseline and 8 weeks. The primary outcome was change in brachial artery flow mediated dilation at 16 weeks. Changes in serum angiogenesis markers (angiopoietin-1, angiopoietin-2, VEGF-A, VEGF-R and tie-2) levels between groups over 16 weeks were compared.

**Results:** A total 120 patients were enrolled. Baseline characteristics showed no differences between groups. Supplementation with cholecalciferol led to significant improvement in FMD. Serum 25(OH)D levels were similar in both groups at baseline (13.21±4.78 ng/ml and 13.40±4.42 ng/ml; p=0.88). At 16 weeks, the serum 25(OH)D levels increased in the cholecalciferol group but not in the placebo group (between-group difference in mean change:23.40 ng/ml; 95% CI, 19.76 to 27.06; p<0.001). Serum level of angiogenic markers were similar at baseline. At 16 weeks, angiopoietin-2 level decreased in cholecalciferol group (mean difference:-0.73 ng/ml, 95%CI, -1.25 to -0.20, p<0.008) but not in placebo group (mean difference -0.46 ng/ml, 95%CI, -0.59 to 0.17, p=0.154), however there was no between group difference at 16 weeks (between-group difference in mean change: -0.27 ng/ml, 95%CI, -0.59 to 0.05). Serum angiopoietin-1 level increased [mean change: 5.63 (0.51 to 10.75), p=0.032] and VEGF-R level decreased [mean change: -87.16 (-131.89 to -42.44), p<0.001] in placebo group but did not show any change in cholecalciferol group. No significant change were noted in VEGF and Tie2 in either group.

**Conclusions:** High dose oral cholecalciferol reduced angiopoietin-2 level in cholecalciferol group but not in the placebo. Further the results suggest that high dose oral cholecalciferol has no effect on serum level angiogenesis marker in subjects with non-diabetic CKD stage 3-4.

**Conflict of interest**

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**POS-402**

**CRUCIAL ROLE OF SERUM RESPONSE FACTOR IN RENAL TUBULAR EPITHELIAL CELL EPITHELIAL-MESENCHYAL TRANSITION IN HYPERURICEMIC NEPHROPATHY**

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**Introduction:** To investigate the role of serum response factor (SRF) in epithelial-mesenchymal transition (EMT) of renal tubular epithelial cells (TECs) in hyperuricemic nephropathy (HN).

**Methods:** The expression of SRF, epithelial markers (E-cadherin and ZO-1) and mesenchymal markers (fibronectin, Z-SMA, FSP-1) was examined in rat renal tubular epithelial cells (NRK-52E cells) or renal medulla tissues following uric acid (UA). SRF was upregulated by SRF plasmids and downregulated by CCG-1423(а small molecule inhibitor of SRF) to investigate how SRF influenced EMT in TECs of HN. Oxonic acid (OA) was used to generate HN in rats.

**Results:** In NRK-52E cells treated with UA and renal medulla tissue samples from hyperuricemic rats, SRF, fibronectin, Z-SMA and FSP-1 expression was upregulated, while ZO-1 and E-cadherin expression was downregulated. SRF upregulation in NRK-52E cells increased slug expression. Blockade of SRF by an SRF-specific siRNA or CCG-1423 reduced slug induction and protected TECs from undergoing EMT both in vitro and in vivo.

**Figure 1 :** UA induced EMT and SRF upregulation in NRK-52E cells.

**Figure 2 :** SRF overexpression mediated EMT and migration in NRK-52E cells.

**Figure 3 :** Inhibition of SRF preserved phenotypes of NRK-52E cells after UA stimulation in vitro.

**Figure 4 :** Inhibition of SRF suppressed slug upregulation in vitro.

**Figure 5 :** Inhibition of SRF improved epithelial phenotype of TECs, renal tubulointerstitial fibrosis and albuminuria in vivo.

**Conclusions:** Together, increased SRF activity promotes EMT and dysfunction of TECs in HN. Targeting SRF by small molecule inhibitor may be an attractive therapeutic strategy for HN.

**Conflict of interest**