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P368-Investigation of the receptor mediated drug-creatinine interaction using trimethoprim in advanced chronic kidney disease- A pilot study

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Background: Creatinine clearance occurs partially by transporter mediated renal secretion. Major transporters included in this mechanism are OCT2, OAT2, MATE1 and MATE2-K in the proximal tubules. Certain drugs like trimethoprim (TMP) cause a reversible increase in serum creatinine without causing change in glomerular filtration rate (GFR) by inhibiting these transporters. There is a growing need for clinical pharmacokinetic studies to investigate these mechanisms and aid in accurate drug dosing.

Objectives: This pilot study aimed to collate creatinine data from CKD patients who were receiving long term TMP and to estimate the change in serum creatinine concentrations after introduction of TMP.

Methods: 20 CKD patients receiving long term TMP prophylaxis with complete dataset and bloods were sampled from the Salford Kidney Study (SKS). SKS is a large longitudinal CKD cohort recruiting patients since the year 2002, with more than 3000 patients recruited. Demographic and biochemical parameters were collected at baseline (prior to TMP therapy) and at follow up. Time trend changes in creatinine levels before, immediately after and at further follow up after TMP initiation was analysed using linear-mixed effect models in SPSS.

Results:
The median age of our cohort was 67 years and it was predominantly female (65%). The median eGFR of the cohort at baseline (prior to TMP) was 30 ml/min/1.73m2. (table). There was a significant rise in mean creatinine from 157 umol/L (pre TMP) to 174 umol/L immediately post TMP ($p < 0.002$). Over a median follow-up of 3 months, the mean creatinine levels improved to 169 umol/L although the mean difference from baseline was still significantly high ($p<0.003$) (figure showing trend in 10 patients). The study was limited by this being retrospective data with variable baseline creatinine and time trends.

Conclusions:Despite limitations, a statistically significant and sustained rise in creatinine was observed after TMP introduction in advanced CKD patients due to competitive inhibition of tubular receptors. This pilot study suggests the need for a further prospective pharmacokinetic study evaluating the receptor mediated drug-creatinine interaction.