SERUM URATE: EFFECT OF ACUTE AND CHRONIC RENAL IMPAIRMENT – A DATABASE ANALYSIS

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Introduction

- Elevated serum urate (SU) in the setting of acute or chronic renal impairment may reflect reduced excretion due to diminished estimated glomerular filtration rate (eGFR).

Aim

Population study: To describe the relationship between SU and eGFR in a large referral population.
- To investigate the contributions of aging and reduced renal function on SU.

Individual study: To investigate the effect of acute changes in renal function on SU in individual patients.

Methods

- An extract was performed on the SydPath database to retrieve results from all samples processed between January 2012 and January 2013 for which analyses for both SU and creatinine had been performed.
- The data was filtered to exclude patients under 18 years of age, as well as patients known to be on dialysis.
- Both inpatients and outpatients were included in the study.
- Results of 21,455 matched SU and creatinine measurements were obtained from samples representing 13,491 patients.
- eGFR was calculated by the CKD-EPI formula.

Population study: SU was graphed as a function of eGFR. Centiles were calculated for various eGFR bins.
- Effect of age: SU was graphed as a function of age, and stratified according to eGFR bins.

Individual study: The change in sequential SU measurements was plotted against the corresponding change in creatinine. Changes were expressed as ratios. 7,987 sequential measurements were available for this analysis.

Results

Population study: An inverse relationship between SU and eGFR extended across the entire eGFR range from <15 to ≥90 mL/min/1.73m² (Figure 1).
- Effect of age: SU was also associated with increasing age, however when stratified for eGFR, SU slightly decreased with aging.

Individual study: Changes in serum creatinine were related to changes in SU with linear regression of the relationship suggesting that changes in SU approximate 48% of the changes in creatinine.

Discussion

Population study:
- SU gradually increases as renal function declines, starting from very mild reductions in eGFR. Median SU was 0.30 mmol/L for eGFR ≥90 mL/min/1.73m², increasing to 0.33 mmol/L and 0.36 mmol/L for eGFR 60 – 89 and 45 – 59 mL/min/1.73m² respectively.
- The observed relationship between SU and eGFR is not perfectly inverse as would be expected for ideal markers of GFR. As eGFR halves from 120 to 60 mL/min/1.73m², median SU increases by 30% from 0.27 to 0.35 mmol/L. Renal handling of urate comprises tubular reabsorption and secretion in addition to glomerular filtration.
- While <10% of this population with eGFR 45 – 60 mL/min/1.73m² have SU above an upper reference limit of 0.5 mmol/L, this proportion increases to 40% in patients with eGFR 15-30 mL/min/1.73m². Increased flagging rates should be expected as the degree of renal impairment worsens.
- Effect of age: if SU were related to age merely via an age-related reduction in GFR, flat profile lines would be expected upon eGFR stratification. The observed down-sloping profile lines suggest factors related to ageing are present which act to decrease SU despite age-related GFR reduction – such as decreased dietary intake, for example.

Individual study:
- The lesser magnitude of observed changes in SU compared to creatinine may be related to differences in the renal handling of SU compared to creatinine.
- The observed short term changes with renal impairment suggest GFR is an important contributor to the observed inverse relationship on the population level.
- As this study was observational in nature, the possibility of reverse causality cannot be excluded, ie, renal impairment due to elevated SU. However, acute urate nephropathy is thought unlikely to be a significant contributor at the SU levels observed in this study.

Conclusion

- At a population level, the increase in SU with decreasing eGFR extends from normal renal function through to end stage kidney disease.
- The age-related increase in SU is less than would be expected from just considering the decline in eGFR with ageing alone.
- At the level of the individual, changes in SU correspond to changes in renal function, which largely explain the relationship between SU and eGFR observed at the population level.