112

The Association Between Hyperkalaemia Risk and Cardiovascular and Renal Comorbidities in a Large Real-World Cohort of CKD Patients

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Background and Aims: Approximately 275.9 million people globally and 5.6 million people in the UK are living with chronic kidney disease (CKD). The risk of hyperkalaemia (HK) is elevated in CKD due to renal impairment and may increase further upon treatment with renin-angiotensin-aldosterone system inhibitors, which are commonly used in many cardiovascular and renal conditions. This study aimed to assess the relationship between comorbidity burden and HK risk in a large cohort of UK CKD patients.

Method: Primary and secondary care data from the UK Clinical Practice Research Datalink (CPRD) and linked Hospital Episode Statistics (HES) were used to identify patients aged ≥18 years who had a diagnosis of stage 3+ CKD (identified as either a READ code for non-dialysis CKD stage 3+ or an estimated glomerular filtration rate (eGFR) <60 mL/min/1.73m2 without a prior READ code for dialysis) during the study period (2008–June 2018) or the five-year look-back period (2003–2007). Patient's index date was 1st January 2008 or the first date of CKD diagnosis, whichever occurred later. Diagnoses based on the presence of READ codes were used to define the accumulation of further cardiovascular or renal comorbidities of interest (resistant hypertension, heart failure, diabetes or dialysis-dependent CKD). The incidence of HK was defined as serum potassium (K+) thresholds of ≥5.0, ≥5.5 and ≥6.0 mmol/L.

Results: In total, 297,702 eligible patients had a CKD diagnosis during the study or look back periods and their mean follow-up was 5.6 (SD 3.2) years from index date. At baseline, mean age was 74.7 (11.3) years, mean body mass index was 28.3 (5.9) kg/m2, and 58.6% of patients were female.
CKD was the first diagnosis in 169,532 patients (56.9% of all CKD diagnoses), second diagnosis in 92,651 patients (31.1%), third in 32,606 patients (11.0%) and fourth or fifth in 2,913 patients (1.0%); however, only 11,129 CKD patients (3.74%) developed four or more comorbidities of interest. In total, 1.5% of the cohort (4,544 patients) progressed to dialysis and 29.6% (88,245 patients) died during the study period.
In general, the incidence of HK increased with the number of comorbidities of interest (Figure 1). At a K+ threshold of ≥5.0 mmol/L, crude incidence rate of HK was 286.5 (95% CI: 285.2–287.8) per 1,000 patient-years in patients with CKD only; this increased 2.8-fold to 806.8 (741.5–876.4) in patients with five comorbidities of interest. A similar trend was observed at K+ thresholds of ≥5.5 mmol/L and ≥6.0 mmol/L. A 5.9 fold increase was observed in crude incidence rate of HK (from 59.7 [59.1–60.3] with CKD only, to 350.3 [307.7–397.1] with all five comorbidities) at a threshold of ≥5.5 mmol/L and a 10.6-fold increase (from 9.1 [8.9– 9.4] to 96.2 [74.6– 122.2]) at the ≥6.0 mmol/L threshold.

Conclusion: This assessment of a large real-world patient cohort showed that the risk of HK in patients with CKD increases with the number of cardiovascular or renal comorbidities. Emphasis should be put on effective prevention and treatment of HK in CKD, especially in patients with high comorbidity burden.