Determining the association of allopurinol prescription on progression of renal dysfunction and progression to renal replacement therapy in patients with chronic kidney disease [CKD].

Andrew S Jeyaruban[1,2], Andrew J Mallett[1,2,3], Anne Cameron[1,2,3], Jianzhen (Jenny) Zhang[2,3], and Helen G Healy[1,2,3]
on behalf of the NHMRC CKD.CRE and CKD.QLD Collaborative
1. Kidney Health Service, Metro North Hospital and Health Service, Brisbane, Queensland, Australia. 2. CKD.QLD and the NHMRC CKD.CRE, The University of Queensland, Brisbane, Queensland, Australia. 3. Faculty of Medicine, The University of Queensland, Queensland, Australia.

www.ckdqld.org https://cre-ckd.centre.uq.edu.au/

Background

Reports in the literature link hyperuricaemia with incident CKD. However, the relationship between allopurinol prescription and progression of renal dysfunction is not well understood.

Aim

To determine the association between allopurinol prescription and changes in kidney function amongst patients with CKD, enrolled in the CKD.QLD Registry.

Methods

- This is a retrospective cohort study of 1,123 patients with CKD in nephrology specialist care within a tertiary hospital in Brisbane, Australia, and who were registered in CKD.QLD Registry between January 2011 and August 2017.
- Each patient included had a minimum of 2 years survival from date of consent.
- Delta eGFR (CKD-EPI) was calculated as the difference between latest eGFR and initial eGFR at time of consent to the Registry.
- Patients who progressed to end stage kidney disease were imputed an eGFR 8mL/min/1.73m^2 at the date of commencement of kidney replacement therapy (KRT).
- Patient comorbidities, prescription of allopurinol, renal function and outcomes (KRT and death) were obtained from electronic medical records.
- Patients were then stratified into groups based on prescription of allopurinol.

Results

- 207 (18.4%) patients were prescribed allopurinol.
- Within the group prescribed allopurinol, 21 (10.1%) commenced KRT and 59 (28.5%) died. In the group not prescribed allopurinol, 105 (11.5%) commenced KRT and 224 (24.5%) died.
- The proportion of patients prescribed allopurinol by CKD stage was 1.5% for stage 1, 7.1% for stage 2; 21.7% for stage 3; 21.4% for stage 4, and 17.3% for those in stage 5.
- Those prescribed allopurinol were older than those not (70.7 vs 65.8 years; p<0.01), had a higher BMI (32.3kg/m^2 vs 30.5kg/m^2; p<0.01), worse renal function at time of consent (35.2 vs 43.6 ml/min/1.73m^2; p<0.01), higher urate levels (0.5 vs 0.4 mmol/L; p<0.01), as well as higher proportions of diabetes (p=0.04), dyslipidaemia (p<0.01) and hypertension (p<0.01). **(Table 1)**
- Prescription of allopurinol did not have a significant association with delta eGFR in patients with hyperuricaemia (p=0.02) or gout (p=0.05). Allopurinol prescription in a subgroup of patients with a serum urate level > 0.36mmol/L was also not associated with a significant change in delta eGFR (p0.17). **(Tables 2, 3, 4 and 5)**
- In multivariate analyses of the outcome of change in eGFR, which included the covariates of age, urate levels, diagnosis of gout and allopurinol prescription, none of these factors were significant.

Table 1: Characteristics of patients with and without allopurinol prescription.

Comorbidity	Allopurinol Mean (SD)	Not on allopurinol Mean (SD)	P value
Total No	207	916	
Age	70.7 (12.4)	65.8 (16.8)	<0.01
eGFR	35.2 (14.1)	43.6 (21.8)	<0.01
Urate	0.5 (0.1)	0.4 (0.1)	<0.01
BMI	32.3 (7.8)	30.5 (7.8)	<0.01

	Allopurinol N (%)	Not on allopurinol N (%)	P value
Diabetes	111 (53.6%)	416 (45.5%)	<0.04
Dyslipidaemia	111 (53.6%)	375 (40.9%)	<0.01
Ischaemic heart disease	78 (37.7%)	253 (27.6%)	<0.05
Hypertension	173 (83.6%)	660 (72.1%)	<0.01
Heart failure	26 (12.6%)	60 (6.6%)	<0.05
Stroke	25 (12.1%)	94 (10.3%)	0.5
Peripheral vascular disease	32 (15.5%)	125 (13.6%)	0.5

Table 2: Delta eGFR by allopurinol treatment (all patients)

	N	Mean (SD)	P-value
Not on Allopurinol	916	2.1 (8)	0.8
Allopurinol	207	1.9 (3.9)	

Table 3: Delta eGFR by allopurinol treatment in patients with baseline urate > 0.36 mmol/L

	N	Mean (SD)
Not on Allopurinol	503	1.8 (4.0)
On Allopurinol	147	1.6 (3.7)
Total	650	1.8 (4.6)

Table 4: Delta eGFR by allopurinol treatment in patients with baseline urate < 0.36 mmol/L

	N	Mean (SD)
Not on Allopurinol	273	1.4 (5.1)
On Allopurinol	36	1.1 (4.4)
Total	309	1.3 (5.0)

Table 5: Delta eGFR by allopurinol treatment in patients with diagnosed gout

	N	Mean (SD)
Not on Allopurinol	273	1.4 (5.1)
On Allopurinol	36	1.1 (4.4)
Total	309	1.3 (5.0)

Conclusion

Allopurinol prescription was more prevalent in patients with advanced CKD. However, it did not appear to be independently associated with deterioration of kidney function.

Limitations of this report include that the patients with the shortest survival were excluded (inclusion criteria: minimum 2 years survival in the CKD.QLD Registry) and that the expression of KRT incidence is by a percent instead of a time dependent variable or rate (per 100 years).

Queries: *please contact the NHMRC CKD.CRE @* ***ckd.cre@uq.edu.au*** *or phone* ***+61 7 3346 4995.***
Primary Author contact details: *Dr Andrew Jeyaruban @ andrewjeyaruban@gmail.com*

Sponsors: