Effect Of Allopurinol On Other Drug Use In Patients With Gout

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Introduction

- Gout affects 1 in 40 people in the UK (roughly 1.5 million) and is the most common form of inflammatory arthritis
- Allopurinol is the most frequently prescribed drug for gout and gout flares
- A multitude of studies have investigated the effects of gout and allopurinol on a wide range of outcomes; however these have mostly been restricted to comorbidity or adverse events

Aim

To estimate the effect of allopurinol on use of other drugs, namely analgesics, colchicine and NSAIDs, using a large database of anonymised primary care electronic health records, and to assess the sensitivity of the findings to missing data.

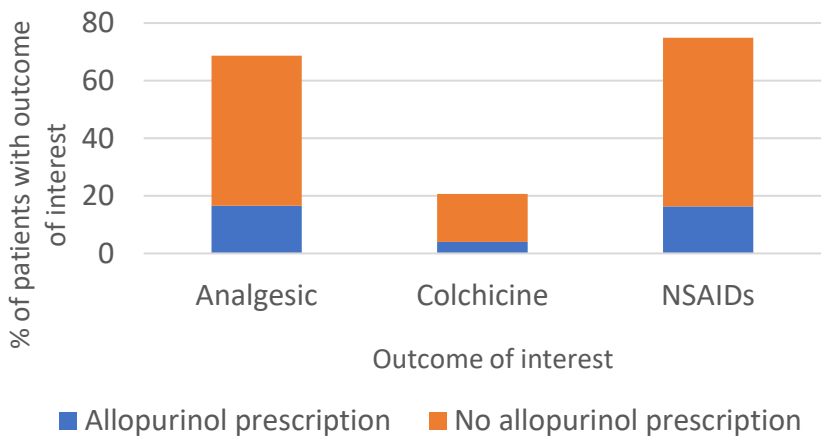
Methods

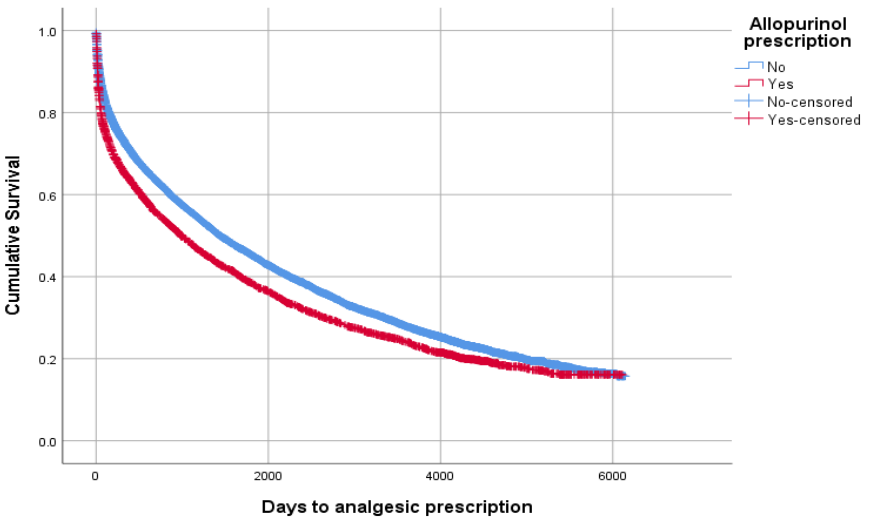
- Retrospective cohort study design
- Data sourced from the Clinical Practice Research Datalink (CPRD)
- Study sample consisted of patients that had incident consultation for gout between 1997-2002 (date defined as index date), with no allopurinol or uricosuric drugs prescription in the two year period prior
- Use of allopurinol was ascertained within 12 month period following index date
- Patients were followed up until the earliest of: prescription of interest, date of death, date of practice transfer, date of last collection of records from practice (31st December 2014)
- Cox model, a semi-parametric proportional hazards model, was used to provide an estimate of the hazard ratios (HR) and 95% confidence intervals (CI), with the hazard function given by:

$$\lambda(t|\boldsymbol{x}) = \lambda_0(t)e^{x\prime\beta}$$

- HR is an estimate of the ratio of the hazard rate in the treatment group (allopurinol users) versus the control group (non allopurinol users)
- Unadjusted and adjusted HRs were estimated; covariates adjusted for were those demographic, comorbidity and lifestyle factors that were significantly associated with either treatment or outcome of interest
- Kaplan-Meier estimator was used to depict survival function empirically
- Sensitivity of study findings on omitting patients with missing data was performed

Occurrence of event of interest in allopurinol vs non-allopurinol users





Kaplan-Meier graph created in SPSS showing cumulative survival over time for allopurinol users and non-allopurinol users

Results

- 16,876 eligible patients consulted for gout between 1997 – 2002
- Median (IQR) follow-up in the three cases of analysis: 11.2(6.5,13) years for analgesics, 9.8(4.8, 12.4) years for colchicine and 8.8(4.3,11.7) years for NSAIDs
- Mean (SD) age: 63 (14.5) years allopurinol users, 62 (14.8) years non-allopurinol users
- Gender: 76% male allopurinol users, 77% male non-allopurinol users
- Treatment groups only differed significantly with respect to:
  - Urate level >360μmol/L : 51% allopurinol users, 32% non-allopurinol users
  - Diuretic use: 46% allopurinol users, 34% non-allopurinol users
- In unadjusted analyses, use of allopurinol was associated with an increased risk of analgesic prescription (HR 1.19), but a decreased risk of colchicine or NSAIDs prescription (HR 0.80, 0.90 respectively)
- On covariate adjustment, size of effect of allopurinol on subsequent colchicine and NSAIDs use was not altered considerably, significance was retained; allopurinol users no longer had an increased risk of an analgesic prescription (HR 1.05 (95% CI 1.00,1.10))
- Removing missing data for urate levels, smoking, alcohol and BMI reduced the sample size to 3609
- Results changed due to missing data: unadjusted and adjusted 95% CIs for all three models overlapped the null (except unadjusted CI for NSAIDs) indicating no significant difference between treatment and control group in the risk of analgesic, colchicine or NSAIDs prescription

Effect of allopurinol on the outcome of interest

Model	Unadjusted HR (95% CI)	Adjusted HR (95% CI)
Analgesic	1.19 (1.14,1.24)	1.05 (1.00, 1.10)
Colchicine	0.80 (0.74, 0.87)	0.73 (0.67, 0.80)
NSAIDs	0.90 (0.87, 0.94)	0.93 (0. 89, 0.97)

Conclusions and further work

- Allopurinol users have a higher risk than non-allopurinol users of analgesic prescription but have a lower risk of being prescribed colchicine or NSAIDs
- Results were sensitive to omission of missing data
- Further work may be performed to model the number of prescriptions of the considered drugs, which will involve use of zero inflated Poisson model

References:

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