Comparing the rate of ACE inhibitor switching to ARB in people with active asthma compared to the general population: outline protocol for a retrospective cohort study

Study investigators

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Background

Asthma is a chronic respiratory disease associated with high morbidity and healthcare cost. Airway hyper-responsiveness is an important determinant in the pathophysiology of asthma and can be affected by a variety of stimuli leading to bronchoconstriction, such as methacholine and bradykinin.

Angiotensin-converting enzyme (ACE) inhibitors are medicines prescribed to treat hypertension, heart failure and chronic kidney disease, conditions which frequently co-exist in people with asthma. Around 10% of normal individuals treated with ACE inhibitors require substitution with an angiotensin-II receptor blocker (ARB). This project aims to examine whether people with asthma are at a greater risk of switching to an ARB after initiation of ACE inhibitor therapy.

Data source

We will use anonymised primary care data from the UK Clinical Practice Research Datalink (CPRD).

Population

An open cohort of all adult asthma patients in CPRD acceptable for use in research will be created. The population will be divided into patients with asthma and the remaining general population (+ COPD). Cohort entry will be defined as the latest of: 18th birthday; registration with a general practice providing up-to-standard data + 365 days. Cohort exit for the general population will be defined as the earliest of: date of deregistration with the general practice; date of death; date of last data collection at the general practice. People with active asthma will be required to have a diagnostic code for asthma and prescription of two more asthma medications. For these patients cohort entry will begin at the latest date of these criteria.

Exposures

The exposures of interest will include incident ACE inhibitor exposure and incident ARB exposure. Patients prescribed an ACE inhibitor on or after the date of an incident ARB prescription will be considered as being treated with dual therapy and will be excluded from the analysis. Incident ACE exposure will be considered as the first prescription for an ACE inhibitor in patients with at least 1 year of observable time prior to cohort entry. Patients prescribed an ARB prior to the incident ACE inhibitor will also be excluded from the analysis.

Outcomes

Outcomes will be the rate of switching from ACE inhibitors to ARB following incident exposure for the asthma and general population.

Descriptive analysis will be undertaken to examine the number of consultations taken from ACE inhibitor initiation to ARB initiation for the asthma and remaining general population and the mean dose of the last ACE inhibitor prescription prior to ARB initiation among people who have switched will be calculated.

Analysis

Trends in the prevalence of ACE inhibitor and ARB prescribing will be plotted over time for patients with asthma. The characteristics of patients within the cohort will be described including by age, gender, body mass index, smoking status and socioeconomic status. The crude rate of ACE switching to ARB following incident exposure will be calculated.

The cohort will be analysed using COX proportional hazards regression to generate hazard ratios for risk of switching to ARB following ACE inhibitor initiation. Comparisons will be made between people with asthma to the remaining general population. Risk of switching will be evaluated over a period of 6 months following ACE inhibitor discontinuation. The analysis will be adjusted for patient characteristics and confounders including age, sex, socioeconomic deprivation and a history of hypertension and cardiovascular disease.

Reporting

Study findings will be reported in the EU PAS register and published in an appropriate medical journal.