Scottish Government Health Directorates Chief Scientist Office

CHIEF SCIENTIST OFFICE

FOCUS ON RESEARCH

MEASURING THE RISK OF BETA-BLOCKER AND NON-STEROIDAL ANTI-INFLAMMATORY DRUG PRESCRIBING IN ASTHMA

Researchers
Dr Daniel Morales, MRCGP MRCP MBChB BMSc(Hons)

Aim
To measure the risk from beta-blocker and non-steroidal anti-inflammatory drugs (NSAIDs) in asthma by analysis of clinical trials of beta-blockers and NSAIDs in people with asthma, and by conducting observational studies using linked UK electronic medical records.

Project Outline/Methodology
Clinical trials provide evidence with good internal validity whilst observational studies survey actual prescribing. Three systematic reviews of clinical trials were conducted measuring: how common aspirin-exacerbated respiratory disease is (AERD); the risk from selective (targeted) NSAIDs in AERD; and the risk of acute (full initial dose) beta-blocker exposure in asthma. Operational studies using electronic primary care data from the Clinical Practice Research Datalink were conducted using two different study designs to measure how often beta-blocker and NSAID prescribing occurs, and risk from different types of beta-blocker or NSAID. Risk from beta-blockers and NSAIDs was assessed according to their selectivity.

Key Results
Clinical trial evidence showed that around 10% of people with asthma are sensitive to aspirin (AERD). Some 'mostly selective' NSAIDs such as meloxicam triggered respiratory symptoms in 8% of people with AERD whilst no significant changes in lung function or respiratory symptoms occurred with completely selective inhibitors of cyclooxygenase-2 (COX2) such as celecoxib. Acute exposure to non-selective beta-blockers reduced a key measure of lung function in asthma called Forced Expiratory Volume in 1 Second (FEV1) by around 11% on average, and caused respiratory symptoms in around 1 in 13 people. In contrast, cardio-selective beta-blockers caused smaller falls in lung function (around 7% on average) and generally no respiratory symptoms. Both classes of beta-blocker had a tendency to cause falls in FEV1 of greater than 20 per cent in around one in 8 asthmatic patients, dependent, at least for selective beta-blockers, on dose. **Observationally**, selective and non-selective beta-blockers were prescribed to 2.8% and 0.6% of people with asthma respectively, having risen by 234% and 87% respectivley between 2000 and 2012. In contrast, NSAID COX2 inhibitors are rarely prescribed. Acute and high-dose non-selective beta-blocker exposure was associated with an increased risk of asthma exacerbations (managed in hospital and in primary care). In contrast, no significant risk was seen with selective beta-blockers. There was no strong evidence to suggest oral NSAIDs prescribed to selected people with asthma in primary care triggered asthma exacerbations.

Conclusions
Beta-blockers and NSAIDs are not uncommonly prescribed in asthma. Results demonstrate that non-selective beta-blockers increase asthma morbidity with their risk varying according to dose and length of exposure. Although selective beta-blockers have the potential to affect lung function in asthma, people are often asymptomatic and no increase in asthma exacerbations was seen. Although 10% of people with asthma may be sensitive to NSAIDs, the current practice of NSAID prescribing in asthma appears to be safe although further evaluation is required.

What does this study add to the field?
These risks were previously poorly quantified and the results should help prescribers better judge their risks versus benefits among individual patients.

Implications for Practice or Policy
These results suggest that selective beta-blockers should not be withheld in people with asthma who experience cardiovascular events over fear of triggering asthma exacerbations, providing they are prescribed for the first time at low dose with appropriate monitoring. COX2 inhibitors may be the safer NSAID alternative in people who are unsure whether their asthma is sensitive to NSAIDs.

Where to next?
Further research measuring how often AERD occurs is needed to better understand the population at risk.

Further details from:
danielmorales@nhs.net
d.r.z.morales@dundee.ac.uk