Important New Evidence Service

In Partnership with The Centre for Medicines Optimisation at Keele University

ScriptSwitch™ Rapid Update 3 – January 2017

Asthma – the importance of diagnosis and reassessment

Asthma is considered a chronic disease and once diagnosed adults are usually thought to have asthma for life. This Canadian study set out to determine whether it is safe to revisit the diagnosis and consider stopping asthma treatment. A third of adults who had asthma diagnosed in the previous 5 years showed no evidence of current asthma on repeated testing and follow-up. Although care needs to be taken in generalising the findings to the UK population, it is important to carefully determine if asthma is the cause of respiratory symptoms, with regular follow-up and reassessment to optimise medicines and to avoid unnecessary prescribing.

Reference: Aaron SD, Vandemheen KL, FitzGerald M *et al*. Reevaluation of Diagnosis in Adults With Physician-Diagnosed Asthma. JAMA 2017;317:269-279.

What do we know already?

- The National Institute for Health and Care Excellence (NICE) is currently preparing a guideline on asthma management and publication is anticipated in June 2017. Another NICE guideline is being developed on asthma diagnosis and monitoring.
- Until the NICE guideline is published, current recommendations for the diagnosis of asthma come from the British Guideline on the Management of Asthma (jointly developed by the British Thoracic Society and the Scottish Intercollegiate Guidelines Network). These were last updated in September 2016. They recommend:
  - A structured clinical assessment (from history and examination of previous medical records).
  - Adults with a typical clinical assessment including recurrent episodes of symptoms ('attacks'), wheeze heard by a healthcare professional, historical record of variable airflow obstruction and a positive history of atopy and without any features to suggest an alternative diagnosis have a *high probability* of asthma and should commence a trial of treatment. Response to inhaled corticosteroids (ICS) is a further diagnostic feature.
  - In determining response to treatment where there is a *high probability*, assess status with a validated symptom questionnaire and/or lung function tests (FEV_1 at clinic visits or by domiciliary serial peak flows).
  - Those patients who have some, but not all, of the typical features of asthma on an initial structured clinical assessment, or who do not respond well to a monitored initiation of treatment, have an *intermediate probability* of asthma.
  - Spirometry, with bronchodilator reversibility as appropriate, is the preferred initial test for investigating an *intermediate probability* of asthma.

What does this evidence add?

- A third of patients in this study were not proven to have current asthma after careful investigation and follow-up. There are two main reasons that may account for this:
  1. It is possible that some initial diagnoses were incorrect, leading to an overdiagnosis of asthma in some people. Lack of subsequent symptoms may then have been interpreted as showing that treatment was effective and that their 'asthma' was being well controlled.
  2. Another possibility is that previously active asthma had gone into remission and that patients no longer had the condition.
- The second explanation seems less likely, as longitudinal follow-up studies of people with a firm or established diagnoses of asthma show low remission rates (3 - 4.8% over a follow-up period of 4 – 8 years).
- The management of asthma in Canada is similar to clinical practice in the UK, but there are differences in healthcare provision, so generalising the results to the UK should be done with caution.
- Whatever the setting, this study emphasises that clinicians (often practice nurses in the UK) need to take great care to avoid overdiagnosis and overtreatment of asthma, and the subsequent inclusion of patients in disease registers. There is evidence that some clinicians may choose to diagnose and treat asthma empirically. This study reinforces the importance of using objective measures to establish the cause of respiratory symptoms, for

example, spirometry and reversibility testing. Clinicians should also be alert to other causes of respiratory symptoms in those thought to have asthma, and be prepared to question the diagnosis.

- Long-term treatment with ICS may cause harms, and can be expensive, so over- or misdiagnosis has important consequences. BTS/SIGN guidance on 'stepping down' treatment should be followed.
- Overdiagnosis of asthma may be a particular problem for those with multimorbidity receiving multiple medications. The burden of treatment can be a significant challenge for individuals and detract from quality of life.
- Another finding from this study was the lack of records that showed how the diagnosis of asthma was reached in some cases. This reinforces the importance of keeping clear records and enabling an audit trail that describes how the diagnosis of asthma was made. This is important if there are subsequent concerns over misdiagnosis.

Study details

Participants:

- This prospective cohort study was conducted in 10 Canadian cities between 2012 and 2016.
  - Randomised telephone dialling was used to contact 16,931 potential participants who were asked if a member of their household had been diagnosed with asthma in the past 5 years. Potential subjects were then contacted by the study coordinator for further telephone screening.
  - Participants had to be 18 years or older. People with a smoking history > 10 pack-years were excluded, as were those using long-term oral steroids or who were unable to undergo spirometry or bronchial challenge testing. Exclusion criteria also included recent myocardial infarction and some other medical conditions.
- Of 1,026 potential participants who fulfilled eligibility criteria during telephone screening, 701 (68.3%) agreed to enter into the study.
  - The mean age of participants was 51 years [standard deviation +/-16 years]; 467 (67%) were women.
  - 181 (44.2%) of subjects were being prescribed daily ICS.
  - 613 completed the study and could be conclusively evaluated for a diagnosis of current asthma.

Intervention and comparison:

- Participants entering the study were initially assessed using pre-and post- bronchodilator spirometry. Where reversible airway obstruction was not confirmed, participants went on to undergo bronchial challenge tests with methacholine (*this is a chemical that causes bronchospasm in those with asthma*).
- Those using daily asthma maintenance medications, who did not exhibit reversible airflow obstruction and who had a negative response to a bronchial challenge, were asked to halve their usual dose of ICS and long-acting bronchodilator, and monitor their symptoms, including recording daily peak flow measurements. Three weeks later, if there was no decline in symptoms and peak flow measurements, and the response to a further bronchial challenge test was negative, ICS and long-acting bronchodilator therapies were stopped. Patients were followed up after an additional 3 weeks, undergoing further bronchial challenge testing.
- Participants in whom a diagnosis of current asthma was ruled out (by having persistent negative tests) were followed up clinically with repeated bronchial challenge tests over a further year of follow-up.
- Information from the diagnosing physician was sought to determine how the diagnosis of asthma was originally made in the community (this was provided in around 75% of cases).

Outcomes and results:

- The primary outcome was the proportion of participants in whom a diagnosis of current asthma was ruled out (defined as participants who exhibited no evidence of acute worsening of asthma symptoms, reversible airflow obstruction, or bronchial hyperresponsiveness after having all asthma medications tapered off and after a study respiratory specialist established an alternative diagnosis.)
- Current asthma was ruled out in 203 of 613 study participants (33.1%; 95% CI, 29.4% - 36.8%).
  - 410 (67%) patients were confirmed to have asthma.
  - Alternative diagnoses for the 203 people who had asthma ruled out included rhinitis (25%) and gastro-oesophageal reflux (8.5%).
  - 12 participants (2.0%) were found to have serious cardiorespiratory conditions that had been previously misdiagnosed as asthma in the community.
  - 181 participants (29.5%; 95% CI, 25.9% - 33.1%) continued to exhibit no clinical or laboratory evidence of asthma after a further year of follow-up.
- Participants in whom current asthma was ruled out, compared with those in whom it was confirmed, were less likely to have undergone testing for airflow limitation in the community at the time of initial diagnosis.
  - 43.8% *vs.* 55.6%, respectively; absolute difference, 11.8%; 95% CI, 2.1% - 21.5%.
- It is not known if the 325 people who declined to participate in the study were different in any way.

Level of evidence: Level 1 High quality diagnostic cohort study (good quality patient-oriented evidence) according to the *SORT criteria*.
Study funding: Funded by the Canadian Institutes of Health Research (not commercially funded).