Risk of asthma exacerbation after stopping inhaled corticosteroids in people with stable asthma

A meta-analysis found that people with well-controlled asthma who stopped regular low-dose inhaled corticosteroids had an increased risk of asthma exacerbations compared with those who continued them.

Overview: The global strategy for asthma management and prevention, produced by the Global Initiative for Asthma suggests that preventive asthma treatment may be stopped if asthma remains controlled on the lowest possible dose of preventive therapy and symptoms do not recur for 1 year.

Current advice: The British guideline on the management of asthma was produced jointly by the Scottish Intercollegiate Guidelines Network and the British Thoracic Society. It recommends that inhaled corticosteroids should be titrated to the lowest dose at which effective control of asthma is maintained, to minimise side effects. Dose reductions should be considered every 3 months, decreasing the dose by about 25–50% each time. Hawkins et al. 2003 suggested that this strategy is realistic and possible without compromising patient care. The guideline states that stepping down therapy once asthma is controlled is recommended but often not implemented, leaving some people over-treated.

‘High-dose inhaled corticosteroids in asthma’ is included in the QIPP document, Key therapeutic topics – medicines management options for local implementation.

New evidence: A systematic review and meta-analysis of randomised controlled trials assessed the risk of asthma exacerbation after stopping low-dose inhaled corticosteroids (Rank et al. 2013). A total of 7 randomised controlled trials from the USA and Europe in 1040 people aged 6–65 years were included, with 8 to 150 participants per study arm.

The run-in period in which participants’ asthma was stable was 4 weeks in 5 trials, 6 weeks in 1 trial and up to 144 weeks in 1 small trial with 28 participants. Follow-up periods ranged from 12 weeks to 52 weeks. The regimens of inhaled corticosteroids studied were: beclometasone 80 micrograms or 500 micrograms per day in 2 trials, budesonide 150 micrograms to 400 micrograms per day in 3 trials and triamcinolone 800 micrograms per day in 2 trials. The definition of an asthma exacerbation was different in each study that was assessed.

Overall, the risk of asthma exacerbations was increased in participants who stopped inhaled corticosteroids compared with those who continued treatment (relative risk [RR]=2.35, 95% CI 1.88 to 2.92, p<0.001). The pooled absolute risk difference for an asthma exacerbation between those who stopped inhaled corticosteroids and those who continued was 0.23 (95% CI 0.16 to 0.30, p<0.001).

Commentary: "This meta-analysis has limitations that severely reduce its clinical applicability. These include a short stable asthma run-in period of as little as 1 month before stopping inhaled
corticosteroids. British and International guidelines recommend reduction of inhaled corticosteroids after at least 3 months of stability.

"The review also included studies in adults and children together. Guidelines have separate sections on children and adults in line with the prevailing view that children and adults may respond differently to asthma drugs. The review was not clear about whether inhaled corticosteroids were stopped abruptly or gradually and the doses included in the studies varied, which could have biased the results. The risk of exacerbation may be lower, for example, in someone who gradually stopped a very low dose of inhaled corticosteroids compared with someone who abruptly stopped a higher dose.

"As a result of these limitations, drawing any firm conclusions is difficult. The review does highlight the need for randomised controlled trials looking at the effect of reducing and possibly stopping inhaled corticosteroids after a stable period of at least 3 months, in line with national and international guidelines." – Dr Kevin Gruffydd-Jones, General Practitioner, Box, Wiltshire and Respiratory Lead, Royal College of General Practitioners

Study sponsorship: The Mayo Foundation.