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Editor: Assoc. Prof. Chris Alderman, University of South Australia – Director of Pharmacy, RGH
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Inhaled corticosteroids and risk of diabetes mellitus

Inhaled corticosteroids (ICS) are first-line therapy for asthma and are also commonly used in the treatment of chronic obstructive pulmonary disease (COPD), in particular for those patients with moderate–severe disease and frequent exacerbations. They are preferred to oral corticosteroids because of a lower risk of systemic adverse effects, although high doses of ICS have been reported to be associated with adrenal suppression, glaucoma, osteoporosis, cataracts, pneumonia, bruising and decreased growth in children.

Oral corticosteroids increase the risk of diabetes mellitus and worsen glucose control in patients already diagnosed with the disease. Case reports have linked high doses of ICS with loss of glucose control, but a randomised controlled trial in patients with mild-moderate COPD (n= 1116) did not find an increased risk of diabetes associated with ICS use. The small number of subjects in this trial is a major limitation.

A possible association between ICS and diabetes has also been investigated in a number of observational studies. The first of these cohort studies in 2002 (n = 21645) did not find an increased risk of diabetes amongst elderly patients using inhaled corticosteroids, after adjusting for the current use of oral corticosteroids. The authors employed a nested case control design using government health insurance databases in the Canadian province of Quebec. The study was unable to measure and control for other risk factors for diabetes, such as family history and obesity.

In 2010 a larger and longer retrospective cohort study (n = 388584) using the same Canadian databases as the 2002 study was published. After excluding patients who had received a prescription for oral corticosteroids during the previous year, current use of ICS was associated with a significant 28% increase in the risk of diabetes, defined as initiation of antidiabetic medications (RR 1.28 (95% CI, 1.22-1.34). Doses of ICS were converted to fluticasone equivalents using defined daily doses and categorised as high (fluticasone 1000 mcg per day or more), moderate (500-999 mcg per day) and low (<500 mcg per day). There was a dose response relationship with the highest rate of diabetes in those prescribed ICS equivalent to fluticasone 1000mcg per day or more (RR 1.64; 95% CI, 1.52-1.76). Higher doses of ICS were also found to be associated with a higher rate of diabetes progression, defined by the need for insulin in patients already treated with an oral hypoglycaemic agent.

The associations observed in this study may not be causal, and other non-pharmacological explanations should also be considered. For example, adjustments for severity of respiratory disease may have been inadequate, and it is possible that patients using high doses of ICS have more severe lung disease which impairs their ability to monitor and manage their diabetes.

At present evidence supports close monitoring of serum glucose concentrations in patients using higher doses of ICS, which can help to identify patients who require improved blood glucose control. COPD patients may gain greatest benefit given the higher incidence of diabetes amongst older patients.

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FOR FURTHER INFORMATION – CONTACT THE PHARMACY DEPARTMENT ON 82751763 or email: chris.alderman@rgh.sa.gov.au
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