

# RGH Pharmacy E-Bulletin

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A joint initiative of the Patient Services Section and the Drug and Therapeutics Information Service of the Pharmacy Department, Repatriation General Hospital, Daw Park, South Australia. The RGH Pharmacy E-Bulletin is distributed in electronic format on a weekly basis, and aims to present concise, factual information on issues of current interest in therapeutics, drug safety and cost-effective use of medications.

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## Risk of fractures with inhaled corticosteroids

The issue of a possible link between inhaled corticosteroids (ICS) and fracture risk in patients with obstructive lung disease has been controversial. Results of subgroup analyses from randomised controlled trials of ICS in chronic obstructive pulmonary disease (COPD) have been conflicting. Three large observational studies have reported an inverse relationship between ICS dose and bone mineral density and another four studies have shown an association between ICS exposure and fracture risk. However there has been debate on whether the observed effects are drug-related or due to confounding factors.

Advanced age, smoking history, cumulative exposure to prednisolone and limited ability to exercise are additional significant risk factors for osteoporosis, falls and fractures in patients with COPD. ICS doses commonly used in severe COPD are high, reflecting the doses used in large randomised controlled trials, and effects on bone mineral density may have greater significance in this high risk population than in patients with asthma.

A recently published study has supplied additional evidence supporting an association between the use of inhaled corticosteroids and fracture risk. UK researchers combined data from a Medical Research Council study on assessment and management of older people in the community with prescribing and diagnostic data from general practice records, an approach which enabled control of a wide range of potential confounding factors such as physical inactivity and falls.

During a mean follow-up of over nine years, 982 elderly patients (59%) with a diagnosis of asthma or COPD received a prescription for an ICS and 187 had a fracture. After adjusting for age and gender, a dose-related increase in fracture risk was observed, with a rate ratio of 2.53 (95%CI 1.65 to 3.89) for those with a mean daily dose of > 600mcg (most commonly beclomethasone). Similar results were obtained after adjusting for potential confounders such as oral corticosteroid exposure, diagnosis, past fracture, bronchodilator use, self-reported falls and activities of daily living. The median annual dose of prednisolone was 144 mg in exposed patients, equivalent to one short course of prednisolone per year. The dose-response relationship between ICS and fracture risk was similar in people with and without exposure to oral corticosteroids. The varying potencies of individual ICS agents and the effects of possible concurrent preventative therapy for osteoporosis were not considered in this study. These results reinforce the importance of titrating the dose of ICS downward to the minimum effective dose in patients with asthma, and highlight the need for ICS dose-ranging studies in COPD patients.

ICS are recommended for those COPD patients with severe disease and frequent exacerbations, or in those with a documented FEV<sub>1</sub> response. Systemic absorption of ICS may be minimised by mouth rinsing regularly after use and by the use of a spacer when the ICS is delivered via a metered-dose inhaler. Consideration should also be given to the prescribing of calcium and vitamin D for at-risk patients, and a bisphosphonate for those with established osteoporosis or history of fractures.

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