Adverse drug reactions in Canada

Bisphosphonates and ocular disorders

Bisphosphonates currently marketed in Canada include alendronate, clodronate, etidronate, pamidronate, risedronate, and zoledronic acid. Indications for their use vary according to product.

International data from spontaneous reporting systems for visual reactions associated with bisphosphonates suggest that, in rare instances, this class of medication can cause serious ocular adverse effects. Adverse effects involving ocular inflammation were initially thought to be related to amine-bisphosphonates, which include alendronate, pamidronate, and risedronate, but clodronate and etidronate, both non–amine-bisphosphonates, have also been implicated. Health Canada received 27 domestic reports of suspected ocular and visual disorders associated with bisphosphonates.

Indications of ocular inflammation include eye pain, redness, abnormal vision (blurred or double vision, decreased vision, "floaters") and photophobia. Although these effects are rare with bisphophonates, the following guidelines have been suggested for care of patients receiving bisphosphonates.

- Patients with visual loss or ocular pain should be referred to an ophthalmologist.
- Nonspecific conjunctivitis seldom requires treatment and usually decreases in intensity during subsequent exposure to bisphosphonates.
- More than one ocular side effect can occur simultaneously (eg, episcleritis in conjunction with uveitis). Sometimes, the drug must be discontinued for the ocular inflammation to resolve.
- For scleritis to resolve, even during full medical therapy, bisphosphonates must be discontinued.

Fluticasone and adrenal suppression

Inhaled corticosteroids are highly effective for control of asthma and prevention of exacerbations. Recently, there have been several reports worldwide of adrenal insufficiency in adults and children using inhaled corticosteroids. Although it can occur with any inhaled corticosteroid, adrenal insufficiency might be more common with fluticasone because of the drug's pharmacologic and pharmacokinetic properties, including its greater potency and hence lower equivalent dose (half the dose of either budesonide or beclomethasone). Health Canada received nine reports of suspected adrenal insufficiency associated with fluticasone.

Adrenal insufficiency can occur with inhaled corticosteroids because of systemic absorption of the corticosteroid and consequent suppression of endogenous glucocorticoids, which leaves insufficient adrenal reserve to respond to stressful stimuli. It might also result from abrupt discontinuation or noncompliance with treatment, which leads to acute steroid deficiency. Signs and symptoms of adrenal suppression and crisis are nonspecific and include anorexia, abdominal pain, weight loss, fatigue, headache, nausea, vomiting, decreased level of consciousness, hypoglycemia, and seizures.

Clinicians are reminded that, beyond a certain limit, increasing the dose of inhaled corticosteroids offers minimal benefit but increases risk of systemic adverse effects. Canadian asthma consensus guidelines recommend that, once best results are achieved, the dose should be reduced at appropriate intervals to determine the minimum dose required to maintain control.

Patients and parents should be informed of the risk as well as the signs and symptoms of adrenal suppression associated with use of inhaled corticosteroids. They should also be cautioned about the risk of serious adverse reactions from abruptly stopping treatment.

Source: Health Canada. *Canadian Adverse Reaction Newsletter* 2003;13(4):1-2. For the complete text of any of these reports, check the website **www.hc-sc.gc.ca/hpfb-dgpsa/tpd-dpt/index_adverse_newsletter_e.html.**