

Inhaled steroids — too much of a good thing?

The goal is to achieve optimal asthma control with the lowest effective dose

OVER THE PAST 20 YEARS, inhaled corticosteroids have become established as cornerstone therapy in the treatment of obstructive pulmonary disorders, ranging from asthma and chronic obstructive pulmonary disease to cystic fibrosis.

The appropriate use of inhaled corticosteroids has transformed the management of asthma in children, improving the quality of life of children and their families, improving exercise tolerance, and reducing hospitalisation and mortality rates. Asthma mortality rates in Australia have fallen by more than 50% over the past 12 years, in parallel with our increased use of inhaled corticosteroids and the development of clinical guidelines.¹

We have gained confidence in the safety of inhaled steroids at recommended doses, supported by national guidelines and extensive reviews.² Local side effects, including oropharyngeal candidiasis and laryngeal dysfunction, can usually be controlled with the use of spacer devices. Further, at recommended doses, initial concerns about growth failure and impaired bone mineralisation have not been realised.²

In recent years, with the advent of more potent steroids and more efficient delivery systems, the relative doses commonly used have increased. There have been several reports of serious adverse events resulting from doses of inhaled corticosteroids in excess of those recommended. These include growth failure,³ and suppression of the hypothalamic–pituitary–adrenal axis^{4–6} — resulting in acute hypoglycaemia, altered consciousness and coma, convulsions^{7,8} and death.⁹ While the majority of these effects have been reported at higher doses, some have occurred at a dose within the recommended range, suggesting that individual susceptibility may also be important. These effects are more commonly associated with one potent inhaled corticosteroid, but this is probably a result of over-representation of that drug in the higher dosage range. Comparative studies would suggest that this is a class effect of inhaled corticosteroids.⁴

Are we overusing inhaled corticosteroids? New evidence-based National Asthma Council guidelines define the need for inhaled corticosteroids in asthma. They recommend an upper limit of 500 µg per day of fluticasone propionate (or equivalent) in children, and 1000 µg per day in adults with severe asthma. In support, a recent meta-analysis, examining the dose response to inhaled corticosteroids in adolescents and young adults, reported that 90% of the maximum benefit was achieved at a daily dose equivalent to 250 µg fluticasone propionate.¹⁰ Minimal further improvement resulted from increases up to 600 µg/day. The introduction of long-acting β-agonists at low doses of inhaled corticosteroids can achieve improved asthma control, avoiding the need for higher doses of inhaled corticosteroids.

When asthma is not controlled by a dose of inhaled corticosteroids equivalent to 500 µg/day fluticasone propi-

onate and long-acting β-agonists, consideration should be given to issues of adherence to the treatment regimen, inhaler technique or an alternative diagnosis. In the UK survey of adrenal crisis due to inhaled corticosteroids,⁹ three of the 28 children did not have asthma and, in five, asthma did not account for all the respiratory symptoms. Inhaled steroids have been shown to be ineffective in children with recurrent cough and those with episodic viral-associated wheeze. Clinicians should be alert to the clinical features of hypoadrenalism, particularly when precipitated at a time of metabolic stress, perhaps indicating adrenal crisis. Children taking excessive doses of inhaled corticosteroids (> 500 µg/day fluticasone propionate) should have their hypothalamic–pituitary–adrenal axis assessed, and their parents should be informed of the risks and the potential need for systemic corticosteroid cover during intercurrent illness and surgery.

The National Asthma Council recommends the introduction of inhaled corticosteroids (alone or in combination) to gain control of symptoms. On clinical review, there should be a reduction (ie, back-titration) to an appropriate dose to optimise symptom control and reduce the likelihood of adverse effects. By comparison with their United States and European counterparts, Australian prescribers have used higher doses of inhaled corticosteroids, but there is now a clear incentive to reverse this trend.

The availability of effective anti-inflammatory therapy, useful and well-publicised guidelines, as well as incentive payments to general practitioners for the treatment of moderate to severe asthma under the 3+ Visit Plan (<http://www.health.gov.au/pq/asthma/3plusgp.htm>), should pave the way for greater improvements in the management of asthma. The goal of asthma management is to achieve optimal control of asthma symptoms with the lowest effective medication dose, allowing children to enjoy a normal quality of life neither burdened by, nor at risk of, serious adverse events. Inhaled corticosteroids remain the cornerstone of asthma management. Responsible use of inhaled corticosteroids will reinforce confidence in the consumer, whereas irresponsible use will promote steroid phobia — a significant barrier to adherence.

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time capsule

Treatment (of asthma)

...As there is no clear understanding of the constant or essential factors of asthma, cures of well established cases are rare, and of advanced cases practically non-existent ... But in so far as certain outstanding biochemical changes have been found, indications for chemotherapy are not lacking. It is but natural that we should apply acid therapy to those whose gastric secretion has been found defective, and administer glucose to children whose blood is below standard in this particular.

In the present state of our knowledge we are forced to rely upon our defence against the contributing factors for the most part. Of these, by far the most important are allergy and infection. Taking infection first, one's immediate duty is to eliminate all obvious foci of infection in the nose and throat. Infected tonsils and adenoids, diseased teeth, sinusitis, anatomical defects in the nose, polypi et cetera, all call for surgical treatment ... The prevention of colds and acute bronchitis should be effected by prophylactic injections of vaccines.

Vaccine treatment

The profession has been accused by bacteriologists of a considerable degree of charlatanism with vaccine therapy. We have been told that our so-called successful results have not been obtained with a proper system of controls; and that, therefore, they do not carry conviction to the scientific mind. There may be some justice in the charge of charlatanism ... Numerous competent physicians, however, have provided such an overwhelming testimony regarding the clinical improvement of their patients undergoing vaccine treatment, that one would require great courage to dismiss their claims with lofty scientific scorn ... Vaccines are employed in asthma to protect against infections and to minimize the effects of established infections.

The vaccines used may be autogenous or stock. There is much to be said for each type. If a stock vaccine is used, it is my custom to have one prepared from mixed sputa obtained from the most virulent cases of respiratory infection undergoing treatment at the time of preparation. I prefer them to be of a strength of 2,000 million per cubic centimetre. I divide the treatment into two stages: (i) an immunizing course lasting about three months, (ii) a maintenance course lasting from twelve to eighteen months.

Desensitization

A similar method is employed when attempting to desensitize allergic patients. A desensitizing solution is prepared, containing the required number of units of the substance found injurious ... In all my allergic cases I have adminis-

tered a bacterial vaccine along with the desensitizing solution, so important do I regard the influence of infection even in these cases.

Prophylaxis

Prophylaxis must, of course, be prominently before one's mind in handling allergic patients. Food, animals, flowers, if found to be injurious, must be avoided. Sometimes allergens, for example, moulds and house dust, are peculiar to the home, in which case another home should be sought. The dwelling should be dry and well ventilated.

Endocrine influences

When asthma occurs at the menopause, ovarian extract is likely to be of use. At this time, on account of the group of symptoms peculiar to the menopause, one cannot possibly say whether the effect of ovarian treatment in asthma is direct or indirect.

Diseases of the respiratory system and structural changes in the chest lead to the employment of breathing exercises ... They are specially designed to diminish the volume of dead air within the lungs, and also to overcome faulty posture and deformity of the chest wall ... Meteorological influences suggest that asthmatics should avoid coastal climates during the months of January and February.

Drug treatment

The anti-spasmodic remedies used in an acute attack of asthma are, of course, adrenaline and ephedrine. Adrenaline is by far the more effective. Patients can be trained to give their own injections. When they are too nervous to do so and no member of the household cares to undertake the responsibility, ephedrine tablets may be relied on...

The other anti-spasmodics are lobelia, stramonium, belladonna, hyoscyamus, grindelia, amyl nitrite, chloroform and ether. Most hospital pharmacopoeias contain an expectorant anti-spasmodic mixture called *mistura lobelie composita*. The continuous administration of this mixture, at intervals of four hours, will frequently enable patients to abandon such proprietary sprays and inhalants as they had previously relied upon.

...Mild sedatives are recommended in the early stages of treatment, so as to minimize adverse psychological influences, such as fear, worry and anticipation. A good method is to administer a mild hypnotic every night, such as potassium bromide or chloral hydrate. This breaks the vicious circle caused by the sequence upon one another of asthma and fear.

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MJA 1933; 2: 174-179