



A **ASTHMA
POEMS**

Asthma POEMs

Patient Orientated Evidence that Matters

Developed by the Best Practice Advocacy Centre
Level 8, 10 George Street
PO Box 6032
Dunedin
Phone 03 4775418
Fax 03 4772622

Acknowledgement

BPAC would like to thank Professor Ian Town and Associate Professor Robin Taylor for their help in the development of this resource.

Contents

SUMMARY.....	1
AIM OF ASTHMA MANAGEMENT	2
WHICH INHALED CORTICOSTEROID?.....	2
DOSE EQUIVALENCE.....	3
DOSE RESPONSE	4
INITIATING ICS THERAPY.....	6
HOW TO REDUCE ICS DOSE	7
HOW TO MINIMISE ADVERSE EFFECTS.....	8
ADULT ASTHMA GUIDELINES ICS RECOMMENDATIONS	9
LONG ACTING BETA AGONISTS	10
EDUCATION & SELF MANAGEMENT	11
REFERENCES.....	12

All information is intended for use by competent health care professionals and should be utilized in conjunction with pertinent clinical data.

Summary

1. The goal of asthma management is to achieve optimal asthma control with the lowest effective doses of medication.
2. Inhaled corticosteroids have a relatively flat dose response curve. The majority of patients will not require maintenance inhaled corticosteroid doses above 500mcg fluticasone or 800-1000mcg beclomethasone or budesonide.
3. Fluticasone is at least twice as potent as beclomethasone and budesonide, therefore equivalent doses for fluticasone are half those for beclomethasone and budesonide.
4. Guidelines differ in the recommended starting doses for inhaled corticosteroids. Some recommend starting with high doses and then stepping back the dose, while others recommend starting with lower doses and titrating to response. Most studies suggest that starting low is adequate unless the presenting symptoms are severe. Either way, “step up” or “step down”, when asthma control has been satisfactory for about 12 weeks, review of the inhaled corticosteroid dose is essential.
5. Back titrate stable patients by approximately 25% of the total daily inhaled corticosteroid dose. When titrating wait 12 weeks to judge effect and before making any further dose reductions.
6. Concurrent use of inhaled long acting β_2 agonist (LABAs) e.g. formoterol, salmeterol, avoids the need to use high dose inhaled corticosteroids in many patients. LABAs should be considered in all individuals who continue to experience symptoms despite taking moderate doses of inhaled corticosteroid (800mcg beclomethasone/day or equivalent).
7. Education is the cornerstone of asthma management. Education enhances self management skills enabling patients to manage their illness and as a result maintain better health, function better, and be less likely to be hospitalised or seen for emergency visits.
8. Side effects from high doses of inhaled corticosteroids are increasingly recognised. Cataracts and osteopenia occur in the elderly. Adrenal insufficiency may occur in children, and fluticasone is of particular concern in this regard. The latter may occur when the 2:1 dose adjustment with respect to beclomethasone is not made.

Aim of Asthma Management

Asthma is a condition that usually responds to appropriate medication and in the majority of patients symptoms are well controlled allowing the person with asthma to live a normal life. An important aspect of care is enabling the patients to be in control of their own management. The aims of asthma management are:

1. to minimise or eliminate symptoms
2. to maximise lung function
3. to prevent exacerbations
4. to adjust medication to the lowest effective dose
5. to minimise adverse effects of treatment
6. to provide enough information and support to facilitate self management

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

Which Inhaled Corticosteroid?

Inhaled corticosteroids are the mainstay of treatment in chronic asthma. There are no clinically significant differences between agents in effectiveness or risk of adverse effects (NZGG 2002). Fluticasone, beclomethasone and budesonide are considered equally effective when used in equipotent doses.

Inhaled corticosteroids (ICS) must be used regularly to obtain maximum benefit, improvement in symptoms is usually evident 3 to 7 days after initiation (BNF, Sept 2002). For the majority of patients symptoms should settle in 2 to 4 weeks of initiating therapy. For those with very severe presenting symptoms an initial short course of oral prednisone may be helpful. Reduced control due to poor compliance may not be apparent for some days or weeks because of the residual benefit of inhaled corticosteroid therapy.

Dose Equivalence

Fluticasone is at least twice as potent as beclomethasone and budesonide (O'Byrne & Pedersen 1998). Doses for fluticasone are therefore half those for beclomethasone and budesonide.

The average daily dose of fluticasone in New Zealand is about the same as for beclomethasone. These doses are likely to be excessive.

The average daily dose (ADD) provides an indication of the prescribed doses of inhaled corticosteroids. The following tables clearly show that fluticasone is being used at almost the same microgram dose as beclomethasone.

National prescribing figures for 1 Nov 2001 to 31 Oct 2002 (PHARMAC analysis of HealthPAC data)

Average daily dose mcg/day	Adults 17+ yr	Overall Adults + children
Beclomethasone	702	624
Budesonide	1027	954
Fluticasone	643	559

Theoretically the ADD for fluticasone should be half that for beclomethasone (assuming that the dose for beclomethasone is optimum). Hence for a calculated ADD of beclomethasone of 624mcg per day the corresponding fluticasone ADD would be expected to be approximately 312mcg per day.

National Average Daily Dose 1 November 2001 - 31 October 2002		
Beclomethasone	Fluticasone	
Actual	Theoretical	Actual
624mcg	312mcg	559mcg

Conclusion

The 2:1 (beclomethasone:fluticasone) conversion necessary for fluticasone dosing has been widely promoted, but in practice this conversion is not routinely occurring. Hence patients are potentially being treated with higher than necessary doses and should be reviewed.

Dose Response

Inhaled corticosteroids have a relatively flat dose response curve. Available studies suggest that increasing the dose above 500mcg fluticasone or 800mcg/1000mcg beclomethasone or budesonide will not provide additional clinical benefit in the majority of patients.

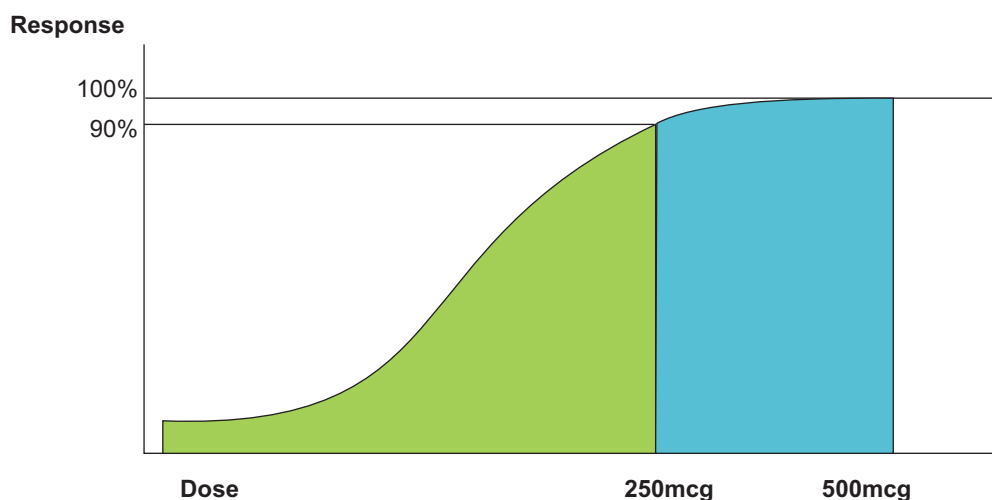
The results from a meta-analysis suggest that nearly all benefit from inhaled fluticasone can be obtained at a total daily dose of 100 to 250mcg and that maximum benefit occurs at about 500mcg/day (Holt *et al* 2001). This meta-analysis included patients with moderate to severe asthma. Eight studies, with a total of 2324 patients, were identified; 5 of the studies included fluticasone dosages as high as 800 to 1000mcg/day. The dose-response curve leveled out at 100 to 200mcg/day and the plateau was reached at 500mcg/day. According to a mathematical model, 90% of possible maximum benefit was achieved at 100 to 250mcg/day, and maximum efficacy was achieved at about 500mcg/day (Holt *et al* 2001).

Doses of fluticasone (mcg/day) at which 80% and 90% of the maximum effect is achieved:

Outcome measure	80% of maximum effect achieved	90% of maximum effect achieved
FEV1	146	209
Morning PEF	172	247
Evening PEF	175	251
Use of rescue medication	71	102
Major exacerbations	108	155
Night awakenings	135	193

(Holt *et al* 2001)

Fluticasone Dose Response Curve



The dose response curve flattens around 250-500mcg per day fluticasone, this is equivalent to 500-1000mcg per day of beclomethasone or budesonide.

Inter-individual variability exists. Some patients will benefit from doses above the “plateau” dose on the dose response curve. Current guidelines allow for doses up to 800mcg fluticasone (1600mcg beclomethasone or budesonide) (NZGG 2002). The proportion of patients that benefit from these very high doses of inhaled corticosteroids is not known. In oral corticosteroid dependent asthmatics, reductions in prednisone requirement may be gained with fluticasone 2000mcg/day (Adams *et al* 2002).

High doses should be continued only if there is clear benefit over the lower dose. The recommended maximum doses of inhaled corticosteroids should not generally be exceeded. However, if higher doses are required (e.g. fluticasone in doses above 500mcg twice daily), then they should be reviewed by a specialist.

Conclusion

The majority of patients will not require inhaled corticosteroid maintenance doses above 500mcg fluticasone or 800mcg-1000mcg beclomethasone or budesonide. Higher doses may be needed if symptoms are severe or if break through symptoms occur after back titration.

Initiating ICS Therapy

Current New Zealand guidelines support a “step up” approach in mild to moderate asthma, starting with 200mcg fluticasone or 400mcg beclomethasone or budesonide in adults.

There has been some debate about the merit of this approach. One of the drivers leading to this recommendation is that patients started on higher doses do not appear to have their dose reduced and therefore remain controlled on higher than necessary doses of inhaled corticosteroid and as a consequence may be exposed to adverse effects.

The main argument for the use of higher initial doses of inhaled corticosteroid, such as beclomethasone 800mcg/day or more, is that it enables quicker control of asthma. Individuals with severe asthma may benefit from starting at higher doses or even using oral steroids to gain control of their asthma. Hence, there may be a place for starting with high dose inhaled steroids followed by back titration in those patients with severe asthma. The New Zealand guidelines suggest that in those newly diagnosed adults with asthma who have moderate to severe symptoms, or a FEV1 < 60% predicted, a short course of oral corticosteroids should be considered to quickly establish control of the asthma (NZGG 2002).

From a patient perspective a “step up” approach may be more acceptable to those who are reluctant to take steroids. A telephone survey of Canadians with asthma found that many have misconceptions and fears regarding these agents (Boulet 1998). Over half of the patients surveyed were “very” or “somewhat” concerned about the regular use of steroids, and most had not discussed these concerns with their doctor. Some specific concerns included fear of side effects, loss of effectiveness over time, weight gain, muscle building, and causing infections.

Hence a “step up” approach, combined with good patient information, is likely to be acceptable to many patients, particularly those with mild to moderate disease, that do not require a more aggressive approach.

Conclusion

Either way, “step up” or “step down”, when asthma control has been satisfactory for 12 weeks, **review** of the inhaled corticosteroid dose is essential. For a significant number of patients this will mean a reduction in therapy.

How to Reduce ICS Dose

Optimising therapy is not always easy, but it is an important part of doing what is best for patients. Many patients are currently being treated using higher than necessary doses of inhaled corticosteroids.

Identify patients that are on maximal rather than optimal therapy.

Steps in reducing inhaled corticosteroid dose:

1. Check compliance, inhaler technique and asthma triggers before making any changes to therapy.
2. Involve the patient. Discuss with the patient their markers of poor control. Try to establish a correlation between their symptoms and peak flow rates. Establish mutually acceptable goals for treatment and a self management plan. Explain to the patient that the effect of inhaled steroids occurs over weeks, not just days. Therefore changing the dose should be done no more frequently than every 12 weeks.

3. Back titration. *Aim low, go slow.*

Step down the dose by about 25% if asthma is well controlled. Repeat this exercise after a further 12 weeks. A small proportion of patients with asthma do not require maintenance therapy except at certain times e.g. for 1-2 months after a cold or during the pollen season.

When titrating the dose, wait 12 weeks to judge effect.

Back titrate stable patients by 25% of total daily dose.

Back titration is safe in almost all patients if they have a self management plan. The self management plan allows the patient to increase the inhaled steroid dose if back titration has been too energetic. If a patient has been admitted to hospital or required prednisone on two or more occasions during the last six months, this suggests the need for particular caution. Higher doses of maintenance therapy are likely to be required. A back titration exercise may be unwise:

1. If the patient is pregnant.
2. If the patient's asthma is occupational.
3. If the patient has proven allergy to aspergillus or other fungi.

Be prepared to adjust dose upwards and add in a long-acting beta₂-agonist for poorly controlled asthma. When control is achieved step down.

Conclusion

Aim low, go slow. Regular review of inhaled corticosteroid requirement is essential. The total daily dose can be reduced by approximately 25% in stable patients. The full clinical effect of the dose reduction may take up to 6 weeks, and a further 6 weeks should be allowed to judge effect.

How to Minimise Adverse Effects

The most important safeguard for patients against any long term systemic effects of inhaled corticosteroids is the regular review and dose adjustment of the inhaled corticosteroid. This will ensure that the lowest dose needed to maintain good control is given.

Aim for the lowest dose needed to maintain good control.

Doses of inhaled corticosteroids < 1000 mcg/day of beclomethasone or equivalent do not cause important systemic effects in adults (Barnes *et al* 1998). A population based case control study suggests that, in older people, inhaled high dose beclomethasone use is associated with a slightly greater risk of nuclear cataracts (RR 1.5, 95% CI 1.2 to 1.9) and posterior subcapsular cataracts (RR 1.9, 95% CI 1.3 to 2.8) (Cumming *et al* 1997). A review found no significant effect of low dose inhaled corticosteroids on bruising or skin thickness (Lipworth 1999). Inhaled corticosteroids can cause oral candidiasis or dysphonia, but these are troublesome in fewer than 5% of people (Toogood *et al* 1980).

Spacer devices reduce oropharyngeal deposition.

Fluticasone should be given at half the daily dose of beclomethasone or budesonide. When given at the same daily dose it appears to have a higher risk of causing side effects (Adams *et al* 2002).

Patients on high ICS doses should be given a 'steroid card'. BNF 2002

Conclusion

Inhaled corticosteroids, while efficacious, are associated with certain adverse effects, including adrenal insufficiency, cataract formation, glaucoma, and bone demineralisation, which occur in a dose-dependent fashion. It makes sense to prescribe inhaled corticosteroids in doses that are effective but minimise the potential for side effects. Based on our current understanding, this means a total daily dose in the long term of less than 500mcg fluticasone or less than 1000mcg beclomethasone or budesonide.

Adult Asthma Guidelines ICS Recommendations

The New Zealand guidelines for the diagnosis and treatment of adult asthma include the following recommendations regarding the use of inhaled corticosteroids (NZGG 2002):

1. Treatment with inhaled corticosteroids is recommended in those who have daily symptoms of asthma or patients requiring short acting β agonists (e.g. salbutamol, terbutaline) daily.
2. Most adults with asthma should be initiated on treatment with low dose inhaled corticosteroids (fluticasone 200mcg/day or beclomethasone dipropionate 400mcg/day or equivalent).
3. Fluticasone propionate is at least twice as potent as beclomethasone dipropionate.
4. Early treatment with inhaled corticosteroid in people with persistent symptoms and impaired lung function leads to better lung function in the medium term, and may help prevent the development of irreversible airflow limitation.
5. Inhaled corticosteroids have a relatively flat dose response curve. Little additional benefit is gained from doses above 500mcg/day of fluticasone propionate or 800-1000mcg/day of beclomethasone dipropionate/budesonide.
6. There is evidence of an increased risk of cataracts, reduced bone mineral density, glaucoma and bruising of the skin with long-term treatment with high dose inhaled corticosteroid (e.g. more than 1000mcg/day beclomethasone dipropionate).
7. High doses of inhaled corticosteroid should be avoided where possible for adults with asthma who have pre-existing conditions or vulnerability to conditions such as osteoporosis or cataracts.



Full text of the guidelines for the diagnosis and treatment of adult asthma are available from:

http://www.nzgg.org.nz/library/gl_complete/asthma/index.cfm

Long Acting Beta Agonists

The introduction of an inhaled long acting β_2 agonist (LABA) (e.g. formoterol, salmeterol) at low doses of inhaled corticosteroid can achieve improved asthma control, avoiding the need for higher doses of inhaled corticosteroid. When asthma is not controlled by a dose of inhaled corticosteroid equivalent to 500mcg/day of fluticasone and a LABA, consideration should be given to issues of adherence to the treatment regimen, inhaler technique or an alternative diagnosis.

With the concurrent use of LABAs, there is now little need to use high dose ICS.

It is estimated that approximately (Markham & Adkins 2000):

- 75% of patients with asthma have clinically mild or seasonal asthma
- 15% to 20% have moderate persistent asthma
- 5% to 10% severe persistent asthma

The LABAs can be considered in those patients that fall into the last two categories and who are not well controlled. They should be used as add-on therapy to achieve control of persistent asthma symptoms as an alternative to increased doses of inhaled corticosteroid. The dose of inhaled corticosteroid can frequently be back titrated once control is achieved.

Availability

Special authority criteria apply as outlined in the Pharmaceutical Schedule. The only preparation that does not require a special authority approval is the low dose formoterol inhaler, Oxis[®] 6mcg turbuhaler. Inhaled formoterol 6mcg can be prescribed by general practitioners when an adult patient is poorly controlled over at least a period of 3 months on a full dose inhaled corticosteroid i.e. ≥ 750 mcg/day beclomethasone/budesonide or ≥ 400 mcg fluticasone. The prescription must be endorsed with the words "poor control on ICS" or "certified condition". For children 12 years and over the inhaled corticosteroid dose is ≥ 400 mcg/day beclomethasone/budesonide or ≥ 200 mcg fluticasone (Pharmaceutical Schedule, Dec 2002).

Conclusion

While the evidence supports the effectiveness of adding in a LABA at low doses of inhaled corticosteroid, this is not possible due to the current access criteria. However those that stand to gain the greatest benefit from their use are eligible. This is reflected in the recommendation made in the New Zealand guidelines that LABAs should always be considered in individuals who continue to experience symptoms despite taking moderate (800mcg beclomethasone/day) doses of inhaled corticosteroid as this is at the top end of the dose response curve and higher doses are associated with increased risk of adverse effects (NZGG 2002). Once control is achieved the inhaled corticosteroid dose can frequently be back titrated and this is acceptable under the PHARMAC criteria.

Education & Self Management

Education is the cornerstone of asthma management, with the idea being that patients who know how to manage their illness will be in better health, function better, and be less likely to be hospitalised or seen for emergency visits.

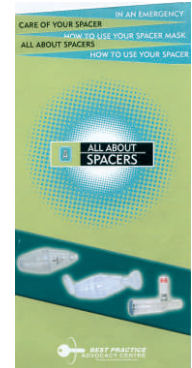
A review found that education about asthma to facilitate self management, whether initiated from a specialist or generalist setting, significantly reduced the risk of hospital admission (RR 0.62, 95% CI 0.41 to 0.96; **NNT 38**, 95% CI 20 to 382), unscheduled visits to the doctor (RR 0.74, 95% CI 0.63 to 0.90; **NNT 12**, 95% CI 8 to 36), and days off work (RR 0.75, 95% CI 0.63 to 0.90; **NNT 7**, 95% CI 5 to 13). Best results were achieved in people who had written care plans (Gibson *et al* 2000).

In adults with asthma, optimum self management and education consists of a structured programme. Essential components of such a programme would include (NZGG 2002):

- Written information about asthma
- Self-monitoring of symptoms and/or peak flow
- Regular review by a doctor or nurse, which involves assessment of medications and assessment of current asthma severity
- Acknowledgement that lung function alone is not an adequate measure of the overall patient status and that quality of life considerations must be incorporated when assessing the impact of disease
- An individualised written self management plan
- Maintaining open dialogue between health professionals and patients with a view to greater involvement of the patients in decision-making but not total abdication of responsibility to the patient.



www.asthmanz.co.nz



Primary health care teams should use a checklist of patient information and instruction, as part of their practice structure for patients with asthma (NZGG 2002).

Conclusion

Education will benefit patients with asthma and will increase self management skills. Information teaches patients how to detect and manage worsening symptoms and encourages the optimal use of medications including good adherence. Hospital admissions, trips to the doctor and days off work may also be reduced.

References

- Adams N, Bestall JM, Jones PW. Fluticasone versus beclomethasone or budesonide for chronic asthma. *Cochrane Database Syst Rev* 2002;(1):CD002310
- Barnes PJ, Pedersen S, Busse WW. Efficacy and safety of inhaled corticosteroids: new developments. *Am J Respir Crit Care Med* 1998;157:1-53.
- Boulet LP. Perception of the role and potential side effects of inhaled corticosteroids among asthmatic patients. *Chest* 1998;113:587-92.
- Bowler S. Inhaled steroids in asthma: Should the doses be reduced? *Aust Fam Physician*, Volume 31, Number 8, August 2002, 746-748.
- British Medical Association, Royal Pharmaceutical Society of Great Britain. *British National Formulary*. BNF 44, September 2002. www.bnf.org
- Cumming RG, Mitchell P, Leeder SR. Use of inhaled corticosteroids and the risk of cataracts. *N Engl J Med* 1997;337:8-14.
- Gibson PG, Coughlan J, Wilson AJ, *et al.* Self-management education and regular practitioner review for adults with asthma. *The Cochrane Library Issue 3*, 2000. Search date 1999; primary sources Cochrane Airways Group Register of Trials, and hand searched references.
- Holt S, Suder A, Weatherall M, Cheng S, Shirtcliffe P, Beasley R. Dose-response relation of inhaled fluticasone propionate in adolescents and adults with asthma: Meta-analysis. *BMJ* 2001 Aug 4; 323:253-256
- Lipworth BJ. Systemic adverse effects of inhaled corticosteroid therapy; a systematic review and meta-analysis. *Arch Intern Med* 1999;159:941-955.
- Markham A, Adkins J. Inhaled Salmeterol/Fluticasone Propionate Combination. A Pharmacoeconomic Review of its Use in the Management of Asthma. *Pharmacoeconomics* 2000 Dec; 18(6): 591-608.
- NZGG (New Zealand Guidelines Group). *The diagnosis and treatment of adult asthma*. September 2002. www.nzgg.org.nz
- O'Byrne P, Pedersen S. Measuring efficacy and safety of different inhaled corticosteroid preparations. *J Allergy Clin Immunol* 1998; 102: 879-86.
- Perneger TV, Sudre P, Muntner P, *et al.* Effect of patient education on self-management skills and health status in patients with asthma: a randomized trial. *Am J Med* 2002; 113:7-14.
- Pharmaceutical Management Agency (PHARMAC). *New Zealand Pharmaceutical Schedule*, December 2002. www.pharmac.govt.nz
- Toogood JH, Jennings B, Greenway RW, Chuang L. Candidiasis and dysphonia complicating beclomethasone treatment of asthma. *J Allergy Clin Immunol* 1980;65:145-153.