



THERAPEUTICS INITIATIVE

Evidence Based Drug Therapy

Changing Concepts in the Management of Asthma

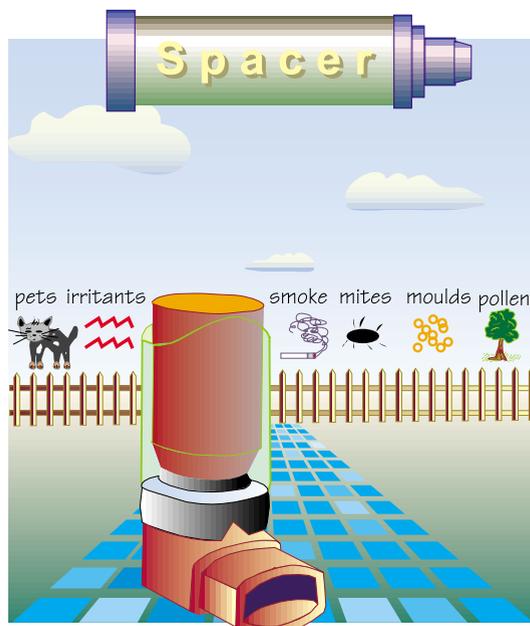
Asthma and other conditions associated with bronchospasm are extremely prevalent and evidence suggests that the prevalence and severity is increasing. A measure of the magnitude of the problem in British Columbia is the fact that the β_2 -agonist salbutamol is the second most frequently prescribed drug, after acetaminophen/codeine combinations. Most β_2 -agonists are prescribed to relieve episodic bronchospasm in ambulatory patients with asthma or chronic obstructive pulmonary disease. This Letter is focused on the optimal management of asthma in the primary care setting.

• What are the goals of therapy?

- To control and prevent symptoms (cough, wheezing, dyspnea).
- To maintain normal activity levels and lung function. (spirometry).
- To prevent exacerbations.

• What are the non-pharmacological therapies?

• Identification and avoidance of environmental allergens and irritants (eg. dust mites, pets, tobacco smoke etc.) as much as possible. **(Environmental control is often neglected, but there is a clear role for physicians and patients to identify triggering allergens and irritants, and to institute a systematic program to eliminate, or substantially reduce such exposures).**



• Education of the patient and family is an essential component of asthma management; in specific settings it has been associated with reduced morbidity¹.

• What is the role of the following drugs in the management of asthma?

• Salbutamol (Ventolin) and other Short-acting β_2 - Agonists.

β_2 -agonists cause bronchodilation by smooth muscle relaxation, and when administered by the inhaled route, are effective and safe for the management of acute asthma exacerbations, in preventing exercise-induced asthma, and for control of intermittent asthma symptoms.

Short acting inhaled β_2 -agonists

Generic Name	Strength	Trade Name	Dose	Cost / Puff
Salbutamol	0.1 mg	generic, MDI	1-2 puffs prn	\$0.03
Salbutamol	0.2 mg	Ventodisk	1-2 puffs prn	\$0.18
Salbutamol	0.2 mg	Rotacaps	1-2 puffs prn	\$0.18
Terbutaline	0.5 mg	Bricanyl, Turb	1-2 puffs prn	\$0.08
Orciprenaline	0.65 mg	Alupent, MDI	1-2 puffs prn	\$0.05
Fenoterol	0.1 mg	Berotec, MDI	1-2 puffs prn	\$0.05
Procaterol	0.01 mg	Pro-air, MDI	1-2 puffs prn	\$0.09

MDI = metered dose inhaler

Turb = turbuhaler



They are not recommended for regular daily therapy, because of evidence that daily use of inhaled β_2 -agonists may lead to a deterioration in asthma control in many patients. One of the better trials,² compared inhaled fenoterol, 0.2 mg QID for 24 weeks with an inhaled placebo for 24 weeks in a double-blind, randomized crossover study (n=64, 50 taking inhaled corticosteroids). Patients were allowed to use a supplementary β_2 -agonist as necessary for symptoms. The total average daily amount of β_2 -agonist was 2.9 and 10.0 puffs in the placebo

and fenoterol groups respectively. Eight out of nine measures of asthma control were worse while the patients were receiving regular fenoterol as compared to placebo. Because of this study and other corroborative evidence, the recent Canadian Asthma Consensus conference recommends that when short-acting inhaled β_2 -agonists are required more frequently than three times weekly (not including their use to prevent exercise-induced symptoms) maintenance therapy with anti-inflammatory drugs is indicated¹. Oral liquid and tablet formulations of β_2 -agonists are not recommended.

• **Inhaled, oral, and parenteral corticosteroids.**

Corticosteroids are anti-inflammatory drugs which reduce two major components of asthma, i.e. the inflammatory changes in the airway and airway hyper-responsiveness. In acute severe asthma, systemic corticosteroids are safe and effective; oral prednisone (50 mg) is just as effective as low or high dose parenteral corticosteroids³. In patients with daily symptoms, regular inhaled steroids are more effective than regular inhaled β_2 -agonists⁴. Administration once or twice daily improves compliance and is effective for most patients; the dose and frequency of administration can be individualized to optimize symptom control and spirometry.

You may have to start with high dose inhaled corticosteroids to control symptoms, but always use the lowest dose of inhaled corticosteroids required to maintain good asthma control; in stable patients repeated trials of dose reduction should be attempted, including stopping the inhaler if possible. Unfortunately, the inhaled corticosteroids do not "cure" asthma; cessation of regular use often results in return to the previous status within weeks to months. Side effects are infrequent; the risk of oropharyngeal candidiasis can be reduced by post-inhalation gargling with water, plus the use of a spacer with metered dose inhalers (MDI) to reduce the amount of steroid deposited in the oropharynx. Inhaled corticosteroids have minimal systemic effects at doses of at least 0.4 mg per day for children and 0.8 mg per day for adults⁵. Higher doses are usually well tolerated.

Low dose inhaled corticosteroids

Generic Name	Strength	Trade Name	Dose [♦]	Daily Cost*
Beclomethasone	0.050 mg	generic, MDI	4 puffs BID	\$0.34
Beclomethasone	0.100 mg	Beclodisk	4 puffs BID	\$1.85
Beclomethasone	0.200 mg	Beclodisk	2 puffs BID	\$1.24
Beclomethasone	0.100 mg	Rotacaps	4 puffs BID	\$0.92
Beclomethasone	0.200 mg	Rotacaps	2 puffs BID	\$1.32
Budesonide	0.100 mg	Pulmicort, Turb	2 puffs BID	\$0.64
Flunisolide	0.250 mg	Bronalide, MDI	2 puffs BID	\$0.68
Fluticasone	0.025 mg	Flovent, MDI [❖]	4 puffs BID	\$0.78
Fluticasone	0.050 mg	Flovent, MDI [❖]	2 puffs BID	\$0.76
Triamcinolone	0.200 mg	Azmacort, MDI	4 puffs BID	\$0.64

* Based on average cost to Pharmacare

♦ Dose to achieve the approximate bio-equivalent of 0.4 mg beclomethasone

❖ Not a Pharmacare benefit at the time of printing

MDI = metered dose inhaler Turb = turbuhaler

High dose inhaled corticosteroids

Generic Name	Strength	Trade Name	Dose [♦]	Daily Cost*
Beclomethasone	0.250 mg	Beclforte, MDI	2 puffs BID	\$1.48
Budesonide	0.200 mg	Pulmicort, Turb	2 puffs BID	\$1.24
Budesonide	0.400 mg	Pulmicort, Turb	1 puff BID	\$1.12
Fluticasone	0.125 mg	Flovent, MDI ❖	2 puffs BID	\$1.20
Fluticasone	0.250 mg	Flovent, MDI ❖	1 puff BID	\$1.20

* Based on average cost to Pharmicare
 ♦ Dose to achieve the approximate bio-equivalent of 1.0 mg beclomethasone
 ❖ Not a Pharmicare benefit at the time of printing
 MDI = metered dose inhaler Turb = turbuhaler

• **Cromoglycate and nedocromil inhalers and oral ketotifen.**

These non-steroidal anti-inflammatory drugs act by preventing the release of inflammatory mediators and are used prophylactically. They are very safe and have a role in some patients, **particularly children**, when

they have been proven effective in a therapeutic trial. In moderate to severe asthma, however, they are not generally as effective as inhaled corticosteroids. They have **no** role in managing acute exacerbations of asthma.

Other anti-inflammatory drugs

Generic Name	Strength	Trade Name	Dose	Daily Cost*
Cromoglycate	1 mg	Intal, MDI	2 puffs QID	\$1.92
Nedocromil	2 mg	Tilade, MDI	2 puffs QID	\$2.08
Ketotifen	1mg tab/syrup	Zaditen	1/2 to 1tab. BID	\$1.78

* Based on average cost to Pharmicare MDI = metered dose inhaler

• **Long-acting β_2 -agonists.**

Because of concerns about chronic adverse consequences of β_2 -agonists⁶, this class of drugs should be restricted to patients who remain symptomatic despite inhaled beclomethasone 1.0 mg or equivalent daily. Two randomized-controlled trials have shown superior control with the addition of salmeterol compared to doubling the dose of inhaled corticosteroids. Patients taking this medication should be carefully monitored and warned

not to discontinue their maintenance anti-inflammatory therapy. It is usually prescribed as a twice daily regimen. Individual n-of-1 studies may allow modification of its use to once daily dosing especially at night for nocturnal symptoms; however, there are no controlled trials using once daily dosing. **Patients should be cautioned not to use this class of drug in acute asthma.**

Long acting inhaled β_2 -agonists

Generic Name	Strength	Trade Name	Dose	Daily Cost*
Salmeterol	0.25 mg	Serevent, MDI	2 puffs BID	\$1.90
Salmeterol	0.05 mg	Diskhaler	1 puff BID	\$2.04

* Based on wholesale cost MDI = metered dose inhaler

• **Oral theophylline.**

Theophylline is a weak bronchodilator which may also have some anti-inflammatory activities. A number of slow release preparations are available. Because of significant dose related toxicity, serum level monitoring is recommended. Theophylline should be reserved for patients who remain symptomatic despite optimization of inhaled corticosteroids.

• **Inhaled ipratropium bromide.**

The evidence is equivocal as to the role of this inhaled anticholinergic bronchodilator in the management of acute or chronic asthma. It acts more slowly than β_2 -agonists and at best is an adjunctive agent in particular patients where it has been proven to be helpful by a therapeutic trial.

• **What is the role of the different inhaler devices and peak expiratory flow (PEF) meters?**

Repeated assessment of the adequacy of patient aerosol technique in the doctor's office is essential. The device that best fits the needs of the patient should be selected. Early reassessment of asthma control is essential, whenever a change in device is made¹. **Home PEF measurements are helpful in managing more complicated patients;** they provide a valuable objective measure of effect when adjustments in medication are attempted.

• **Conclusion:**

Regular inhaled corticosteroids are the main therapy in asthmatic patients with frequent symptoms or exacerbations. Use inhaled β_2 -agonists for intermittent relief or breakthrough symptoms only. **For all treatments always have an objective goal and measure of efficacy and titrate the dose to identify the lowest dose that will achieve that goal.**

References

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Information on the Therapeutics Initiative and the **Therapeutics Letter** is now also available on the **internet** at the web site below.



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