Asthma Treatment

"Questions, Tips, Pearls & Comparisons"

March 2006

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www.RxFiles.ca
See also: Asthma Drug Chart, Devices & Action Plan.

What is acceptable control of asthma? [1]

Asthma is often under-controlled or even unrecognized. Three reasons for poor control are 1) non-compliance, 2) other causes such as hyperventilation, or 3) worsening asthma. **Asking questions** to assess asthma control is essential. E.g. Does the patient have nocturnal symptoms? How much are they using their PRN reliever? See also Table 1.

Table 1: What constitutes acceptable control of asthma?

PARAMETER	FREQUENCY or VALUE
Symptoms (dyspnea, cough, tightness, wheezing, ↑sputum)	**Day**: <4 day/week **Night**: none
Physical activity	Normal
Exacerbations	Mild, infrequent
Absent (work/school)	None due to asthma
Need for a ß$_2$ agonist (Reliever medication)	**<4** doses/week (1 dose/day before exercise is acceptable)
FEV$_1$ or PEF	≥90% of personal best

FEV$_1$=forced expiratory volume in 1 second **PEF**=peak expiratory flow

What is the role of an "action plan"?

Comprehensive education programs work, but the role of the written action plan alone is still inconclusive.[2,3] Benefits have included reductions in hospital admissions, emergency visits & days off work.[4,5] Patients should **monitor** their **symptoms** and have **action plans** for self-management.[1,6] (PEF can be an insensitive measure of airway obstruction, effort dependent & less sensitive than symptoms for exacerbations; may be useful in select cases e.g. poor perceivers, occupational asthma, aid to caregiver).[7,8]

Action plan: What to change with poor control?

- Increasing the **inhaled corticosteroid** (**ICS**) dose is an option, although one should first assess for non-compliance. In patients who regularly take an ICS, **doubling** the maintenance dose may not have a beneficial effect on the pattern of the exacerbation.[9,10] Some specialists use up to **3-4x** the maintenance ICS dose **until control is restored**.
- Alternately consider **oral steroids** depending on severity of exacerbation or failure to respond to more intensive controller therapy given for at least a few days.[1,11,12,13] Tapering is not required for short term steroids.
  Prednisone: Adults 30-60mg po od x 7-10day;
  Kids 1-2mg/kg/d x 3-5day; Max 50mg.
- Viral exacerbations often respond poorly to steroids.

Do inhaled steroids affect growth?

ICS do not appear to have a long term affect on total height but may decrease short term growth rate.[14,15,16,17,18,19] {Observational data: budesonide [400ug/d] x 9.2years ⇨ kids attained normal adult height[20]. A longer term randomized control trial found a ~1cm decrease in growth mainly in the 1st year [21] Camp 4.3yr}.

ICS: Use regularly in mild persistent asthma?

Yes. ICS (eg. budesonide Pulmicort, fluticasone Flovent, beclomethasone QVAR) are the most effective therapy.[22, 23] Long acting ß$_2$ agonists (**LABA**s) should not be a substitute for ICS.

However, for those unable or unwilling to take ICS, leukotriene receptor antagonists (**LTRA**s eg. montelukast Singulair) appear reasonable.[24] One preliminary trial has evaluated the effect of **intermittent ICS** in **mild persistent** asthma. Intermittent therapy with ICS, appeared as effective as continuous therapy with budesonide or zafirlukast Accolate (but worse inflammatory markers).[25] Impact However, patients had a clear action plan when breathless. {Recent SK data found that **37%** of the poorly controlled asthmatics did **NOT** fill an ICS prescription[26]}.

ICS: Are they safe in pregnancy?

Yes. Failure to control asthma during pregnancy may lead to poor outcomes.[27] Control with ICS or even systemic steroids may be required. Prospective ICS cohorts & trials managed by NAEPP guidelines have shown no evidence of increased maternal or fetal morbidity or mortality, especially with budesonide.[28,29] A recent review found viral illness and ICS nonadherance led to 6% of all pregnant asthma patients requiring hospitalization for asthma.[30]

Is monotherapy with salmeterol reasonable?

No. A US study [SMART n=26,355 28weeks] comparing salmeterol Serevent or placebo added to usual asthma therapy, showed no primary difference for respiratory-related deaths or life-threatening experiences, but more **asthma-related deaths** and other serious respiratory-related outcomes with salmeterol. {*Post hoc* analysis: ↑risk in patients who did **not** report using **ICS** at study entry and in **African-American's.}** Data for formoterol generally does not suggest ↑risk,[31,32] but the FDA Advisory Committee could not exclude that the risk may apply to all long-acting ß$_2$ agonists including the **faster acting** formoterol Oxeze.[33]

Which is better: increasing the corticosteroid dose or adding a LABA or a LTRA?

Adding a LABA is often preferred.[34] In asthmatic adults poorly controlled on low dose ICS, the addition of **LABA is superior** to LTRA for preventing exacerbations requiring systemic steroids, and for improving lung function, symptoms, and use of rescue ß$_2$-agonists.[35,36,37,38] In adults with chronic asthma, using moderate to high maintenance doses of ICS, the addition of LABA may have a ICS-sparing effect.[39]

ICS: Is high dose necessary?

Low maintenance doses of ICS will be adequate for many patients. Some evidence suggests that ICS have a fairly flat dose-response curve (e.g. much of the benefit at doses of 200ug/day fluticasone[40] & 400ug/day budesonide[41]). When initiating ICS therapy, starting with a **moderate dose** (fluticasone ≤500ug/d; budesonide ≤800ug/d) is equivalent to starting with a high dose and stepping down. Initial moderate ICS doses appear to be more effective than an initial low ICS dose.[42,43,44] High dose ICS may be most effective for airway hyper-responsiveness or to reduce dependence on oral steroids. A Cochrane review found no benefit

when doubling doses in subjects with stable asthma.[45] Novel ways to reduce ICS are being studied.[46,47] (eg. nitric oxide)

Combination products: What are their roles?

Budesonide/formoterol Symbicort & fluticasone/salmeterol Advair are recommended for moderate-severe persistent asthma, when moderate dose ICS alone is **not** controlling symptoms. Combinations may not be beneficial in mild asthma.[48,49] Optima Availability of samples may lead to overuse in such patients; however, when add-on therapy necessary, these products may be cost-effective. Company sponsored trials have found:

- Symbicort **regular and as necessary** was better than fixed dose regimens of either Symbicort or budesonide with a PRN short acting β_2-agonist (SABA) as reliever.[50] Stay, [51]
- With Advair, control was more rapid and at a **lower ICS dose** than in the fluticasone only arm.[52] Goal In another trial, stable Advair dosing was better than adjustable dose Symbicort but often dosed OD in persistent adult asthma.[53] Concept

What herbal options are available for asthma?

There is not enough evidence to assess the possible role of herbal medicine or homeopathy in asthma therapy.[54,55,56] (ASHMI-3 herbs?) Popularity aside, there is an urgent need for relevant clinical trials. Some natural products may contain constituents/impurities that exacerbate asthma.

What about concerns about drug cost?

↓**Cost**: Giving SABA ~$20 separately with Pulmicort <$50 minimizes cost; Symbicort $80-100 may be cheaper than Advair $90-150 depending on dose. Combivent $30 & Theophylline ~$25 Uniphyl are options in rare cases.

↑**Cost**: **nebulizers** salbutamol $70, Combivent $120; Singulair $80; Spiriva $80; Xolair $600/vial; & although expensive Oxeze $45-60 is usually cheaper than Serevent $70.

Should we be using wet nebulization options?

MDI with spacer/holding chambers have been shown to be equivalent to nebulizer therapy [57,58,59,60,61,62]. In Nova Scotia [63] & BC [64] restrictions on neb coverage reduced costs without extra GP visits and hospitalizations. The decision of which type of device to choose should be based on the practical considerations of the patient's performance and preference.[65]
(At least 1200 patients in Sask.~5% use nebs especially 6-9yr olds HQC-2005 26)

Do kids require lower doses of ICS?

No. In very young kids, medication lung deposition is about a tenth of an adult dose.[66,67] This reflects an "auto-scaling" of dosage. Nevertheless, strive for the **lowest effective dose**.

We would like to acknowledge the following contributors and reviewers: Dr. D. Cockcroft (Int Med SHR), C. Bayliff, PharmD (London, ON), D. Turner (RT, PA), Dr. T. Laubscher (FM SHR), Dr. J. Alport (FM), H. Sharpe RN, MN, CAE (AB), J. Pilla MScPhm (ON), D. Jorgenson PharmD (SHR/HQC), & the RxFiles Advisory Committee.
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