When and how to step down asthma treatment?

Björn Stridh[1],
Kerstin Romberg[2], Björn Ställberg[3], Lars Ahlbeck[4], Hampus Kiotseridis[5], Holger von Fircks[6], Christer Janson[7]

1. MD, GP Kista Primary Care Unit. 2. MD, PhD, Respiratory Medicine and Allergology, Lund University. 3. MD, PhD, Dep of Public Health and Caring Sciences, Uppsala University
4. MD, Allergy Center, University Hospital Linköping 5. MD, PhD, Respiratory Medicine and Allergology. 6 M Sc Pharm, Medical Advisor Meda. 7. MD. Prof, Dep of Medical Sciences, Uppsala University

Introduction

The Swedish National Board of Health and Welfare published new guidelines in treatment of COPD and asthma 2015. These guidelines recommend to correct and step down unnecessary combination therapy with ICS and LABA. Current international guidelines from GINA presents a general stepwise treatment in 5 steps. The model is widely accepted internationally including by the Swedish Medical Product Agency.
Clear instructions of how and when to step up asthma treatment is given by GINA, the Swedish MPA and Swedish National Board of Health and Welfare. A strategy or clear instructions for stepping down asthma treatment is less described.

The Swedish MPA guidelines state that:
- The stepwise model can be used both for stepping up and stepping down asthma treatment
- The treatment should be adapted so that the asthma patient is well controlled with the lowes medication possible.

The Swedish national board of welfare estimates:
- That 120.000 patients in step 3 treatment should step down from combination therapy (Step 3).

The Swedish statistical report “Öppna jämförelser av hälso- och sjukvård”, comparing regions and development in different medical fields, showed 2013 that new asthma diagnoses accounted for ≈50% of all combination therapy initiated in Sweden. The prescription pattern contradicts the indication of combination therapy medication. All combination medication in Sweden is indicated to be considered first after asthma control is not achieved with regular use of ICS.

Here we present an evidence based treatment algorithm for Step 1-3 in adults for use in clinical practice (Fig. 1 and 2), including instructions of how to step down asthma treatment. The algorithm is presented as a tool to follow current guidelines to achieve optimized treatment, as the best alternative for the patient and the most cost-effective alternative for the health care system.

Study analysis

In our screening of studies that addresses a step down approach of asthma treatment in step 1-3, we found 3 published meta-analysis [1-3], 2 Cochrane reviews [4, 5] and 10 RCT trials and 2 observational studies.
The meta-analyses differ in their conclusions.
When carefully studying every single RCT study we found some scientific shortcomings:

- Studies not showing negative outcome from step down were not always included in the meta analyses.
- Shown significant outcome was not clinically relevant.
- Several studies included low numbers of patients and gave wide confidence intervals.
- Primary outcome was often PEF or FEV1, in which the actual clinical relevance can be discussed.
- Patients were included after a short period of asthma control. Normally 1-2 months.
- Studies were not clear concerning the definition of asthma control and which patients that were included.
- Every clinical study found was sponsored by the pharmaceutical industry of companies with interests promoting the market of combination asthma medication.

Based on the data available we concluded that step down in asthma treatment while maintaining asthma control is possible to do in a safe way. If the risks are taken into consideration, step down can be considered after minimum 3 months of full asthma control (Fig 1 and 2).

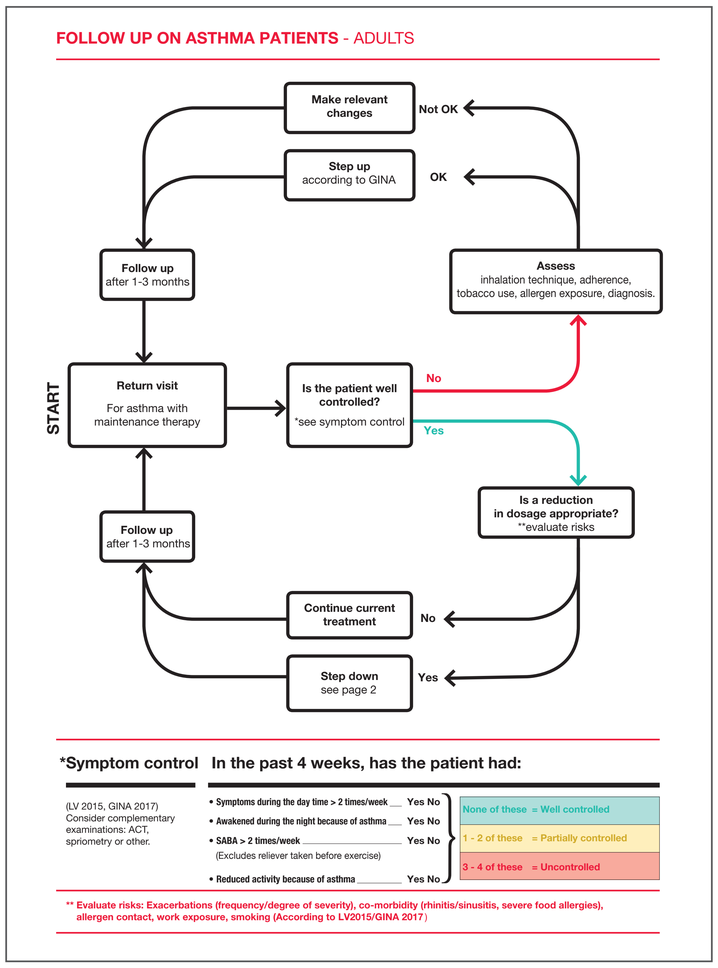
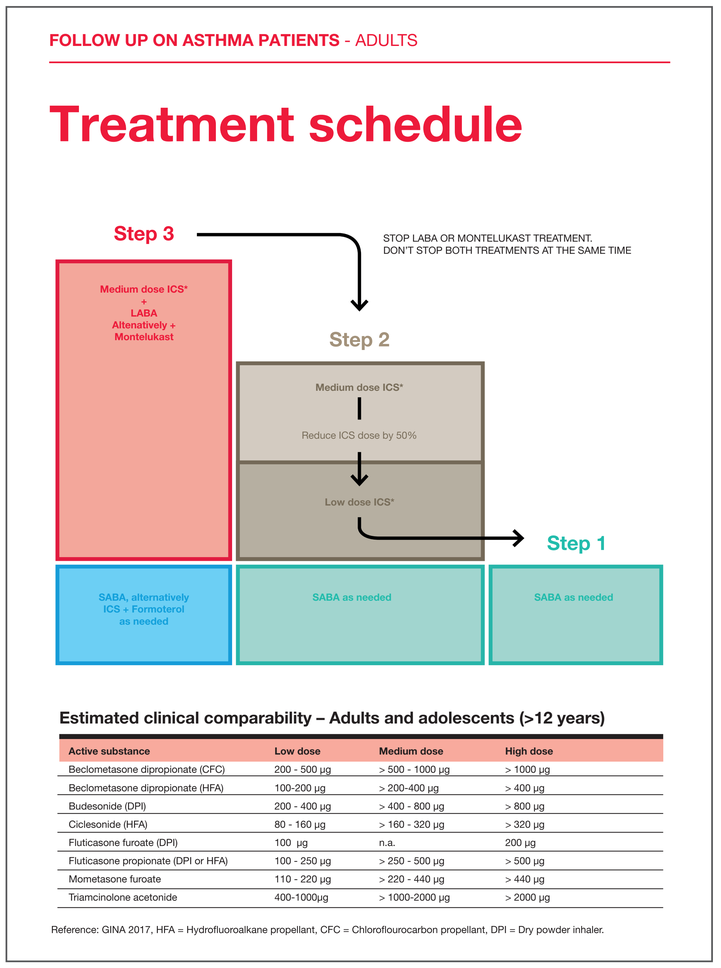


Figure 1. Treatment algorithm for asthma in adults



Estimated clinical comparability – Adults and adolescents (>12 years)

Active substance	Low dose	Medium dose	High dose
Beclometasone dipropionate (CFC)	200 - 500 µg	> 500 - 1000 µg	> 1000 µg
Beclometasone dipropionate (HFA)	100-200 µg	> 200-400 µg	> 400 µg
Budesonide (DPI)	200 - 400 µg	> 400 - 800 µg	> 800 µg
Ciclesonide (HFA)	80 - 160 µg	> 160 - 320 µg	> 320 µg
Fluticasone furoate (DPI)	100 µg	n.a.	200 µg
Fluticasone propionate (DPI or HFA)	100 - 250 µg	> 250 - 500 µg	> 500 µg
Mometasone furoate	110 - 220 µg	> 220 - 440 µg	> 440 µg
Triamcinolone acetonide	400-1000µg	> 1000-2000 µg	> 2000 µg

Reference: GINA 2017, HFA = Hydrofluoroalkane propellant, CFC = Chloroflourocarbon propellant, DPI = Dry powder inhaler.

Figure 2. Step down schedule according to GINA.

When to step down asthma treatment?

It is recommended that clinicians discuss the option of stepping down asthma treatment with patients when asthma symptoms are under control, lung function is near normal, and biomarkers (if measured) are near normal [1]. We suggest that the patients should have shown full asthma control for at least 3 months before considering to step down.

Risks

When initiating step down, the physician should be aware that step down is mostly initiated and executed by the patient her-/himself. First the physician must make sure that a step down has not recently been made by the patient already.

We consider some patient categories being at higher risk of complications when conducting step down. These categories includes patients with:
co-morbidity (rhinitis/sinusitis, severe food allergies), allergen contact, work exposure, smoking and season has to be considered for those patients with seasonal asthma allergy we therefore suggest that these risk factors are considered before deciding to proceed step down.

The medical risks for the patient while being in the process of a step down includes exacerbations and worsening of asthma control.
We therefore suggest to follow up these symptoms while stepping down.

Conclusion

With a selection of patients for stepping down asthma treatment using the criteria presented, a step down process can be done at every clinical setting in a safe way together with the patient.

References

1. Rank, M.A. and S.P. Peters, The risks, benefits, and uncertainties of stepping down asthma medications. J Allergy Clin Immunol Pract, 2014. 2(5): p. 503-9; quiz 510.
2. Hagan, J.B., et al., The risk of asthma exacerbation after reducing inhaled corticosteroids: a systematic review and meta-analysis of randomized controlled trials. Allergy, 2014. 69(4): p. 510-6.
3. Brozek, J.L., et al., Long-acting beta2-agonist step-off in patients with controlled asthma. Arch Intern Med, 2012. 172(18): p. 1365-75.
4. Crossingham I, E.D., Halcovitch NR,Marsden PA, Stepping down the dose of inhaled corticosteroids for adults with asthma (Review). Cochrane Database Syst Rev, 2016.
5. Ahmad, S., K.M. Kew, and R. Normansell, Stopping long-acting beta2-agonists (LABA) for adults with asthma well controlled by LABA and inhaled corticosteroids. Cochrane Database Syst Rev, 2015(6): p. CD011306.

MEDA