



Asthma and Medicines – Long-Term Side-Effects, Monitoring and Dose Titration

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Abstract

Asthma is a major pediatric respiratory morbidity requiring long-term management. A thorough knowledge of long-term medication side-effects in children is, thus, essential for every physician dealing with childhood asthma. Establishing diagnosis and initiating treatment is just a beginning of the journey. Ongoing monitoring is an essential component of comprehensive asthma management programme. Monitoring includes not only assessment of asthma control but also checking for adherence to treatment, technique of inhaler device use, associated co-morbidities, if any, and potential environmental exposure. Various tools – both subjective and objective – are available for assessment of asthma control. However, evidence for their optimum use in different settings and patient groups is lacking and monitoring has to be customized depending on available resources and individual patient characteristics. Patient education is an important component of long-term asthma therapy. The ultimate aim is to achieve optimum asthma control *i.e.*, achieve and maintain control of clinical symptoms, decrease future risk to patients (risk of exacerbations, progressive loss of lung function and development of fixed airflow obstruction, adverse effects of medications) and enabling the child to lead a life without restrictions, at lowest possible dose of drugs. This article reviews the side-effects of medications used for long-term management of asthma and discusses current literature on asthma monitoring and dose titration in pediatric population to help the asthma therapist not only prescribe the drugs rationally but also help the family make right choices for treatment.

Keywords Childhood asthma · Management · Side-effects · Monitoring · Dose titration · Step-down

Introduction

Asthma is the most common persistent respiratory disease of childhood. It imposes a significant health burden on pediatric population and is one of the major contributor to emergency department visits, hospitalization and frequent school absenteeism. Globally, childhood asthma prevalence is increasing (0.06% per year in 13–14 y age group, 0.13% per year in 6–7 y age group) with wide variation in prevalence across globe [1]. International Study of Asthma and Allergies in Childhood (ISAAC) phase III reported that 6.8% of 13–14 y and 7.1% of

6–7 y age group children surveyed by them in India had current wheeze [2].

As asthma causes a significant health burden and often requires long-term management with controller drugs, this article reviews the side-effects of prolonged use of controller medications and discusses current literature on asthma monitoring and dose titration in pediatric population.

Asthma Medications

Drugs used for asthma management can be categorized into 3 categories –

1. Reliever/Rescue Medications – These are used on ‘as needed basis’ and include Short Acting Beta Agonist (SABA) and anticholinergics.
2. Controller Medications – These are used for long-term management to reduce airway inflammation, control symptoms and minimize risk of exacerbations and

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development of fixed airflow limitation. These include inhaled corticosteroids (ICS), combination ICS/long-acting beta₂-agonists (ICS/LABA), leukotriene receptor antagonists (LTRA) and chromones.

3. Add on therapies for severe asthma – These are used to treat truly refractory severe asthma that remains uncontrolled despite optimized treatment with high dose ICS controller medications. These include Anti IgE (Omalizumab), Anti IL-4, Anti IL-5. Theophylline, *etc.*

The authors herein briefly review the side-effects of controller and add on medications.

Inhaled Corticosteroids (ICS)

ICS are the most effective controller drugs used for management of asthma and are recommended first line management of persistent asthma. Table 1 lists the various ICS with their dose range. Though, ICS are generally considered safe in pediatric population, side-effects, both local and systemic, remain a concern especially at high doses. 'Defined' high doses are those that have been associated with systemic adverse effects with long-term use.

Local Side-Effects

There is a paucity of literature in general and particularly for pediatric population, regarding magnitude and mechanism of local side-effects of ICS as these are generally considered minor and insignificant. However, local side-effects can impair quality of life and affect compliance. Reported incidence of local side-effects is highly variable, varying between 5 and 60%, perhaps reflecting the difference in the used steroid dose, formulation, delivery device and study methodology (questionnaire *vs.* clinical examination) [3, 4]. Common oropharyngeal side-effects

include oropharyngeal candidiasis, dysphonia, pharyngitis and reflex cough. Perioral dermatitis and tongue hypertrophy have been reported rarely. Exact cause of these side-effects is not known. Pro-inflammatory effect of propellant and lubricant component of metered-dose inhaler (MDI), non-specific irritant effect of ICS, decreased oral immunity, increased salivary glucose and vocal cord dyskinesia have all been proposed as possible contributory factors.

A pediatric study (n = 639, age range 3 mo – 16 y) reported as many as 60% of the users reporting local side-effects. The adverse events reported included cough during inhalation (39.7%), hoarseness (14.1%), oropharyngeal candidiasis (10.7%), perioral dermatitis (2.9%) and tongue hypertrophy in (0.1%) users [4]. In addition, they also reported that about one-third of children reported a feeling of thirst that may be related to pharyngeal irritation. In contrast, two earlier pediatric studies did not find dysphonia/hoarseness to be a significant side-effect in children taking inhaled budesonide/beclomethasone [5, 6]. Local side-effects are dose related and are seen more with increasing dose and frequency of use of all ICS; though events are reported more frequently with fluticasone as compared to inhaled beclomethasone or budesonide [3, 7]. From the reported literature, it appears that local side-effects are common and can be bothersome. Screening for these side-effects should be a part of regular assessment and monitoring of asthmatic children to prevent non-adherence. Rinsing of the mouth after ICS inhalation, use of volume holding chambers, or both, can ameliorate many of these side-effects.

Systemic Side-Effects

1. **Effect on Growth** Growth in children is a dynamic process and is influenced by a number of factors including

Table 1 Inhaled corticosteroids with their dose range in different age groups (as per GINA Guidelines 2016)

Drug	Children 6–11 y			Children <5 y
	Daily Dose			Low Dose
	Low	Medium	High	
Beclomethasone dipropionate (HFA)	50–100	>100–200	>200	100
Budesonide (DPI)	100–200	>200–400	>400	200 (pMDI + spacer)
Budesonide (nebules)	250–500	>500–1000	>1000	500
Fluticasone propionate (HFA)	100–200	>200–500	>500	100
Fluticasone furoate (DPI)	N.A.	N.A.	N.A.	–
Fluticasone propionate (DPI)	100–200	>200–400	>400	–
Ciclesonide	80	>80–160	>160	160
Mometasone furoate	110	≥220–<440	≥440	N.A.
Triamcinolone acetonide	400–800	>800–1200	>1200	N.A.

Not a table of equivalence but estimated clinical comparability based on available literature

growth phase (infancy - childhood – prepubertal -pubertal), genetics and presence as well as severity of chronic diseases (including asthma). All these factors can and do confound the result of studies evaluating growth suppressing effect of ICS. Our understanding of real impact of ICS is affected by a relative lack of well powered, long-term studies to evaluate effect of ICS on final adult height. Thus, while it is generally agreed that there is some decremental effect of high doses of ICS on growth velocity and but its impact on final adult height continues to be a subject of debate as it cannot be said how much would have been the impact of uncontrolled disease in the absence of ICS use. Another difficulty in assessing the impact of ICS on growth is due to wide variation in type, dose and device of ICS used.

A recent Cochrane review in children with mild-moderate persistent asthma concluded that regular ICS use, even at low to medium doses, caused about half centimeter/year reduction in linear growth velocity with maximal growth suppression occurring in 1st year of treatment. Subgroup analysis showed statistically significant difference between six studied molecules with CFC-Beclomethasone dipropionate and Budesonide *via* dry powder inhaler (DPI) causing relatively greater reduction in growth velocity than HFA- Flunisolide, Fluticasone propionate and Mometasone furoate [8]. Only a few studies have tried to assess the impact of ICS on final adult height. Long-term follow up of CAMP trial participants showed a mean reduction of 1.2 cm in final adult height in prepubertal children treated with budesonide 400 µg/d for a mean duration of 4.3 y [9]. In contrast, study by Agertoft et al. showed no difference in adult height between asthmatic patients treated with Budecort (mean daily dose 412 µg for 9.2 y) and healthy non-asthmatic siblings [10]. Another Cochrane review done to assess the dose response impact of ICS in prepubescent school-aged children with mild to moderate persistent asthma showed a small but statistically significant group difference in growth velocity between low and low-medium doses of HFA-beclomethasone equivalent (mean 0.20 cm/y, observed over 12 mo) [11]. Limited number of trials comparing head to head, the various ICS molecules have reported that Fluticasone Propionate has more favourable therapeutic index compared to Beclomethasone or Budesonide [12, 13]. A Cochrane review is underway to investigate the effect of different drugs and delivery devices on long-term growth in children with persistent asthma [14].

To summarize, in spite of small measureable effect of ICS on linear growth, their safety profile is much better than oral glucocorticoids and benefits of treatment far exceed the risk. Furthermore, it is still not clear if reduction in growth is permanent or a temporary slowing. Effect of different ICS formulations (especially newer ones), doses

and inhalational device on linear growth needs to be confirmed. Physicians should be mindful of this small but definite effect and should neither prescribe ICS carelessly nor withhold ICS where needed. Use of appropriate devices, mouth rinsing after inhalation, regular monitoring and titration of dose can help to decrease the adverse impact of ICS further.

2. **Adrenal Suppression** Hypothalamic-pituitary-adrenal axis (HPA axis) suppression is the most severe potential adverse effect of ICS therapy. Clinical presentation of adrenal insufficiency is variable, ranging from non-specific symptoms of fatigue, headache, abdominal pain to more severe manifestations of generalized weakness, hypotension, hypoglycemia, hyponatremia and shock. Historically, HPA axis suppression was considered likely only in patients taking high dose ICS. An earlier meta-analysis reviewing systemic adverse effects of ICS concluded that adrenal suppression occurred with high doses of ICS (1500 µg/d of Beclomethasone) with almost no risk at low doses (400 µg/d or less) [15]. However, subsequently, cases of adrenal insufficiency have been reported even in children taking standard recommended doses of ICS [16]. Smith et al. reported that about one in nine of the 214 children on ICS (low-moderate doses) had HPA axis suppression [17]. Concomitant use of nasal steroids and low body mass index (BMI), have been shown to increase the risk [18].

Canadian Society for Allergy and Clinical Immunology (CSACI) has brought a position paper on adrenal suppression and it recommends targeted screening of:

- (a) Children taking high dose ICS (>500 mcg of Fluticasone propionate or equivalent, >400 mcg of Fluticasone propionate or equivalent in those under 12 y of age) for more than 6 mo
- (b) Those on medium dose ICS in the presence of risk factors for increased systemic corticosteroid exposure (*viz.* ICS dose in the higher end of the dose band, prolonged duration of treatment at such dose, concomitant use of nasal and topical corticosteroids, recent or frequent short courses oral steroids, and smaller body mass for age), and
- (c) Children with signs and symptoms suggestive of adrenal insufficiency (regardless of ICS dose) [19].

Morning serum cortisol level is used as a screening test with abnormal results confirmed with low dose ACTH stimulation test. Confirmed adrenal suppression should be managed with physiological doses of hydrocortisone (8–10 mg/m²/d) until morning serum cortisol returns to normal and that usually takes 6–12 mo [19].

Such cases should be managed in conjunction with an endocrinologist. Written instructions regarding situations where stress dose of steroids is needed should be provided to parents.

In summary, adrenal suppression can occur in patients on high doses and/ or those on prolonged standard doses of inhaled steroids, particularly in presence of risk factors referred to before. Usage of ICS at lowest possible effective dose should be practiced.

3. **Effect on Bone Mineral Density** The oral steroids increase risk of fracture in children with cumulative effect of multiple courses, however, effect of high dose ICS on bone health in children has not been sufficiently studied. In adults, both oral corticosteroids and high dose ICS are associated with decreased bone mineral density, osteoporosis and dose dependent increased risk of fractures [20]. A few available cross sectional/cohort studies and randomized trials in children on low-medium dose ICS have not shown to have any effect on bone mineral density (BMD) [21, 22].

A follow up study of CAMP cohort (to assess cumulative effect of both inhaled and oral doses of corticosteroids on bone mineral accretion), reported that multiple bursts of oral corticosteroids were associated with dose dependent decrease in bone mineral accretion and increased risk of osteoporosis while the cumulative inhaled corticosteroid use resulted in a small decrease in bone mineral accretion in boys alone without an increased risk for osteopenia [23]. Further, another follow up study with same cohort showed that modifying effect of oral corticosteroids on decreased bone mineral accretion was more marked in those with insufficient vitamin D concentration [24].

Another important contention about effect of ICS on bone health is whether decreased bone mineral accretion in childhood is associated with decreased peak bone mass and thus increased risk of osteoporosis and fractures in adults. However, it has been proposed that bone mass regulation is a homeostatic system that returns to a set point after any perturbation and thus transient changes in bone mineral density in childhood may not persist into adulthood [25].

To conclude, ICS in low-medium doses have not been shown to affect bone mineral density in children and by decreasing asthma severity and risk of asthma exacerbation (thereby oral corticosteroid use), their use in asthma outweighs any potential risk. Adequate nutrition, especially sufficient intake of vitamin D and calcium, should be ensured in asthmatic children on long term ICS.

4. **Ocular Complications** Though ocular complications are reported among adults, ICS are not associated with increased risk of cataract/ glaucoma in children [6, 26, 27].

5. **Immunity** Studies have not shown any evidence of impaired cell-mediated immunity (CMI) (using delayed hypersensitivity skin tests as marker of impaired CMI) in pediatric asthmatic patients taking low or high dose ICS [28–30]. Though, oral corticosteroids are known to suppress CMI and ICS have been associated with increased risk of pneumonia and tuberculosis in adult chronic obstructive pulmonary disease (COPD) patients, evidence regarding increased risk of infection in pediatric asthma is lacking.

6. **Effect on Glucose Metabolism** Pediatric studies examining the effect of ICS on glucose homeostasis are limited. Most studies implicating ICS in contributing to clinical hyperglycemia and diabetes mellitus have been conducted in adults. The only pediatric cross sectional study on this subject reported a small but statistically significant increase in HbA1C levels ($5.44 \pm 0.75\%$ in asthmatic vs. $5.14 \pm 0.41\%$ in healthy controls) in non-diabetic asthmatic children taking ICS [31]. However, no dose response association was found. Furthermore, the only pediatric study to examine effect of asthma treatment on glucose homeostasis in asthmatic children with pre-existing diabetes, had small sample size to draw any meaningful conclusion [32]. More studies are warranted in this domain.

To be on the safe side, more careful blood glucose monitoring, especially with any change in ICS regimen, should be done in diabetic children on ICS therapy.

7. **CNS Effects** Though behavioral abnormalities (hyperactive behavior, aggressiveness, insomnia, uninhibited behavior) and impaired concentration with ICS use have been described in isolated case reports and in a study analyzing adverse drug reporting pattern in pediatric population in Netherland, same has not been confirmed in two long-term controlled trials of inhaled budesonide [27, 33, 34].
8. **Skin Effects** High dose ICS have been associated with dermal thinning and increased bruising/purpura [35]. Hypertrichosis has also been reported in association with ICS therapy in children [36].

Long Acting Beta-2 Agonist (LABA)

Studies have suggested increased risk of severe exacerbation, hospitalization and death in children, when LABA is used without concomitant ICS [37]. A recent Cochrane review done to assess safety and efficacy of adding LABA to ICS in children and adolescent concluded that LABA addition to ICS, though superior in improving lung function compared with same/higher dose of ICS, was not associated with significant reduction in rate of exacerbations requiring systemic steroids. However, there was a trend, though not statistically

significant, towards increased risk of hospital admission irrespective of dose of ICS [38].

Leukotriene Receptor Antagonist (LTRA – Montelukast, Zafirlukast)

Psychiatric (agitation, anxiety, depression, sleep disturbance, hallucinations, suicidal thinking) and non-psychiatric effects reported in isolated case reports and retrospective studies have not been confirmed in randomized controlled trials [39]. A meta-analysis of randomized placebo controlled trials in children concluded clinical and lab safety profile of montelukast to be similar to that observed for placebo/usual care therapies [40].

Chromones (Sodium Cromoglycate, Nedocromil Sodium)

Though both these agents have good safety profile with no significant reported adverse effects, they have limited role in long-term treatment of asthma in children. Reported adverse effects include unpleasant taste, sore throat, headache, nausea and sleepiness [41, 42].

Anti IgE (Omalizumab)

Omalizumab has been recommended to be used as a treatment trial for children >6 y with confirmed IgE dependent allergic asthma that is uncontrolled despite optimal pharmacological and non-pharmacological management. Its long-term safety has not been studied in children. Reported adverse effects include injection site pain, urticaria, rash, flushing, and pruritus [43].

From the foregoing discussion, there is enough evidence to say that there is a definitive but largely modifiable risk of adverse effects to asthma therapy. The key to decreasing the adverse effects is proper selection of the type of drug, its formulation, dosing, correct selection of route and device, correct technique, *etc.* Appropriate monitoring can help get the best risk benefit ratio by appropriate adjustment of therapy on follow up.

Monitoring

Ongoing watchful monitoring is an essential component of asthma management so as to achieve and maintain optimum asthma control at lowest possible dose of drugs. Frequency of follow up visits depends upon initial disease severity, presence of risk factors for future adverse outcomes, response to treatment, age and training of caregivers. IAP National Respiratory Chapter Guidelines recommend follow up visit 2–4 wk after starting treatment, every month thereafter routinely and within

1 wk of any exacerbation. The monitoring takes into account the response to therapy, control of symptoms and exacerbations, technique of inhalation, adherence to therapy, adverse effects to therapy, *etc.* The effort is to optimize the treatment for maximum control with least amount of drugs.

The authors discuss below the factors that need to be monitored at each visit.

Assessment of Asthma Control

Asthma control is assessed in terms of impairment (frequency and intensity of daytime, nocturnal and exercise related symptoms; activity limitation, school absenteeism, impaired sleep, and; variation in lung function) and future risks (of exacerbation, progressive loss of lung function, adverse effects of medications).

Currently available tools to monitor asthma control include subjective (patient reported), semi-objective (asthma questionnaires) and objective (physiologic and inflammatory measures). Till date, there is no universally recognized gold standard assessment that captures both subjective and objective measures of lung function and for many aspects of monitoring pediatric asthma, the evidence is lacking. A judicious combination of measures from each category is needed to ensure optimal delivery of health care services. Table 2 outlines various available tools for pediatric asthma monitoring. The list shows the various tools that may be applicable at different age groups but many of these tools are meant only for research purpose and may not be useful for routine clinical monitoring. The maintenance of a daily symptom diary is simplest, cheapest and effective manner suitable for all cultures and socio-economic groups. However, certain composite score have also been developed and are in use in the developed world. Use of composite asthma control scores has not been shown to improve symptom control over and above interview based clinical assessment of symptoms/exacerbation/ use of rescue medications or patient / caregiver maintained symptom diaries. Peak expiratory flow rate monitoring also has not been shown to improve asthma management compared to management based on symptoms alone [44–46].

Spirometry with measurement of maximum expiratory flow volume curve [especially FEV1 (Forced expiratory volume in 1 sec) and FEV1/FVC ratio (FVC: Forced vital capacity)] is recommended routinely for asthma monitoring in children >5 y of age. There is insufficient evidence for routine monitoring of interrupter resistance (Rint) or using Impulse oscillometry or tidal flow volume loop for pre-school wheezy children. Bronchial hyperresponsiveness (BHR) measurement is not useful for routine monitoring but may be used in children with exercise limitation/poor symptom perception/poor response to treatment.

Table 2 Asthma monitoring tools for children of different ages

	0–2 y	2–4 y	4–6 y	>6 y
Subjective Tools				
Symptoms	✓	✓	✓	✓
Exacerbations	✓	✓	✓	✓
Asthma Control Questionnaires				
C-ACT			✓	✓
ACQ				✓
TRACK	✓	✓	✓	✓
QoLQ				✓
Objective Tools				
Lung Function Assessment				
Flow-volume curve/BDR	Tidal	Tidal	✓	✓
PEF			✓	✓
ILF	✓			
Rint-IOS-FOT		✓	✓	✓
LCI	✓	✓	✓	✓
BHR				
Direct (methacholine/histamine)			✓	✓
Indirect (exercise/mannitol)			✓	✓
Inflammatory Markers				
FeNO	✓	✓	✓	✓
Induced Sputum				✓
EBC			✓	✓

ACQ Asthma control questionnaire; BDR Bronchodilator response; BHR Bronchial hyperresponsiveness; C-ACT Childhood asthma control test; EBC Exhaled breath condensate; FeNO Fraction of exhaled nitric oxide; FOT Forced oscillation technique; ILF Infant lung function; IOS Impulse oscillometry; LCI Lung clearance index; PEF Peak expiratory flow; QoLQ Quality of life questionnaire; Rint Interrupter resistance; TRACK Test for respiratory and asthma control in kids

There is no evidence for any advantage for routine “Inflammometry” - monitoring of airway inflammation markers like Exhaled Nitric Oxide (FeNO), sputum eosinophil counts, *etc.* In a recent meta-analysis, it was concluded that using FeNO to guide treatment decisions showed little clinical benefit, although FeNO levels were significantly higher in children who had an exacerbation in the year following the FeNO measurement and there was complete overlap in FeNO values between children with and without exacerbations [47]. Some experts believe that ‘inflammometry’ is an important part of asthma management at the more severe end of the spectrum [48].

Adherence to Treatment

Poor adherence to treatment is a rule rather than exception in chronic conditions including asthma. About 50% of adults and children do not take controller medication as advised [49]. While treatment adherence is one of the main determinant of successful outcome, illness perception and medication beliefs

are strong determinants of adherence in asthma. Trent et al. reported that the caregivers of children with controlled asthma answered more questions on asthma knowledge test correctly and had a lower score on the asthma barrier questionnaire as compared to those with uncontrolled asthma [50]. Therefore, close monitoring of adherence with provision of repeated tailored education that addresses parent/patient’s beliefs and concerns, is the most effective way to achieve asthma control. There is no gold standard measure to assess adherence. Methods used include interviews, self reporting by parents/patient, pharmacy re-fill rates and more recently, electronic data monitoring. Interviews, self-reporting and pharmacy re-fill rates tend to over estimate adherence [51]. E-monitoring has been reported to be the most reliable way to assess adherence [51] though it does not by itself improves adherence.

Inhalation Technique

Correct inhalation technique and device use is cornerstone for optimum asthma control. Correct inhaler technique means prescribing an age appropriate device and teaching adequate breathing maneuver along with correct device handling and maintenance. Many authors have reported poor usage of devices across all ages; particularly among children. Caponoglu et al. reported that only about 1/3 of patients using DPI and 68% using MDI/spacer performed all steps correctly [52]. Inhaler technique needs to be taught, checked and re-taught as even well performing patients/ caregivers can forget or miss some steps later on. Studies have shown that correct device usage was higher in patients given repeated instructions and in those who had been asked to demonstrate usage, with technique improvement occurring up from 37.4% to 97.4% after 3 comprehensive instruction sessions [52].

Monitoring and Managing Co-morbidities

Asthma, especially severe asthma, often has associated co-morbidities. These include allergic rhinitis/rhinosinusitis, gastro-esophageal reflux disease (GERD), obesity and food allergy. Active monitoring and management of these is recommended as some of these not only contribute to symptom burden and impaired quality of life but are also associated with poor asthma control [53]. Many patients with asthma have allergic rhinitis (AR) and 10–40% patients with allergic rhinitis have asthma [54]. The improvement in symptom control requires appropriate management of AR. Gastro esophageal reflux (GER) can cause cough in asthmatic as well as non-asthmatic children [55]. Though GER has been suggested as a cause of poorly controlled asthma, there is not much evidence to support this. In a recent trial of children with poorly controlled asthma, without symptoms of GER, lansoprazole neither improved symptoms nor lung function [56]. However, in patients with asthma and symptomatic GER, a trial of anti

reflux medications may be considered but there is no role of routine diagnostic tests for GER in all asthmatic children.

Relationship between asthma and obesity is complex and not fully elucidated. Lack of fitness, reduced lung volume due to abdominal fat, mechanical factors and associated obstructive sleep apneas and GER may all contribute to symptoms. Therefore, in obese patients it is important to confirm the diagnosis of asthma with objective measures rather than relying on symptoms alone. A recent study showed that asthma is more difficult to control in obese asthmatic children [57]. Weight reduction should be a part of comprehensive management plan for obese asthmatic children.

Food allergy has been associated with severe and even fatal asthma exacerbations. However, it is not food allergy *per se* but sensitization to multiple food and aero-allergens that may be a risk factor for poor asthma control and severe exacerbations. There is no role for routine food allergy screening in asthmatic children without history of food allergy.

Review of Environmental Factors

Multiple environmental triggers can worsen asthma and a discussion about these exposures should be part of comprehensive asthma management. A detailed discussion on this is beyond the scope of this article.

Dose Titration

After starting asthma treatment, further management decisions are based on continuous monitoring (as discussed) with cycle of treatment adjustment, as required, with further review of response to adjusted treatment. The ultimate aim is to maintain optimum asthma control and reduce future risk to patient on minimal possible dose of controller medications.

Stepping Down Treatment

Efforts are always to be made to step down therapy provided the patient is showing a good control of symptoms for a long period of time, say 3 mo. Studies evaluating objective measures of control have shown variable results and currently there is no consensus on role of these in monitoring and dose titration. Literature on step down of therapy in children is sparse and current guidelines are based on limited evidence. Any step down should be considered a therapeutic trial and further treatment adjustments should be done on follow up depending on subsequent symptom control and exacerbations. Providing written asthma action plan before any step down is of paramount importance. Dose of ICS should be gradually reduced to low dose (25–50% reduction every 3 mo). Even in patients on combined ICS-LABA controller treatment, before discontinuing LABA, ICS dose should be reduced to low dose,

as a meta-analysis in older children has shown an increased risk of loss of asthma control with LABA discontinuation [54]. Subsequently, ICS can be given once daily. Stopping ICS should be considered once good symptom control is maintained for 6–12 mo on once daily ICS. Stopping of therapy may not always be successful and a proportion of patients may require re-introduction of therapy depending on the frequency and severity of the returning symptoms. A trial of withdrawal of therapy should always be attempted after a prolonged period of remission on lowest dose, as discussed above.

Stepping Up Treatment

If asthma is not well controlled despite 4 wk of regular, correctly taken controller treatment, a step up of the therapy is planned. It is important to first rule out problems related to correct diagnosis, adherence, inhaler technique, persistent environmental exposure and co-morbidities before augmenting therapy.

To conclude, monitoring is an integral component of comprehensive asthma management and should be customized as per the available resources and individual patient characteristics with the aim to provide optimum asthma control at lowest possible dose of drugs. Monitoring of asthma care should not fall short of monitoring for treatment efficacy, treatment of any co-morbidities, treatment technique, environmental control and trigger avoidance, treatment related adverse effects in addition to continued support and education of the patient and their care givers.

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Compliance with Ethical Standards

Conflict of Interest None.

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