Special Article

Montelukast in Pediatric Asthma Management

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Abstract. Leukotriene modifiers (receptor antagonist and biosynthesis inhibitor) represent the first mediator specific therapeutic option for asthma. Montelukast, a leukotriene receptor antagonist is the only such agent approved for use in pediatric patients. Montelukast modifies action of leukotrienes, which are the most potent bronchoconstrictors, by blocking Cysteinyl leukotriene receptors. Systemic drug like mountelukast can reach lower airways and improves the peripheral functions which play a crucial role in the evolution of asthma. Review of existing literature showed that montelukast compared to placebo has proven clinical efficacy in better control of day time asthma symptoms, percentage of symptom free days, need for rescue drugs and improvement in FEV_1. Studies also demonstrated improvement in airway inflammation as indicated by reduction in fractional exhaled nitric oxide, a marker of inflammation. Studies comparing low dose inhaled corticosteroids (ICS) with montelukast are limited in children and conclude that it is not superior to ICS. For moderate to severe persistent asthma, montelukast has been compared with long acting beta agonists (LABA) as an add-on therapy to ICS, montelukast was less efficacious and less cost-effective. It has beneficial effects in exercise induced asthma and aspirin-sensitive asthma. Montelukast has onset of action within one hour. Patient satisfaction and compliance was better with montelukast than inhaled anti-inflammatory agents due to oral, once a day administration. The recommended doses of montelukast in asthma are- children 1-5 years: 4 mg chewable tablet, children 6-14 years: 5mg chewable tablet, adults: 10mg tablet; administered once daily. The drug is well tolerated. Based on the presently available data montelukast may be an alternative treatment for mild persistent asthma as monotherapy where ICS cannot be administered. It is also an alternative to LABA as an add-on therapy to ICS for moderate to severe persistent asthma. The other indications for use of montelukast include: allergic rhinitis, exercise induced bronchoconstriction and aspirin-induced asthma. **[Indian J Pediatr 2006; 73 (4) : 275-282]**
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Asthma is the most common chronic disease of childhood and its prevalence has substantially increased worldwide, particularly in pre-school children.[1] It is associated with significant morbidity and economic burden. Chronic inflammation and smooth muscle dysfunction are consistent features of asthma pathophysiology, responsible for disease progression and airway remodeling. The acute and chronic inflammation in asthma is the result of extensive infiltration of the airway by inflammatory cells including T cells, eosinophils, mast cells and release of inflammatory mediators- cytokines and leukotrienes from these cells.

Current clinical practice guidelines from National Asthma Education and Prevention Programme (NAEPP)[2] and Global Initiative for Asthma (GINA)[3] recommend use of anti-inflammatory controller therapy to attenuate long term inflammation and smooth muscle dysfunction in persistent asthma, thus preventing permanent airway changes. In this regard inhaled glucocorticosteroids (ICS) are the recommended first line controller agents because of their broad anti-inflammatory properties. However, for some patients with persistent asthma, ICS fail to achieve adequate response without increasing the dose. These issues led to trials of adding alternative agents like long acting beta-2 agonists (LABA), cromolyn sodium and leukotriene modifiers to achieve optimal disease control. Research into asthma pathophysiology enabled to understand the role of leukotriene as one of the pro-inflammatory agents in asthma. This initiated research and development of leukotriene modifiers as first mediator specific therapy for asthma.

Recent years have witnessed a favorable preference among health care givers for montelukast, a leukotriene antagonist in asthma management of children. The present article intends to review the scientific evidence concerning the role of montelukast in childhood asthma and understand its current position in pediatric asthma management.

PHARMACOLOGY

Leukotrienes (LT), previously known as slow reacting substance of anaphylaxis, are linear C20 endogenous

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metabolites of arachidonic acid (icosa-5,8,11,14-tetraenoic acid) containing a terminal carboxy function and four or more double bonds (three or more of which are conjugated) as well as other functional groups. Membrane bound arachidonic acid is released by phospholipase A2. Free arachidonic acid can be converted to prostanoids (prostaglandins, prostacyclin, thromboxane) by cyclo-oxygenase or via the 5 lipo-oxygenase pathway (5-LO) to form leukotrienes. Arachidonic acid (AA) is presented to the 5-LO enzyme by the 5-LO-activating protein (FLAP) resident in the nuclear membrane. The 5-LO pathway results in the formation of 2 classes of LTs, the non-peptide LTs- LTA_4 and LTB_4 and the cysteinyl leukotrienes (Cys-LTs) LTC_4, LTD_4, and LTE_4. The 5-LO enzyme is primarily restricted to various myeloid cells-neutrophils, eosinophils, monocytes/macrophages, mast cells/basophils and B lymphocytes. CysLTs are essentially generated in mast cells, alveolar macrophages and eosinophils. LTB_4 is predominantly produced by neutrophils.[4]

Leukotrienes exert their biological effects by acting on leukotriene receptors present on cell membranes. LTB_4 activates the BLT receptor, while the CysLTs activate CysLT receptors 1 and 2 (CysLT1 and CysLT2) subtypes. The CysLT1 receptor has recently been cloned[5] and is found mainly localized to the pulmonary smooth muscle cells and macrophages and peripheral blood monocytes. The biological effects of CysLT1 receptor activation are pertinent in asthma pathophysiology.

The biological properties of leukotrienes (LT) are protean. CysLTs are the most potent bronchoconstrictor agents yet discovered, about 100-1000 times more potent than histamine[6]. They enhance airway hyperresponsiveness, increase microvascular permeability and impair ciliary activity. They are shown to induce airway smooth muscle proliferation and may play a role in airway remodeling in chronic asthma. LTC_4 and LTD_4 are potent airway secretagogues *in vitro*, although similar effect is not proven to occur *in vivo*.[7] They have a direct chemotactic activity for eosinophils, an effect that is found to persist for up to 4 weeks in guinea pig models.[8] These biological properties suggest that CysLT play key biological role in asthma pathogenesis. LTB_4 role remains obscure, but is found to be strongly chemotactic for neutrophils. This property may be associated with the neutrophilia observed in late response to allergen challenge and acute severe asthma.[9]

Leukotriene modifiers represent the first class of mediator specific therapeutic option in asthma, tailored to the understanding of asthma pathophysiology. They include two groups of drugs: leukotriene receptor antagonist and leukotriene biosynthesis inhibitor. Zileuton is the only marketed drug available as Leukotriene synthesis inhibitor via inhibition of 5-LO enzyme. Pranlukast, Zafirlukast and Montelukast are CysLT receptor antagonists approved in various markets.

PHARMACOKINETICS AND DOSAGE

Montelukast is rapidly absorbed following oral administration. For the 10 mg film-coated tablet, the mean peak plasma concentration (C_{max}) is achieved three hours (T_{max}) after administration in adults in the fasting state. The mean oral bioavailability is 66%.[10] The oral bioavailability and C_{max} are not influenced by a standard meal. For the 5 mg chewable tablet, the C_{max} is achieved in two hours after administration in adults in the fasting state.[11] The mean oral bioavailability is 73% and is decreased to 63% by a standard meal. After administration of the 4 mg chewable tablet to pediatric patients 2 to 5 years of age in the fasting state, peak plasma concentration is achieved 2 hours after administration.[12] Montelukast is more than 99% bound to plasma proteins. The steady-state volume of distribution of montelukast averages 8-11 litres.[10,13] Studies in rats with radiolabelled montelukast indicate minimal distribution across the blood-brain barrier. In addition, concentrations of radiolabelled material at 24 hours post-dose were minimal in all other tissues. Montelukast is extensively metabolized.[14] In studies with therapeutic doses, plasma concentrations of metabolites of montelukast are undetectable at steady state in adults and children. *In vitro* studies using human liver microsomes indicate that cytochromes P450 3A4, 2A6 and 2C9 are involved in the metabolism of montelukast.

The plasma clearance of montelukast averages 45 ml/min in healthy adults. Following an oral dose of radiolabelled montelukast, 86% of the radioactivity was recovered in 5-day faecal collections and <0.2% was recovered in urine. Coupled with estimates of montelukast oral bioavailability, this indicates that montelukast and its metabolites are excreted almost exclusively *via* the bile.[15] However, no dosage adjustment is necessary for the elderly or mild to moderate hepatic insufficiency. Studies in patients with renal impairment have not been undertaken. Because montelukast and its metabolites are eliminated by the biliary route, no dose adjustment is anticipated to be necessary in patients with renal impairment.

A once-daily 10 mg dose (film-coated tablet) was selected as the optimal adult dose based on dose-ranging studies. As asthma is a similar disease and is treated with the same medications in children and adults, it is logical that a dose of montelukast in children providing overall drug exposure (i.e. montelukast plasma concentrations) similar to that of the 10 mg film-coated tablet dose in adults would be efficacious, well tolerated, and obviate the need for separate dose-ranging studies in children. Therefore, the dose of montelukast for 6–14 year old children was selected by identifying the chewable tablet dose of montelukast yielding a single-dose area under the plasma concentration-time curve (AUC) comparable to that achieved with the adult 10 mg film-coated tablet

dose. Based on this approach, which included dose normalization of data from several pediatric pharmacokinetic studies, a 5 mg chewable tablet dose of montelukast was selected for use in clinical efficacy studies in 6–14 year old children with asthma.[11] Various studies have provided the pharmacokinetic basis for selection of the 4 mg dose for children 2-5 years of age.[12,16] Migoya *et al*[17] evaluated the pharmacokinetic comparability of a 4-mg dose of montelukast oral granules in patients between 6 to 24 months old to the 10-mg approved dose in adults. The authors observed that the area under curve (population) estimate ratio (pediatric/adult 10 mg film coated tablet) and the 95% confidence interval (CI) for children compared with adults were within the predefined comparability bounds. Observed plasma concentrations were also similar. Based on systemic exposure of montelukast, a 4-mg dose of montelukast appeared to be appropriate for children as young as 6 months of age The efficacy of these doses has been established in clinical trials, as discussed below.

DOSAGE

Children between 2–5 years: 4 mg chewable tablet or granules per day.
Children between 6–14 years : 5 mg chewable tablet daily.
Adults and adolescents above 14 years; 10 mg tablet daily.

ADVERSE EFFECTS OF MONTELUKAST

Pediatric studies on montelukast found that it was well-tolerated. The majority of the reported adverse effects were mild and included headache, ear infection, nausea, abdominal pain and pharyngitis. In clinical trials the incidence of these adverse effects was not higher than with placebo. In some patients receiving oral corticosteroids and Zafirlukast, reductions in steroid dose have been associated with Churg-Strauss syndrome.[18] This is thought to be due to reduced steroid dosage and not causally related to Zafirlukast. Similar phenomenon have not been reported with montelukast. No dose adjustment with montelukast is necessary for patients with renal and mild-moderate hepatic dysfunction. It crosses the placenta and is excreted in breast milk. Montelukast should not be prescribed to pregnant and lactating women, due to lack of controlled trials.

MONTELUKAST IN CHILDHOOD ASTHMA

Montelukast Compared with Placebo

Several randomized double blind comparative studies in pediatric patients comparing therapeutic efficacy of montelukast and placebo have been conducted[19-30] (Table 1). The asthma severity was mild to moderate persistent in these trials. Two of these studies were in patients less than 2 years of age.[19,21] The results from these studies depicted significant improvements in multiple parameters of asthma control with montelukast compared to placebo: day time asthma symptoms (cough, wheeze, breathing difficulty, and activity limitation), overnight asthma symptoms (cough); percentage of days with asthma symptoms, percentage of days without asthma, need for beta-agonist or oral corticosteroids; physician global evaluations and peripheral blood eosinophils. There was a significantly greater improvement in FEV_1 from baseline for montelukast group compared to placebo group. Studies comparing the effect on fractional exhaled nitric oxide (FeNO), a marker of airway inflammation in asthma, found a significant reduction in FeNO in the montelukast arm. Montelukast was found to have a rapid onset of action (within 1 day of dosing). It was well tolerated, with no notable differences between treatment groups in incidence of clinical and laboratory adverse effects. A study by Bisgaard *et al*[20] showed that Montelukast effectively reduced viral induced asthma exacerbations in 2-5 year old patients with intermittent asthma over 12 months of treatment and also delayed the median time to first exacerbation by approximately 2 months.

Two randomized controlled trials (RCT) studied the efficacy of montelukast in very young children (6-24 months and 10-26 months) with early childhood asthma.[19,21] It was found to have a positive effect on lung function, airway inflammation and symptom scores in very young children with early childhood asthma.

MONTELUKAST COMPARED WITH INHALED CORTICOSTEROIDS

In comparison to adults, randomized controlled studies comparing montelukast with inhaled corticosteroids in childhood asthma are scarce [31-35](Table 2). A recently published randomized controlled trial compared montelukast with inhaled fluticasone in 6-14 year old children with mild persistent asthma and concluded that montelukast was comparable to fluticasone in increasing the percentage of asthma rescue free days.[33] Secondary end points including FEV_1, beta 2-agonist use, and quality of life improved significantly more in fluticasone treatment group. Earlier studies found daily symptom scores, nocturnal awakenings, percentage asthma exacerbation was similar in montelukast and inhaled corticosteroids (ICS) arm. Randomized "real world" observational studies also found relative efficacies in the two treatment groups similar.[35] However, patient and parent satisfaction, convenience and adherence to treatment were better with montelukast than ICS.[35] Owing to its easy and simple oral once a day administration montelukast was found to be advantageous over ICS. One RCT showed that response

TABLE 1. Studies Comparing the Efficacy of Montelukast *vs* Placebo in Childhood Asthma

Study	Design	Study population	Intervention	Main outcome measures	Conclusions
Straub *et al*[19] 2005	RCT, DB	10-26mo (n=24) early asthma	MT (4mg) *vs* placebo	FeV0.5 FeNO Symptom score	Significant improvement in all parameters
Bisgaard *et al*[20] 2005	RCT, DB	2-5y (n=549) intermittent asthma	MT(4 or5mg) *vs* placebo, 12mo	Asthma exacerbation episodes	Reduced exacerbations
Van *et al* [21] 2005	RCT, DB	6-24mo	MT (4 mg granules) *vs* placebo 6 wks	Adverse events, Asthma attacks, beta agonist use	MT was well tolerated over 6wk period
Becker *et al*[22] 2004	RCT, DB, multicenter	6-14y (n=138) mild persistent asthma	MT(5mg) *vs* placebo, 8wk	% change FeV1	Significant improvement (p=0.005)
Phipatanakul *et al* [23] 2003	RCT, DB	6-14y (n= 36) persistent asthma	MT *vs* placebo, 24wk	Rescue free days (RFD)	MT as add on therapy to ICS increased RFD
Strauch *et al*[24] 2003	RCT	6-14y (n=25) steroid dependent asthma	MT(5mg) *vs* placebo, 4wk	Sputum ECP Sputum Eo count FeNO, QOL	MT suppressed Sputum ECP, improved QOL. No change in rest of parameters
Stelmach *et al*[25] 2002	RCT, DB	Mild –mod atopic asthmatic children (n=39)	MT *vs* placebo 6wk	Serum levels:IL2R, IL-4, sICAM 1, ECP, FeV1	MT significantly reduced Inflammatory markers
Phipatanakul *et al*[26] 2002	RCT, DB	6-14y (n=18) cat allergen induced asthma	MT *vs* placebo, 1wk	Respiratory tract (RT) symptoms FeV1, acoustic rhinometry	MT attenuated RT symptoms
Knorr *et al*[27] 2001	RCT, DB, multicenter	2-5y (n=689) persistent asthma	MT(4mg) *Vs* placebo, 12wk	Clinical parameters of asthma control, Adverse effects, QOL scores	Clinically significant efficacy well tolerated
Bisgaard *et al*[28] 2000	RCT, DB	3-5y (n=13)	MT(5mg) vs Placebo 2d	Cold air induced bronchoconstriction	Significant bronchoprotection by MT
Bisgaard *et al*[29] 1999	DB, cross over	6-15y	MT(5mg) (n=26)	FeNO *vs* placebo 2wk	Significant reduction in FeNO
Knorr *et al*[30] 1998	RCT, DB, multicenter	6-14y (n=336) chronic asthma	MT(5mg) *vs* placebo, 8wk	Morning FeV1 % change	p<0.001 MT *vs* Placebo

Abbreviations: RCT: randomized control trial, DB: Double-blind, MT: montelukast, FeNO: fractional exhaled nitric oxide, QOL: quality of life, ECP: Eosinophilic cationic protein, sICAM:soluble intercellular adhesion molecule

to ICS and montelukast may vary between subjects.[32] Children with low pulmonary function or high levels of inflammatory markers had a better response to ICS therapy.

MONTELUKAST COMPARED TO LONG ACTING β AGONIST AS ADD ON THERAPY TO INHALED CORTECOSTEROIDS

Pediatric studies comparing montelukast with long acting beta2-agonist (LABA) as add on therapy to ICS in persistent asthma are lacking. One study by Buchvald *et al*[36] found that FeNO levels were significantly higher after salmeterol add on treatment compared with both placebo and montelukast. FEV_1 levels were comparable between the two groups. A Cochrane review [37] of eight randomized controlled trials involving 5,895 adult patients concluded that asthmatic adults inadequately controlled on low doses of inhaled steroids, the addition of LABA is superior to leukotriene receptor antagonist for preventing exacerbations requiring systemic steroids, and for improving lung function, symptoms, and use of rescue beta2-agonists.

TABLE 2. Studies Comparing Efficacy of Montelukast and Inhaled Glucocorticosteroids (ICS) in Childhood Asthma

Study	Design	Study population	intervention	Main outcome measures	Conclusions
Stelmach *et al*[31] 2005	RCT, DB, DD	Children(n=51) House dust mite asthma	MT vs Inh BD 6mo	S. IgE	Inh BD & MT decreased S.IgE
Szefler *et al*[32] 2005	Randomised, DB, multicenter	6-17y, (mild-mod persistent asthma	MT(5/10mg) *vs* Inh FP 18wk	FeV1	Those with Low pulm function, high markers, better response to FP
Garcia *et al*[33] 2005	RCT, DB	6-14y(n=914) mild persistent asthma	MT(5mg) *vs* Inh FP, 12mo	Asthma RFD	RFD in two groups comparable, FeV1, QOL, beta2 agonist use better in FP
Karaman *et al*[34] 2004	Randomized, Parallel group	8-14y (n=63) mild persistent asthma	MT vs ICS	FeV1, symptom score	Similar effects by two drugs

Abbreviations: RCT: randomized control trial, DB: double-blind, DD- double-dummy, FP: fluticasone propionate, BD: budesonide, MT: Montelukast

MONTELUKAST IN EXERCISE INDUCED BRONCHOCONSTRICTION

During exercise, evaporation of water from the airway surface is the stimulus for release of inflammatory mediators such as histamine and cysteinyl leukotrienes [50]

Accumulating evidence shows that cysteinyl leukotrienes are the most important mediators in exercise induced bronchoconstriction (EIB). Few long term studies however exist in children with EIB. One study showed following 8 weeks treatment with montelukast, asthma symptom score and FEV_1 significantly improved in patients with EIB. [38] Montelukast was found to attenuate immediate and late phase response to exercise challenge in asthmatic children. The timing of drug administration is critical. The timing of onset and duration of action of montelukast compared to placebo on exercise induced asthma in children was conducted on 19 subjects by Peroni *et al.*[39] Patients undertook three consecutive treadmill exercise tests, respectively 2, 12, and 24 hours after a single dose administration. Bronchoconstriction after exercise challenge was assessed by comparing the percentage fall in FEV_1. Maximum protective effect with montelukast was observed after 12 hours of administration. There was no difference in the effect on FEV_1 detected at 2 and 24 hour.

Recent study[40] also confirmed that montelukast was effective in exercise induced bronchoconstriction when given in the morning or in the evening.

EXPERIMENTAL ROLES OF MONTELUKAST IN ACUTE ASTHMA

Studies are presently exploring the efficacy of intravenous montelukast in management of moderate- severe acute asthma in adults. In a randomized study of 201 adults[41] with moderate- severe asthma, intravenous montelukast was compared to placebo, in addition to the standard therapy. Montelukast was found to improve FEV_1 in comparison to placebo and the benefit was found to last for more than 2 hours following administration. Patients treated with montelukast tended to require less beta agonists and treatment failures were less. Further studies are required to explore the role of montelukast in acute asthma.

ROLE OF MONTELUKAST IN SEASONAL ALLERGIC RHINITIS

The efficacy of montelukast for the treatment of seasonal and perennial allergic rhinitis was evaluated in a number of randomized double blind trials.

In one of the studies[42] the effect of montelukast 10 mg was compared with loratidine in adult patients and was found to be equally effective with loratidine for suppression of flare and itching. In another study[43] montelukast 10 mg was compared with pseudoephedrine hydrochloride (240 mg) for 2 week in the treatment of allergic rhinitis in adult patients. The study concludes that pseudoephedrine and montelukast are equivalent in the improving symptoms of rhinitis and quality of life index.

Montelukast was compared with cetrizine for the treatment of allergic rhinitis in children aged between 2-6 years. Nearly 60 children were selected and treated with either of these drugs and compared with Pediatric Rhinoconjunctivitis Quality of Life Questionnaire (PRQLQ) and total symptom score (TSS). The result of this[44] study revealed that both montelukast and cetrizine were equally effective in all symptom scores. For night sleep quality montelukast was significantly superior to cetrizine.

ROLE OF MONTELUKAST GRANULES IN PEDIATRIC PATIENT BETWEEN 6- 24 MONTH OLD

Montelukast granules have been evaluated in pediatric patients with asthma aged 6-24 month in two trials.[45,46]

In one study, montelukast 4 mg granules was compared with placebo in children aged between 6-24 months with asthma. This was double blind placebo control trial. The efficacy parameter of the study was rescue medicine for asthma, un-scheduled physicians or hospitals visit for asthma, discontinuation of drug due to worsening of asthma and total blood peripheral eosinophil counts. This study concludes that montelukast 4mg granule was well tolerated over 6 weeks of treatment in children aged between 6-24 months with asthma.[45]

In another study, pharmacokinetic of montelukast granules in pediatric asthma patients of 6-24 months old was evaluated. The pharmacokinetic parameters of 4mg granules were similar to adult dose. Based on the evidence of montelukast 4 mg granule dose was found to be appropriate for children as young as 6 months age.[46]

ROLE OF MONTELUKAST IN OTHER CONDITIONS:

The potential role of montelukast in ameliorating symptoms and lung function abnormalities associated with RSV bronchiolitis and its potential in preventing post-bronchiolitis reactive airway disease is being investigated. [47] The inflammatory response in viral induced bronchiolitis includes bronchial obstruction, mucosal edema and release of inflammatory mediators including cysteinyl-leukotrienes. In a randomized placebo controlled trial of 130 infants, 3-36 months of age received either montelukast or placebo for 28 days starting with 7 days of onset of acute RSV bronchiolitis symptoms. Infants on montelukast were free of any symptoms on 22% of the days and nights compared with 4% in placebo group ($p=0.015$). Daytime cough and exacerbations were significantly delayed with montelukast compared with placebo ($p<0.05$).

Apart from asthma other emerging roles for montelukast include seasonal allergic rhinitis[48], chronic urticaria[49], cystic fibrosis[50], migraine[51], eosinophilic gasteroenteritis [52] and vernal keratoconjuctivitis.[53]

COST OF THERAPY

The monthly cost of therapy with montelukast is approximately Rs 180 for 4 mg tablet, Rs 210 for 5 mg tablet and Rs 300 for 10 mg tablet. This cost is higher than that of low dose ICS for mild persistent asthma (approx. 120 per month for budesonide). However, the cost of holding chamber has to be considered for ICS. Also the cost of adding montelukast to ICS in moderate persistent asthma is higher than that of adding inhaled LABA .

POSITION OF MONTELUKAST IN CURRENT PEDIATRIC ASTHMA MANAGEMENT GUIDELINES

Mild Intermittent Asthma

The present guidelines [2,3] recommend use of rapid acting inhaled beta-2 agonists for the relief of symptoms. No daily medication is recommended. Occasional patient with intermittent asthma but having severe exacerbations should be treated as moderate persistent asthma.

Mild Persistent Asthma

These patients require controller medications every day to achieve and maintain control over symptoms. Treatment with an inhaled glucocorticosteroid is preferred. Sustained release theophylline, cromolyn and leukotriene receptor antagonist are other options. Research has shown that montelukast although efficacious compared to placebo in this category of patients, but is not superior to inhaled glucocorticosteroids. However, patient-satisfaction and compliance was better with montelukast, attributed to oral intake and convenience.

Moderate Persistent Asthma

The preferred therapy for moderate persistent asthma is regular treatment with a combination of inhaled glucocorticosteroid and a long acting inhaled beta-2agonist (LABA) twice daily or a medium dose of inhaled steroids. Leukotriene receptor antagonist or sustained release theophylline are alternatives as add on therapy to low dose inhaled steroids. Several studies in adults and one study in pediatric patients has shown that ICS-LABA produce consistently greater improvements in lung function and asthma symptom score than ICS-montelukast combination. In addition, ICS-LABA is a more cost-effective treatment option than ICS-montelukast for patients with moderate persistent asthma.

Severe Persistent Asthma

The primary therapy for severe persistent asthma includes inhaled glucocorticosteroids at higher doses, plus a long acting inhaled beta2-agonist twice daily. Alternatives/combination to LABA as add on therapy to steroids are oral sustained release theophylline, leukotriene modifier or oral beta 2 agonist.

CONCLUSION

Anti-inflammatory therapy is the backbone of asthma management and inhaled glucocorticosteroids continue to be the cornerstone of asthma therapy as controller agents. Although clinical trials have proven efficacy of montelukast in comparison to placebo in pediatric asthma, its efficacy and cost-effectiveness in comparison to ICS and ICS-LABA for the management of mild and

moderate-severe persistent asthma, respectively is inferior. It however has the advantage of single daily oral administration and hence better compliance. It has beneficial effects in exercise induced asthma and aspirin-sensitive asthma. Judicious use of montelukast based on available scientific evidence is warranted in pediatric asthma management for optimal control of asthma symptom score and prevention of deterioration of lung function.

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