



Budesonide and formoterol combination therapy is an optimum and effective therapy option for long-term control of moderate persistent asthma in children above 4yrs of age than budesonide alone.

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ABSTRACT:

Childhood asthma management always been a challenge for paediatricians. First of all the diagnosis of asthma in children particularly young children less than 5yrs is often delayed due to various factors like various asthma phenotypes as well as asthma mimic conditions and also lack of definitive biomarkers.

Various treatment guidelines by both national and international bodies have stringent recommendations to reduce asthma related morbidity and mortality in children with uncontrolled symptoms. There have emphasized on use of newer combination therapy using budesonide and formoterol as a long term controller in case of moderate and persistent asthma in children above 4yrs of age. This combination is proved to be quite safe and effective in treatment by various studies.

This article reviews and discusses the use of budesonide and formoterol combination inhalation therapy in children above 4yrs for long term management of moderate persistent asthma.

Key

words: Asthma, childhood asthma, control, budesonide, formoterol, long-term control

I. INTRODUCTION:

Asthma is one of the most common chronic inflammatory non infective disease in children..

Long term control of asthma symptoms is very crucial in order to reduce the morbidity and mortality associated with it.

The main goals in asthma treatment are to control symptoms, prevention of acute exacerbations with use of lowest possible effective dose of medications to avoid unnecessary adverse effects along with a good compliance in children and making it cost effective.

Various national and international guidelines are emphasizing on use of combination therapy such as long acting Beta2 agonists (LAMA) and inhaled corticosteroids (ICS) for long term control of asthma in children above 4 yrs of age.

Budesonide is a potent Steroid which reduces the airway inflammation and responsiveness effectively. Formoterol, a rapid LABA drug that helps to improve asthma control and prevent acute exacerbations when added with budesonide due to its rapid onset of action. These benefits has helped to develop the combination therapy of budesonide and formoterol in a single inhaler device for use in maintenance and reliever therapy (SMART)

Ideal dose to start with 100 micrograms of budesonide with 6 micrograms of formoterol as twice daily dose.

This article is a prospective article that reviews and discusses various studies that shows positive encouraging results by use of budesonide and formoterol combination therapy for long term control of moderate persistent asthma symptoms in children above 4 yrs of age.

Diagnosis of asthma in children

Diagnosis of asthma is very important before starting long term controller therapy. Many studies have shown that asthma is often underdiagnosed or there is a delay in diagnosis.

It is a chronic inflammatory disease characterized by episodic reversible airflow obstruction leading to wheezing, cough and breathlessness, chest tightness.

There is no single test to prove. Spirometry is gold standard in children above 5yrs of age. FEV1 being an important indicator and the reversibility of airways shown by increase of 12% after bronchodilator therapy. Newer tests have come like



FENO and impedance oscillometry which is quite helpful in diagnosis as well as monitoring of treatment in long term control.

It is often difficult to diagnose in younger children as cough and wheezing is very common due to do many other reasons like viral infections, congenital respiratory problems, bacterial infections, foreign body etc. It's not possible to assess lung function in children less than 5 yrs.

Most of the time it's the clinical history and detailed physical examination that helps in diagnosis.

Use of Asthma predictive index (API), a tool developed by Castro-Rodriguez and colleagues and modified asthma predictive index (MAPI) in children less than 3 yrs helps in clinching the diagnosis.

API- Major criteria (American thoracic society, 2008)

1. parent with physician diagnosed asthma.
2. physician diagnosed eczema

Minor criteria:

1. wheezing apart from cold
2. physician diagnosed allergic rhinitis
3. eosinophilia > 4%

API with at least 1 major criteria or two minor criteria has a positive predictive value of 76% and negative predictive value of 95%.

Long term control of asthma in children

As per GINA (Global Initiative for Asthma) and NAEPP (National asthma education and prevention program) treatment guidelines, there are two important aspects of asthma control. One is current symptoms control and second into prevent the long-term adverse outcomes. This can be achieved by early and proper diagnosis, starting inhalation therapy with right drug combination and right dose. Besides monitoring the compliance and adherence to treatment in addition to assessing the improvement intermittently by the physician.

Counselling of both parents and child is important.

For long term control of symptoms inhaled corticosteroids like budesonide play an important role. In case of moderate to severe and persistent asthma symptoms it has been established by various randomized control studies that addition of long acting Beta2 agonists to inhaled inhaled corticosteroids is very effective in reducing future severe exacerbations besides controlling the current symptoms in day to day life.

Numerous studies have done to show 1. good control of moderate persistent asthma.

2. improved lung function.

3. reduced asthma exacerbations.

in adults and adolescents. One of the important trial was OPTIMA trial.

Few clinical trials in children from 5 to 11 yrs of age have shown similar benefits like adults with use of combined preparation of budesonide and formoterol in metered dose inhaler instead of budesonide alone or both given in separate MDI or in placebo.

Examples:

1. Study by Tal and colleagues, A 12 wk double blind, parallel multicentric trial in 286 asthmatic children with mean age 11 yrs. This study revealed that budesonide and formoterol combination in single inhaler therapy was more effective than budesonide alone as far as improved lung function (FEV1, PEF) and tolerability of drug is concerned.

2. Pohunek and colleagues - 630 children with persistent asthma between 4 to 11 yrs of age were selected for a 12 wks double blind randomized trial for budesonide and formoterol combination therapy. Similar results were noted as Tal and colleagues trial.

3. O'Byrne and colleagues - It was a pivotal double-blind parallel group study where 2760 asthma patients between 4 to 80 yrs were randomized with inhaler therapy of various combination and single drugs such as budesonide and formoterol for MART and individual budesonide and terbutaline as reliever therapy in various diseases combination. It showed better efficacy as well as improved lung function, reduced asthma exacerbations with minimal adverse effects with budesonide and formoterol combination as MART therapy.

4. A prospective cohort study conducted on 164 children in China aged 12 to 17 yrs with persistent asthma had shown better outcome with the use of budesonide and formoterol combination twice a day and as-needed basis as far as hospitalization and ER visit, cost effectiveness and control, steroid exposure compared to use of high dose Salmeterol and fluticasone plus SABA as reliever therapy.

5. Sofia Cividini and colleagues (2023) - a systematic review and network meta analysis of individual participation data in children with uncontrolled asthma symptoms has revealed that the reduction of acute exacerbations and improvement in lung function was superior with the use of medium dose ICS and LABA than any dose of ICS alone.

6. An open-label randomized controlled parallel group trial with 6 month treatment with budesonide and formoterol combination MART therapy in



Belgian children and adult above 22 yrs of age with persistent asthma had shown to be as effective as conventional Steroid treatment with lower ICS dose and at significantly reduced cost.

Since early 1990 both LABA Salmeterol and formoterol are available for use in asthma.

Rapid onset of action in case of formoterol is an advantage compared to Salmeterol. As per Salmeterol Multicentre research trial there is increase patient death with salmeterol use than placebo group in adult asthmatics.

As per GINA and NAEPP (National Asthma Education and Prevention Program)-

.In children 12 yrs and above, SMART (single inhaler maintenance and inhaler therapy) is highly effective in moderate to severe asthma.

. Children between 5 to 11 yrs of age when symptoms are not controlled well with low dose ICS and as needed SABA then ICS plus LABA is effective in controlling symptoms as well as prevention severe asthma exacerbations.

.only one study has been done in children aged 4 to 11 yrs to show that there is benefit and low risk of growth suppression with use of budesonide and formoterol combination.

As per REACT study a 16 wk trial on Taiwanese Asthma patients the real world effectiveness of budesonide and formoterol combination in MART therapy (Maintenance and reliever therapy) is better than any other fixed dose combination like fluticasone and salmeterol along with SABA.

Most of the current and newer recommendations suggest use of budesonide and formoterol combination as MART or SMART for effective control of asthma symptoms.

There are so many other options available which is beyond the scope of this article to discuss.

II. CONCLUSION

For treatment of persistent asthma symptoms in children above 4 yrs combination therapy with budesonide and formoterol in a single inhaler is an effective and optimum method of treatment. It not only control symptoms but also improves lung function. The compliance is much better in children. SMART therapy reduces the number of acute exacerbations with a lower dose of corticosteroid. Additionally the high cost with multiple inhaler devices is avoided along improved compliance.

Abbreviations

API-Asthma predictive index

MAPI-Modified asthma predictive index

SABA-short acting beta2 agonist

LABA-long acting beta2 agonist

ICS-Inhaled corticosteroid

MART- Maintenance and reliever therapy

SMART-single maintenance and reliever therapy

GINA-Global initiative for Asthma

NAEPP-National asthma education and prevention program

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