Original research article

Pediatric Pharmacological Implications of Medications in Asthma

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Abstract

A common allergic reaction that more frequently affects youngsters is an asthma attack. Both the risk and the morbidity may rise as a result. It is a fatal illness that poses a serious threat to life. Children who have chronic asthma are more likely to experience drug-induced side effects, medication errors that aggravate their illness, and negative outcomes. Poor medication adherence, ignorance of the disease, and improper inhaler use can all result in a lower quality of life and make it challenging to treat a severe condition. Uncontrolled aggravation and lingering symptoms are the usual causes. Children who are in a serious state should be referred to a pulmonologist and instructed on the proper inhaler technique.

Keywords: asthma, allergic attack, morbidity, inhaler

Introduction

An inflammatory illness of the lower respiratory pathways is asthma. This is characterised by episodic and symptomatic wheezing, chest tightness, shortness of breath, and coughing and can affect persons of all ages. A severe asthma attack can be brought on by dust, pet dander, pollen, and other environmental allergens. The aim of the medications used in asthma is to reduce the inflammation and severity of the disease. Children with severe and chronic asthma will show psychotic symptoms like anxiety and difficult to adapt their disease this can lead to poor medication adherence and management of asthma. Asthma attack can be life threatening and particularly recurrent, so it is difficult to treat.

In children aged 5 to 11 years and 12 to 17 years, the prevalence of asthma was 9.6% and 10.5%, respectively in 2016, according to the CDC (Centre for disease control and prevention). Genetics, environmental variables, triggers, and different illnesses are among the causes of asthma. The characteristics of asthma will be affected by a variety of environmental factors and lifestyle choices [1]. Exposure to indoor allergens like food allergen, cockroach, mold, pets and outdoor includes pets and pollen. Some studies reported that the certain infection viruses protect against asthma, and some will initiate the asthma. The most common viruses for the exacerbation of the asthma are human rhinoviruses. In addition, the other triggers include the tobacco smoke, irritants, pollutants, exercise, weather, stress and drugs.

In comparison to adults, children have a much larger number of eosinophils, IgE, and allergen sensitivity, according to the severe asthma research programme (SARP). The health-related quality of life (HRQOL) can be significantly lowered by severe asthma, which can also result in life-threatening exacerbations and adverse drug reactions. For children with asthma who are in school, simple and reliable HRQOL questionnaires have been developed. Diagnosis is crucial for the treatment because it helps to classify the severity of the asthma [2, 3]. The asthma can be more focused on cell type (mast cell, eosinophil etc.), timing of

symptoms (morning and night), trigger (allergens, viral, exercise and food) and reversibility (often). This can be done by the detailed analysis of the history of patient, physical examination of upper respiratory tract (chest and skin) and the outcome of spirometry. The diagnosis of asthma is based on the episodic symptoms and the allergic triggers [2, 3].

PATHOPHYSIOLOGY

Airway restrictions, hyperresponsiveness, and chest tightness can all be symptoms of asthma. Mast cell mediators (prostaglandins, histamines, leukotriene, and thromboxane) released during these events generate an inflammatory response that can result in bronchoconstriction, lining irritation, edema, and mucus plug development. Leukotriene has potent role in asthma, which will show more inflammation responses and their effect can also enhance inflammation response on the eosinophil, neutrophils and lymphocytes [4]. This inflammation causes smooth muscle contraction, increased collagen deposition and chest tightness. This can also lead to damage on the airway epithelial cell. Thus the anti-inflammatory drugs have fundamental role in the bronchial asthma [5, 6].

CLINICAL MANIFESTATION

The symptoms of asthma, an allergic illness, include coughing, wheezing, sneezing, shortness of breath, and tightness in the chest. The severity of a disease is influenced by its symptoms. This can happen at any age, although it happens to males more often than to women. Most of the time, an asthma attack occurs in the early morning or late at night. The most symptom of the asthma is breathlessness due to the chest tightness. Usually the cough is dry but sometimes it is wet. Wet cough of different sputum colour, the colour can be white or green. Green colour is due to the release of peroxidase from the eosinophil and neutrophils.
Hyperreactivity to allergens can result in allergic rhinitis, eczema, conjunctivitis, and skin irritation. Asthma has two subtypes: intrinsic (non-allergic) and extrinsic (allergic), each with a unique set of triggers.

Table 1: Extrinsic vs Intrinsic

Allergic trigger factors	Non allergic trigger factors
House dust mite	Exercise
Pollen	Food and drinks
Fungal spores	Drugs and disease
Pet	Air pollution, smoking and climate change

Clinical evaluation is crucial to the therapy process in order to determine the severity accurately. The clinical signs comprised of

- Respiratory rate
- Pulse rate
- Amount of wheezing
- Degree of breathlessness
- Degree of consciousness

The common presentation of asthma for pediatrics include-

- Transient wheezing

The child may wheeze occasionally, but there may be no family history. This will be up to the 3 years and later disappear.

- Non atopic wheezing

This is another type, where the wheezing is continued after 3 years to the child. This may be occurring due to the family history. These children will respond to leukotriene antagonist.

- Late onset childhood asthma

In some cases, the bronchial hyperresponsiveness can be seen in puberty age. This is more affect to girls compare to boys. This is called late onset childhood asthma.

DIAGNOSIS AND INVESTIGATION

Based on the medical history and physical examination, asthma can be diagnosed early. A pulmonary function test is performed to assess the disease's severity and scope.

Spirometry- When checking for restrictive and obstructive airway illness, the forced vital capacity (FVC) and forced expiratory volume (FEV) in 1 second test is the most popular. The object is called a spirometer. Ratio of FEV1/FEVC:

<0.7 = obstructive lung disease

>0.7 = restrictive lung disease

In severe asthma condition the forced exhalation rate is very low, because the obstruction of airflow.

Peak flow meter- Similar to a spirometer, a peak flow metre measures the peak expiratory flow rate following a full inspiration. The simplicity and low cost are advantages. This can identify airflow obstructions.

Exhaled nitric oxide test: This test assesses inflammation. Nitric oxide levels are higher in patients with severe asthma. This happens as a result of increased nitrous oxide synthase levels in the respiratory mucosa. Nitric oxide synthase may increase as a result of the eosinophilic inflammation.

Eosinophilic count: Severe asthmatic conditions are characterised by an elevated eosinophil count (>15%). Eosinophil levels should be between 1 and 6%. Both allergic bronchopulmonary aspergillosis and tropical eosinophilia can result in an increase in eosinophil levels.

Total IgE- The level of total IgE is elevated in allergic asthma (>1000 ABPA). Anti IgE can be given to this patient.

Sputum test- It is to analyze the amount eosinophil in sputum. This can check the differential cell count. Higher number of eosinophil count indicates the severe inflammation of airways.

Pulse oximetry- The measurement of oxygen saturation is very important in asthma patients and this can be reduced in case of chronic wheezing.

Blood gases- If the condition is very poor the measurement of blood gases can be done. The enhances of pco2 can be seen in worsen condition of asthma.

Chest x-ray- This can be done only in case of persisting unilateral severe emphysema.

Categories of asthma medications

The use of bronchodilators, pain relievers, controller drugs, and risk-reduction medications are all part of the pharmacological management of asthma. The medications used to treat bronchial asthma include leukotriene modifiers like montelukast, beta 2 adrenergic blockers, and corticosteroids. Since asthma can affect anyone at any age, it's crucial to treat it with the

right medication. The high effective therapeutic drugs and appropriate drugs can reduce the severity and complications of asthma. The step wise allergic management (table 2) in children has been proposed. Treatment starts from step 1 at a low dose. And stepping up the medication for the control the disease. Step 5 is most worsening condition [7, 8, 9].

Table 2: Stepwise pharmacotherapy management in asthmatic children

Step 1	Step 2	Step 3	Step 4	Step 5
Reliever Therapy	As Needed SABA	As Needed SABA	Or Low Dose	ICS/LABA
Controller Therapy	Low Dose ICS	Low/Medium ICS/LABA	Medium ICS/LABA	Add On Treatment
Other Common Controller	Low Dose ICS LTRA	Medium/High Dose ICS+LTRA	High Dose ICS+LTRA	Low Dose OCS Option

MEDICATIONS USED

Short Acting Beta 2 Agonist

Acute asthma attacks are treated with short-acting beta 2 agonists. They consist of pirbuterol, levalbuterol, salbutamol, and terbutaline. The primary medication of choice for SABA is salbutamol inhalation. The other terbutaline, however, is not recommended for patients who are younger. They typically administer medications as needed, the greater the demand, the stronger the anti-inflammatory effect. This medication may have a stronger bronchodilator effect. Compare to other drugs SABA have faster and more rapid action. Oral SABA are generally discouraged. The other second line agents are anticholinergics which include Ipratropium bromide.

Combining SABA with anti-cholinergic drugs may have a synergistic effect. Combining the two can lessen the hospitalisation and asthma's severe effects. Three doses of 2.5 mg salbutamol (6 puffs on an MDI through spacer) are administered every 20 minutes for an hour to patients younger than 6 years old. The mechanism of action includes beta agonist causes bronchodilation by inducing airways smooth muscle relaxation, reducing the inflammation and edema, improve broncho clearance. This drug has with less tachycardia and tremor. In adults, salbutamol or short acting theophylline can be prescribed. Oral short acting theophyllines are alternative to SABA, have slower action and higher risk of adverse effects than SABA. So they are not recommended in children [9-11].

Long Acting Beta 2 Agonist

Salmeterol and Formoterol are examples of long-acting beta 2 agonists that are frequently used in conjunction with inhaled corticosteroids like fluticasone or budesonide. The addition of ICS at a set dose is showing good results and is not producing any major asthma-related adverse effects compared to using ICS alone [9]. Long acting beta 2 agonists should not be administered as monotherapy. Salmeterol is available in both aerosol and an inhaled dry powder. Both forms are more effective than short acting beta 2 agonist in treating with moderate asthma and bronchodilation action last for 12 hours [12]. The agonist binds on G protein and activating the adenylyl cyclase, which in turn activate protein kinase A, which trigger uncoupling of myosin and actin. This leads to smooth muscle relaxation and bronchodilation.

Salmeterol is less active and effective than formoterol. While salmeterol is only a partial agonist, formoterol is. 50 mcg twice daily of salmeterol and 12 mcg of formoterol are the recommended dosages for patients older than 4 years [13]. The combination of LABA and ICS will show synergism effect compared to monotherapy. LABA were better than the SABA for different of lung function and there monitoring [14].

ORAL CORTICOSTEROIDS

Only if the asthma has persisted for a longer period of time may this be used. The therapy of severe asthma exacerbations is also possible with the use of systemic corticosteroids. When compared to systemic CS, inhalation corticosteroid (ICS) is superior in youngsters. The mechanism of corticosteroids is targeting the reduction of inflammatory mediators including eosinophil, mast cell, lymphocytes and proinflammatory proteins which causing the inflammation in the airways. This can also reduce the hyper responsiveness and bronchoconstriction in airways.

The ICS dose varies depending on age [15]. Oral corticosteroids are the other medications; they are used extremely infrequently. When asthma is under control, the dosage of these medications should be decreased. Corticosteroid side effects, such as obesity, osteoporosis, and hypertension, might be exacerbated by repeated use. This does not have a recommended protocol in child therapy [16]. However, this can be added if the patient has severe asthma (stage 6). Prednisolone (1-2mg/kg/day) is given early in treatment. Betamethasone (0.1-0.2 mg/kg/dose) in 2 to 3 times of administration. The other steroid includes Inj hydrocortisone (5-10 mg/kg 6-8). Steroid treatment should not exceed more than 14 days. Prednisolone is short acting and dexamethasone is long acting. Most of the oral and intravenous agents have the same efficacy [7].

Leukotriene Receptor Antagonist

These medications include zileuton, pranlukast, zafirlukast, and montelukast. This can lessen lung bronchospasm and exacerbation. The medications will prevent cysteinyl leukotrienes from activating. Leukotrienes play a crucial part in asthma. Bronchoconstriction, mucus sequestration, plug development, etc. are among conditions that cysteinyl leukotrienes might lead to. According to studies, these drugs have a less significant impact than ICS and LABA. The most common drugs in this category are montelukast and zafirlukast. Studies also report that montelukast are effective in exercise induced asthma. The montelukast (4mg) chewable tablet is given in the bedtime for the 2-5 year old child [16]. Montelukast has less adverse effect than zafirlukast, but hepatic dysfunction should be monitored [10]. It can be used first line agent in the mild to moderate asthma if ICS is not possible because many reports concluded that these agents are safe, convenient, non-steroidal, less side effect and oral administered agents [17].

PREVENTION

The treatment's main objective is to avert the allergic disease. Additionally, it is exceedingly challenging to identify and manage asthma in children. Medication has the effect of reducing problems and symptoms. Despite the fact that the disease's severity and morbidity can be decreased by the controller medication. A worsening of the ailment may result from ignorance of the disease and medications. For a better therapeutic outcome, there should be proper medication adherence. The correct way to use inhalers and medications should be explained to paediatric patients. He should avoid being in close proximity to any allergies or exposures to different allergens [18].

CONCLUSION

Salbutamol is used the most frequently of all the beta 2 agonists, according to the majority of guidelines. Although the addition of ipratropium bromide will strengthen the effect, this can treat acute asthma. A synergistic impact is shown when corticosteroids are used with SABA or LABA. Children should not be given epinephrine. Only moderate to severe asthma requires the use of oral corticosteroids, and systemic steroids should not be administered in place of high doses of inhaled steroids. Only after the other initial treatment fails to work will the usage of Mgso4 in severe asthma show results. Since the asthma in children is common and life threatening, the appropriate dose and right drug should be preferred for the treatment. Alternative treatment should be followed only if the initial treatment is unresponsive. However implementation of standard asthma guidelines will prevent the co morbidities and complications. And more research needs to be done regarding the disease and drugs [8].

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