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The Effectiveness of Combining Ipratropium Bromide and Salbutamol for the Treatment of Acute Severe Exacerbation of Asthma in Children: A Literature Review

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Author's contribution

The sole author designed, analyzed, interpreted and prepared the manuscript.

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Review Article

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ABSTRACT

The most common symptoms of asthma include episodes of wheezing, shortness of breath, and cough. When a person develops asthma in their childhood, it is usually seen to arise as a consequence of hay fever or allergic rhinitis and eczema, or atopic dermatitis. Maternal factors during the prenatal period have been found to be responsible to some extent in some infants, however, the role of breastfeeding and other nutritional allergies as the causes of asthma stands out to be unclear and controversial. The maintenance therapy of asthma in children comprises the following options, which are recommended to be used symptom-wise and only after keeping all the safety guidelines in mind. The combination therapy has been found to be very useful in treating asthma and reducing the complications that arise due to it.

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1. INTRODUCTION

Asthma is one of the most common respiratory illnesses prevalent worldwide. It is a chronic inflammatory disease of the airways, in which the air passages are inflamed and thus, narrowed. This inflammation of the air passages occurs due to bronchospasm, edema, and the resultant increased production of mucus, which manifests in the form of various symptoms in the affected patients. Usually, asthma is found to begin in the early years of a person's life, that is when they get exposed to allergens or triggers that cause their airways to get compromised [1].

The most common symptoms of asthma include episodes of wheezing, shortness of breath, and cough. When a person develops asthma in their childhood, it is usually seen to arise as a consequence of hay fever or allergic rhinitis and eczema, or atopic dermatitis [2].

Currently, there are about 260 million people all over the world that suffer from asthma. This was calculated from a study that was carried out in 2019 and concluded that the prevalence estimates of asthma were in the upgoing trend, with a current trend of about 11.95% at that time [3].

Although adults and children are both seen to be affected with asthma, this condition mainly develops in the childhood of an individual, thus proving that exposure to a particular allergen or trigger at that very young age makes them vulnerable to becoming sensitized to it.

There is no particular cause behind the pathogenesis of asthma, although it has been found that both genetic and environmental factors affect a person equally. In children, another important cause that has been found to be the culprit is maternal smoking. Expectant mothers, who continue smoking during the prenatal period are found to give birth to children who have increased sensitivity to cigarette smoke and at the same time, are predisposed to develop episodes of wheezing. This ultimately increases the chances of developing asthma in such children [4].

Other factors that contribute to the development of asthma in children are delivery through cesarean section, maternal stress, the exaggerated use of antibiotics, and poor maternal nutritional intake. All in all, whatever the mother goes through during her pregnancy ultimately reflects in one way or the other in the child once they are born.

According to the CDC, approximately 8.5% of children suffer from asthma in the United States alone. This equals up to 6 million children in the United States. Nowadays, the trend of asthma is seen to increase in children, with its acute exacerbations or acute episodes as one of the leading reasons behind children missing school [5].

As far as the predominance factor of asthma is concerned, it was found that before puberty, males are affected more than females. The severity of asthma was also found to be higher in boys at this stage, to the point that it garnered admissions in the hospitals.

However, the opposite case was seen in the post-pubertal or adolescent phase, where it was also seen that the severity of asthmatic attacks decreased significantly. It has also been found through studies that adolescent children in African American and Hispanic states are more likely to suffer from hospitalizations, severe acute episodes, and an increased prevalence in the occurrence of asthma as compared to other Americans [3].

2. CAUSES AND DIAGNOSIS OF ASTHMA IN CHILDREN

Even in today's modern world, asthma has been labeled as one of the leading, chronic respiratory diseases affecting children in their primary years. Although it is clear that asthma is a multifactorial disease and does not arise due to a single cause, it is still unclear as to what factors possibly play their role in developing this condition.

Maternal factors during the prenatal period have been found to be responsible ot some extent in some infants, however, the role of breastfeeding and other nutritional allergies as the causes of asthma stands out to be unclear and controversial [6].

Family history is another factor that has been found to be responsible for the development of asthma and so, an increased family size has been proposed as a risk factor for the development of asthma, as there are various secondary factors such as lifestyle and habits of

the family members attached to it, that could give rise to asthma. The same applies to a poor socioeconomic status among the affected families as their modes of living might in themselves be responsible for exposing the individuals to various allergens [7].

Respiratory Syncytial Virus (RSV) and other viral infections were also found to be responsible for the development of asthma.

Although asthma has a high morbidity rate, its mortality rates are found to be low, mainly because it decreases in intensity as the child grows older. However, this does not deny the existence of life-threatening, severe asthmatic attacks that some children might experience.

According to the National Review of Asthma Deaths (NRAD) carried out in 2014, it was concluded that of all the children that died of asthma or its complications, there were several deaths that could have been avoided had their causative factors been caught within time [8].

In all the cases of asthma, misdiagnosis is a major issue. It could lead to both over and underdiagnosis and in both the citations, the situation spans out unfavorably for the children as starting the treatment in any case could also lead to them experiencing the side effects of these drugs in the long term.

As far as the gold standard diagnostic test for asthma is concerned, there is not a single test that falls in this category. Therefore, the diagnosis of asthma is based on several characteristics and these include the presentation of symptoms in the child, the variability pattern of airflow limitation present in the airways, and the response to whatever treatment is given. These factors help in diagnosing asthma in the majority if not all the suspected children [9].

However, now, lung function tests (LFTs) are also reliable for helping diagnose asthma in patients. Spirometry and peak expiratory flow (PEF) tests are found to be reliable when testing for asthma in children, above the age of 5 years. The latter (PEF) is also found to be useful in testing out the diurnal pattern that is characteristically seen with asthma, whereas lung function tests (LFTs) are seen to be periodically used in children with asthma to look for any progressive signs or symptoms or signs of resolution. In school-aged children who suffer mainly from eosinophilic asthma, the Fractional Exhaled Nitric Oxide (FeNO) test was also found to be of fundamental value when used for diagnosing asthma [10].

3. METHODOLOGY

For this literature review, the search engines and research journals used were Google Scholar, PubMed, NCBI, Frontier's, Hindawi, ResearchGate, among others. A total of about 80-100 research papers were reviewed and useful information was extracted from them to authenticate the information used in this review.

3.1 Management Protocols in Children with Asthma

Pharmacological therapy is the mainstay of treatment in all patients with asthma. Over-the-counter medications do little to nothing to help with asthma and therefore, it is required for physicians to prescribe either a maintenance therapy or reliever therapy for the management of asthma and its acute attacks, whatever is needed at that particular time [11].

For the purpose of convenience, it is better to understand the treatment protocols of asthma by dividing them into these main divisions - maintenance and reliever therapy.

3.2 Maintenance Therapy for Asthma in Children

The maintenance therapy of asthma in children comprises the following options, which are recommended to be used symptom-wise and only after keeping all the safety guidelines in mind.

3.2.1 Inhaled corticosteroids

These inhaled corticosteroids are recommended as the first line of treatment for asthma in children. However, in all the guidelines that recommend this as the first line of treatment, it has also been said that the dosing should start with the lowest possible dose to minimize the chances of any side effects that may arise with its usage. Moreover, inhaled corticosteroids are also the preferred choice of treatment in children with persistent asthma [12].

3.2.2 Long-Acting Beta Agonist (LABA)

The option of using LABA as the preferred treatment option for maintenance therapy in asthmatic children arises when other treatment modalities namely inhaled corticosteroids and short-acting beta-agonists fail to suppress the symptoms. Since they are long-acting in nature, they have been found to delay or prolong bronchodilation by up to 12 hours [13].

3.2.3 Leukotriene receptor antagonists

In some children with persistent asthma, even if inhaled corticosteroids or LABA are showing little to no effect, these leukotriene receptor antagonists such as Montelukast are recommended as an add-on therapy. This is the third line of treatment and so, only recommended for persistent or poorly controlled symptoms.

3.3 Reliever Therapy for Asthma in Children

Reliever therapy refers to those modes of treatment that are used for relieving acute exacerbations of asthma or acute asthmatic attacks that may arise spontaneously, without any prior symptoms or warning signs.

In patients who are diagnosed with asthma, it has been recommended that reliever therapy that has been prescribed to them should be kept within their reach at all times so as to prevent any life-threatening conditions.

In children, there are two popularly used pharmaceutical agents that are used as reliever therapy:

3.3.1 Short-Acting Beta Agonists (SABA)

Short-acting beta-agonists are safe and effective and have been labeled as the first line of treatment in many guidelines. They provide a rapid mode of action and quickly relax the smooth muscles of the airways, thereby providing a bronchodilation action for up to 4 hours.

However, there are some limitations to using SABA - they are either delivered through a hand-held spacer device or delivered via supplemental oxygen through a nebulizer machine.

The mechanism of action in both situations remains the same, although the time taken to achieve the action is different in both ways [14].

3.3.2 Oral corticosteroids

Although not exactly recommended as a first-line of treatment, oral corticosteroids are used for the rapid relief of symptoms from an acute asthma attack. However, their long-term usage might lead to poor symptom control and thus, they may turn out to be ineffective in the long term. For these reasons, their usage is usually prevented in children with asthma.

4. USING IPRATROPIUM BROMIDE AND SALBUTAMOL IN COMBINATION TO PREVENT ACUTE EXACERBATIONS OF ASTHMA IN CHILDREN

In cases where monotherapy does not work out or fails to provide effective symptom control, it is seen that combination therapy is usually prescribed. These combination therapies vary in their existence, and different combinations have been used for providing symptom relief to patients [15].

In the previous section, it has been discussed how Salbutamol or short-acting beta-agonists (SABAs) are recommended as the first line of reliever therapy in patients with acute asthma attacks. However, in some of the recent guidelines, it has been directed that the usage of Salbutamol alone is not as effective as it was considered in its initial days. Moreover, it is also related to the risk of developing asthma-related fatalities and so, should no longer be used as a monotherapy in both adolescents and older adults. In its place, it has been proposed that a short-acting muscarinic acetylcholine-receptor blocker called ‘Ipratropium Bromide’ (IB) could be used instead. This combination therapy has been reserved for treatment only in acute exacerbations of asthma, as it helps control its extreme symptoms. There is no role of Ipratropium alone in providing symptom relief, but the role of both the medicines being used together in combination [16].

All the studies that were carried out to test the effectiveness of Slabultamol and Ipratropium bromide have shown that their combination is very effective. It has helped several patients in improving their peak expiratory flow rate (PEF), while also helping reduce the number of hospital admissions that occur as a consequence of acute asthma attacks. These effects were better than the effects of Salbutamol (SABA) alone when used as a monotherapy regime [17].

However, there is still a lot to explore on this topic since it was only a primary-level study. More studies on the long-term usage and the variations of effects seen when tested out in different circumstances such as in different ages and for different time durations would further help in elaborating the role of either of these pharmaceutical agents.

This was indeed a good effect seen that Salbutamol and Ipratropium bromide helps in reducing the incidence of acute asthma attacks, however, the same combination therapy did not show much effect when dealing with side effects such as vomiting, tremors, and dry mouth that also occur as a consequence of acute asthma attacks.

However, it is only a matter of time until more research gets done on the subject, and would then help in deciding whether this combination therapy this indeed safe to be used in all age groups with asthma [18].

5. CONCLUSION

Asthma is one of the leading chronic respiratory illnesses that affect millions of people worldwide. It is found to have a multifactorial etiology, with genetics and environment both playing a leading role in its development.

There are several treatment regimens that are used for the prevention and control of asthma, however using short-acting beta-agonists (SABAs) and inhaled corticosteroids are the most preferred ones worldwide as they help in rapidly reversing the acute cases of asthmatic attacks. Recently, there have been some studies found that propose using SABAs and Ipratropium bromide together for maximizing the beneficial effects of either of them alone. So far, this combination therapy has been found to be very useful in treating asthma and reducing the complications that arise due to it. However, more research is needed to expand the topic and introduce this treatment combination on a large-scale, only if found to be very effective and safe for all the people using it.

CONSENT AND ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Author has declared that no competing interests exist.

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