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A Review on Evolution and uses of inhaled corticosteroid for the management of asthma

Govind Upadhyay, Divyansh Kateja, Pushparghya Pal, Mohd Hanief, Dr. Mekha Monsi Chenthiyethu

1234 Pharm D NIMS Institute of Pharmacy NIMS UNIVERSITY RAJASTHAN
Assistant Professor Dept of Pharmacy Practice NIMS Institute of Pharmacy NIMS UNIVERSITY RAJASTHAN

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ABSTRACT
Asthma is an obstructive airway disease that affects millions of people worldwide. It is a complicated disorder where genetics and environment interact and where numerous inflammatory cells release a variety of mediators. Inhalation of inhaled corticosteroids is a common medication used to treat asthma. This medication is often used on a consistent basis to help treat inflammation. The use of corticoids to treat asthma has significantly increased during the last few decades. In this paper, we will discuss the evolution and use of the beta-2 adrenergic receptor agonist as a valuable agent in managing respiratory diseases and COPD. This activity will highlight the mechanism of action, adverse effects, current topics of discussion, and different key factors (e.g., tolerance, pharmacology, and pharmacodynamics) relevant for inter professional team members within the care of patients with respiratory disease, COPD, and connected conditions.

Keywords:- Asthama, COPD, Salbutamol, Corticosteroids, antimuscarinic agents,

I. INTRODUCTION

The word asthma was used in ancient Greek probably meant noisy breathing today to describe asthma, a particular kind of an obstructive airway disease [2]. Asthma is a chronic respiratory disease that affects people all over the world. According to WHO asthma will affect an estimated 262 million population in 2019 and cause 45500 deaths. Air containing oxygen goes through your mouth or nose and travels down in your airways at the end of airways, the airfield with small sacs called alveoli. A large number of inflammatory cells that release a diverse variety of mediators are involved in the complex condition of asthma, which results from the combination of heredity and environment. By acting on the cells in the airway, these mediators generate rapid muscle contraction, hyperactive secretion, plasma outflow, edoema, activation of cholinergic reflexes, and stimulation of sensory nerves, which intensify the ongoing inflammatory response [2, 15]. The chronic inflammation results in structural changes, together with sub-epithelial pathology and swish muscle hypertrophy and dysplasia.

1.1 Pathophysiology

Asthma is divided into three main immunopathological phenotypes: WBC, neutrophilic, and paucigranulocytic lymphocytes Increased WBC infiltration of the airways characterizes the WBC makeup [11]. Patients are frequently discussed. Asthma attacks are triggered by allergens and typically respond well to corticosteroids [14, 3]. Increased neutrophilic infiltration of the airways characterizes the neutrophilic makeup. Patients frequently experience severe, aggressive, and poorly controlled asthma attacks. Furthermore, they typically do not respond to corticosteroids because of the WBC kind. Within the paucigranulocytic makeup, cartilaginous tube neutrophils and eosinophils are abundant lower. Allergens including pollen, animal dander, dust mites, and mold; viral respiratory tract infections; irritants such as smoke and dust; cold air and exercise trigger asthmatic patients.

1.2. History of Treatment of Acute Asthma

There may have been multiple "asthmas" in the early 1800s because the term "asthma" was used to describe any episode of shortness of breath [11, 3]. The doctor had to take care that the first cause was not an infectious disease or an internal organ disease (e.g., mitral stenosis); each was quite common at the time. Once a designation of respiratory disorder (as we all know it now) was established, the quantity of effective treatments was quite limited; inhalation of smoke from burning jimson weed was most likely the simplest. This

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agent had anticholinergic properties and was the forerunner of the currently used antimuscarinic agents like ipratropium and tiotropium [9]. There have been various different treatments, like inhalation of the fumes of hydrocyanic acid or inflation of the lungs with a bellows. Luckily, such treatments and lots of others that made no profit and doubtless caused harm are no longer used. 7

In the eighth edition of the Principles and Practice of Medicine, published in 1914, Osler (8) states that hypodermic injections of alkaloid will be effective in the treatment of bronchial asthma. He additionally claims that the sedative antispasmodics, like belladonna, "may be run in resolution or employed in the shape of cigarettes [4, 11]. Nearly all the popular remedies, either of this type or in pastilles, contain some plant of the potato family... Wonderful cigarettes are currently factory-made and asthmatics strive for varied types since one type advantages one patient, another type another patient. Thus, in 1914, anticholinergics by injection or inhalation were thought of as first-line bronchial asthma therapies. Additionally, Osler additionally created the vital observation of the intraindividual variations within the response to bronchial asthma treatment. We have a tendency to currently appreciate that these variations might replicate genetic variations within the mechanisms resulting in the unhealthy response among subjects. In the 1927 edition of Cecil's A Textbook of Drugs, Francis Rackemann once more suggests the employment of the smoke of stramonium leaves, atropine, and belladonna. In the seventh edition of Cecil's A Textbook of Drugs, published in 1947, Rackemann (10) still suggests the employment of respiratory disease, respiratory illness, respiratory disorder powders or asthma cigarettes with the active ingredient consisting of belladonna-type alkaloids. However, by 1975, once the ordinary edition of the textbook was revealed, belladonna alkaloids weren't thought to be a major enough part of asthma attack treatment to be enclosed by J.B.L. Howell. Between 1928 and 2012, our understanding of respiratory illness underwent three major shifts. First, spirometry, which had been developed within the decade, was refined by adding time to volume output, and measurements of forced exhalations were used in the diagnosis and treatment of respiratory illness between the late 1940s and early 1950s. 14 different lung-function tests were developed and used, elucidating the links between clinical physiology and symptoms. 15 Second, glucocorticoids were recognized as an effective and beneficial treatment for respiratory illnesses. They were first used systemically in the early 1950s16 and were later made available in inhaled form1. These agents continue to improve patient care today. Third, we have gained a better understanding of the immunobiology of respiratory illness. On the other hand, it was discovered that the primary mechanism was an on-the-spot hypersensitivity. Unfortunately, advances in understanding the cell biology of respiratory illness have not yet been translated into new therapies, even though new therapies are derived from our improved understanding of immediate hypersensitivity responses — specifically, the use of leukotriene modifiers21 and anti-IgE antibodies [19]. Our patient is up-to-date on her medical information and is using online medical data to help her manage her chronic condition. The authorities quantified her physiological deficit using measures of respiratory organ function. The authorities also measured the patient's immune globulin level, which was consistent with allergic respiratory illness, and provided the information needed for anti-IgE treatment, if the patient chose this option. The patient has exhausted all quality respiratory illness therapies but still has symptoms. The author outlines various respiratory illness treatments that the patient may try and emphasizes the need to try a variety of treatments to see if one or more will work. Unfortunately, we still do not have any way to predict a given patient's response to medical care.

LEVELS OF ASTHMA

There are four levels of asthma based on how severity it is

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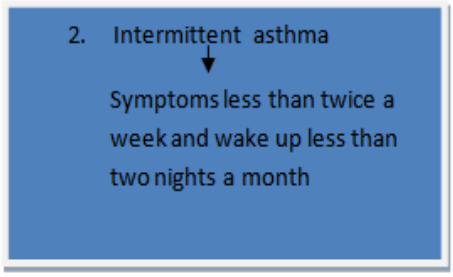

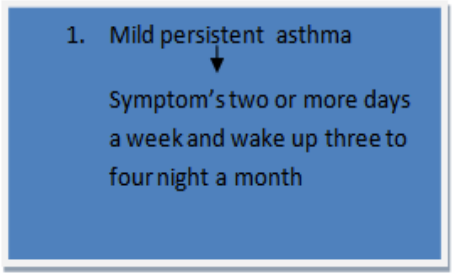

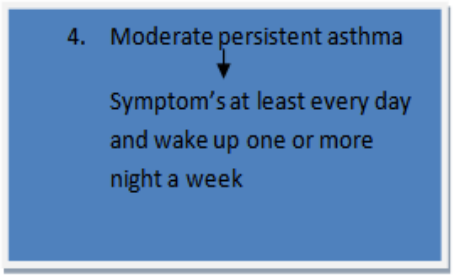

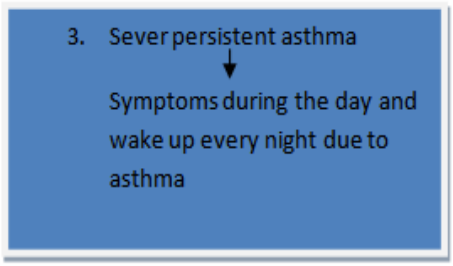

When you have asthma, it's important to know what is happening in your airways, as well as common asthma symptoms. Understanding asthma symptoms can help you know what your triggers are, when you need quick-relief ("rescue") medicines, and when you are having a medical emergency. There are three changes in your airways when you have asthma:

1. Swelling inside the airways
2. Excess mucus clogs the airways
3. Muscles tighten and squeeze around the airways

This swelling, clogging, and muscle tightening makes your airways smaller or narrower. This makes it harder for air to flow easily through your airways, and it becomes harder to breathe [5, 6]. This causes asthma symptoms, also known as an asthma episode, flare-up, or attack**.** It can happen at any time. While more severe asthma symptoms might last hours or days, milder symptoms may just last a few minutes.

It becomes unpleasant and challenging to breathe, like trying to do so through a straw filled with cotton.

Methodology

Asthma is characterized by the chronic airway inflammation and increase airway hyper responsive leading to wheeze, cough and dyspnoea [1]. Pharmacological treatment steps:-

Step 1:- occasional use of short acting beta 2 adrenoreceptor agonist. This medication is used for the patient with mild intermittent asthma (symptoms Symptom's less then twice a week and wake up less then two night a month)

Step2:- regular preventer therapy is regular inhaled corticosteroids (ICS) are used for any patient who experience exacerbation in last 2 years. Uses inhaled beta 2 agonist >3 times /week report symptoms >3 times/week or is awakened by asthma1 night/ week.

Step3 – Add- on therapy: If poor control remains despite regular ICS add-on therapy should be considered long acting beta 2 agonist (LABAs, e.g., salmeterol, formoterol) are first choice, and combination ICS/LABA inhalers may increase compliance[18,19]. LABAs have consistently been demonstrated to improve asthma control and reduce exacerbations. Compared to increase doses of ICS alone. Leukotriene receptor antagonists (e.g. montelukast 10 mg daily) are ales effective add-on therapy

Step 4 –poor control on moderate dose of inhaled steroid and add-on therapy: The ICS dose may be increased to 2000µg BDP or equivalent daily. A nasal corticosteroid should be used if upper airway symptom is prominent.

Step 5 –continuous or frequent use of oral steroids. Patients receiving more than three or four course/yr or long term corticosteroid (>3 mths) are at risk of systemic side effects. Osteoporosis should be prevented using bisphosphonates. In atopic patient, omalizumab, a monoclonal antiIgE antibody, may help to limit steroid dose and improve symptoms.

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Step-down therapy: once asthma control is established, inhaled (or oral) corticosteroid should be titrated to the lowest doses at which effective control of asthma is maintained [19]. Beta-2 adrenergic receptor agonist's are a category of medicines utilized in the frontline management and treatment of respiratory disease and COPD. This activity outlines the importance, action, and current problems with concern for the beta-2 agonist as a valuable agent in managing respiratory disease and COPD. This activity can highlight the mechanism of action, adverse effects, current topics of discussion, and different key factors (e.g., tolerance, pharmacology, and pharmacodynamics) relevant for interprofessional team members within the care of patients with respiratory disease, COPD, and connected conditions [4].

Activation of β adrenergic receptors leads to relaxation of smooth muscle in the lung, and dilation and opening of the airways.

Mechanism of action

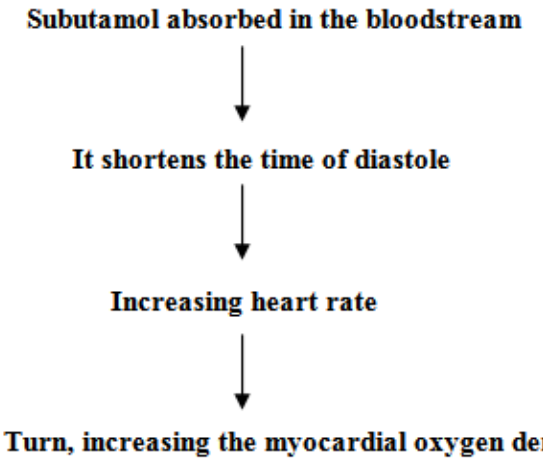
Adrenergic receptors are coupled to a stimulatory G protein of adenylyl cyclase. This enzyme produces the second messenger, cyclic adenosine monophosphate (cAMP). In the lung, cAMP decreases calcium concentrations within cells and activates protein kinase A. Both of these changes inactivate myosin light-chain kinase and activate myosin light-chain phosphatase. In addition, 2 agonists open large conductance calcium-activated potassium channels and thereby tend to hyperpolarize smooth muscle cells in the airways. The combination of decreased intracellular calcium, increased membrane potassium conductance, and decreased myosin light chain kinase activity leads to smooth muscle relaxation and bronchodilation.

Effect of Inhaled Salbutamol on Heart Rate in Healthy Volunteers:

Tachycardia is a potential side effect of salbutamol inhalation. Salbutamol nebulization, even at a low dose, can lead to a significant increase in heart rate.5

Mechanism of action:

Salbutamol causes an increase in the heart rate by the following propositioned mechanisms:



Second, it acts on beta-adrenergic receptors of the heart, resulting in an increased sympathetic outflow.

Inhaled corticosteroid

Inhaled corticosteroids are a type of medication that is often used to treat patients with asthma and COPD. Glucocorticoids are lipid-soluble drugs that provide anti-inflammatory effects on the airways. Considered maintenance or controller medications because they work by decreasing inflammation seen in obstructive diseases. They should not be used during an acute attack or exacerbation because they do not provide immediate relief. (e.g., budesonide, ciclesonide, beclomethasone, flunisolide hemihydrates, fluticasone propionate, fluticasone furoate)

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Mechanism of action

The cytoplasmic steroid receptor is where glucocorticoids bind.The complex with the receptor is transferred from the cytoplasm to the nucleus and binds to DNA there. inducing the synthesis of specific mRNA that exhibits anti-inflammatory activity through the synthesis of several proteins that help to decrease the formation of cytokines. Inhibit PG synthesis, induce lipocortin, increase the activity of LK and PAF synthesis, reduce eosinophil influx into the lungs and thus suppress the release of inflammatory mediators, and decreasing the important IL-3 synthesis in the respiratory tract.

Anti-inflammatory effect of corticosteroid in asthma:

It reduces the inflammation by decreasing the eosinophil number and increasing the apoptosis of eosinophils [24]. It decreases the cytokine release from T lymphocytes, decreases the activity of mast cell numbers, and decreases the cytokine release from macrophages; it also decreases the dendritic cell numbers, which contain antigen. It has structural cells in the respiratory track; it decreases cytokine and other inflammatory mediators' release from epithelial cells, decreases plasma leak from the endothelial cells, decreases the cytokine and increases the beta 2 receptor numbers so bronco relaxation can occur, and it also decreases the mucus secretion from mucus glands [25].

Inhaled Corticosteroids and the Risks of Diabetes:

The use of inhaled corticosteroids is associated with a significant 34% increase in the risk of incident diabetes, defined as the initiation of anti-diabetic medications, in a large population-based cohort of asthma and COPD patients [12, 20]. Higher doses of inhaled corticosteroids increased the risk, with 1000 g of fluticasone per day or equivalent associated with a 64% increase in risk. Furthermore, we discovered that in patients already receiving oral hypoglycemic agents for diabetes, the risk of progression to insulin increased by 34% with the use of inhaled corticosteroids, with higher doses associated with a 54% increase in this risk [10, 26].

Common myth considered corticosteroids:

Inhaled corticosteroids are a common medication used to treat asthma. Inhaled corticosteroids are often used on a consistent basis to help treat inflammation. This medication is extremely effective. when used with the proper dose and technique. However, there are many misconceptions regarding steroids. When used properly, inhaled steroids reach the lungs [23]. With very minimal side effects throughout the rest of the body. There are very different effects when seen in the mouth versus through an intravenous. In this case, the steroid concentration is very high. There are a few common misconceptions regarding corticosteroids. Inhaled corticosteroids are most effective when used every single day, often twice a day. Even this symptom was not present. Many people have misconceptions about the side effects associated with steroid use. As big muscles weigh more, irritation of the stomach, and cataracts, they simply do not occur with a proper dose of inhaled corticosteroid. in proper technique. The most common side effect is local deposition of medication inhaled through the mouth or throat. Use a spacer device to avoid local deposition of medication [27].

Respiratory tolerance is inhibited by the administration of corticosteroids.

Respiratory tolerance is extremely effective at preventing airway inflammation, and it is thought to limit immune responses to the large amounts of innocuous Ags that enter the lungs suspended in inspired air. We discovered that dexamethasone treatment prevented the development of respiratory tolerance, allowing Ag-specific T cell proliferation and cytokine secretion, as well as AHR, to develop [21, 22]. Dexamethasone also inhibited IL-10 production in DCs from the lungs of tolerized mice, as well as their ability to transfer tolerance and induce the development of Ag-specific TReg cells. Thus, while corticosteroids can reduce acute allergy inflammation, they may also impede the development of respiratory tolerance, an immune response that regulates Th2-driven allergic pulmonary inflammation.

II. DISCUSSION

Inhaled corticosteroids are a common medication used to treat asthma. Inhaled corticosteroids are often used on a consistent basis to help treat inflammation. This medication is extremely effective. when used with the proper dose and technique. However, there are many misconceptions regarding steroids. When used properly, inhaled steroids reach the lungs [23]. With very minimal side effects throughout the rest of the body. There are very different effects when

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seen in the mouth versus through an intravenous. In this case, the steroid concentration is very high. There are a few common misconceptions regarding corticosteroids. A large population-based cohort of individuals with asthma and COPD who take inhaled corticosteroids has a significant 34% increased risk of incident diabetes, which is defined as the start of anti-diabetic drugs.

III. CONCLUSION

Asthma is characterized by chronic airway inflammation and increased airway responsiveness, leading to wheezing, coughing, and dyspnea. Asthma can be treated with a short-acting beta-2 adrenoreceptor agonist or a combination of ICS and LABA inhalers. Beta-2 adrenergic receptor agonists are a category of medicines utilized in the frontline management and treatment of respiratory disease and COPD. The smooth muscle of the lung relaxes as well as the airways widen and open as a result of the activation of beta-adrenergic receptors. Patients with asthma and COPD frequently use inhaled corticosteroids as a form of treatment. Glucocorticoids are lipid-soluble drugs that provide anti-inflammatory effects on the airways. They act on beta-adrenergic receptors in the heart, resulting in an increased sympathetic outflow. Corticosteroids are medications used to control inflammation seen in obstructive diseases such as asthma. They should not be used during an acute attack or exacerbation because they do not provide immediate relief. Glucocorticoids inhibit PG synthesis, induce lipocortin, increase activity of LK and PAF, reduce eosinophil influx into the lungs, and thus suppress the release of inflammatory mediators. Inhaled corticosteroids are a common medication used to treat asthma and COPD. When used properly, inhaled steroids reach the lungs with minimal side effects throughout the rest of the body. The most common side effect is local deposition of medication inhaled through the mouth or throat.

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