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RESEARCH ARTICLE

Novel Therapeutic Approaches to a Chronic Inflammatory Disorder - Asthma

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ABSTRACT

Asthma is a chronic inflammatory disease of respiratory tract that attacks more than 300 million people all over the world. It is gradually identified that larger percentage of patients suffering from asthma persists terribly governed with severe exacerbations inspite of giving conventional treatments by inhaled corticosteroids or even by various other agents. The evolution of various therapies and therapeutic agents has shown a greater response in treating severe asthma. This review focuses upon the various proceeding therapeutic approaches in treating this chronic inflammatory airway disease. Asthma is a respiratory disease that causes the uncertain and reversible obstruction of airflow and may also cause bronchospasm. The symptoms in the patient may include continuous coughing, breathing audibly, pain in the chest, difficulty in breathing. This chronic disease is a union of various environmental and genetic factors. This may also become chronic in young children and infants. This may be due to the background of pneumonia, bronchitis or diligent cough along with cold. The pathophysiology of asthma is a complicated one and involves the inflammation in the airways, obstruction of airflow, hyper responsiveness of bronchi etc. Diagnosis may include Spirometry accompanied by post bronchodilating response as the main test for confirmation of asthma. Other test may also include radiography of chests etc., which may help in the detection of severe symptoms of asthma. The therapeutic approach may include Anti-IgE therapy, Anti IL-5 therapy, thermal bronchoplasty, Antifungal therapy etc. These are considered to be the novel therapies in the treatment of asthma. The present study based on providing better therapies in the treatment of chronic disorder, Asthma.

KEYWORDS

Chronic, Inhaled Corticosteroids, Bronchospasm, Spirometry, Anti IL-5 Therapy

INTRODUCTION

Asthma is a chronic or long term inflammatory disorder of respiratory system. This inflammation is a base and elevates the hyper responsiveness of the airways which may ultimately promote repetitive or periodic wheezing, which is the breathing out audibly (usually during expiratory breathing), acute pain in the chest, shortness of breath or feeling difficulty while breathing, tightness of the chest etc.

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This may be due to the obstruction or blockage of airflow in the respiratory tract.[1] It was estimated that more than 300 million people all over the world and also around 7 million children become the victims of this chronic inflammatory disorder.[2] Asthma is usually of two types, they are Atopic asthma and Anatopic asthma.[3]

Every year in UK, around 1,200 people die because of Asthma attack. Despite of making people aware about the disorder, this rate of deaths has persisted since many years.[1] Many patients suffering from asthma, attain better control of disease which are the cornerstone of

the disorder is the use of inhaled corticosteroids and long- acting β_2 adrenoceptor agonists (LABAs). But however the use of these therapies has shown unsuccessful results in patients and could not prevent the severe exacerbations. There are various causes due to which these conventional therapies are not working out for providing the safety and efficacy to the patient.[4]

Pathophysiology of Asthma

The pathophysiology of asthma is a complicated one. Asthma is generally conciliated by IgE (immunoglobulin-E) response and also this is triggered by the hypersensitive or allergic responses due to various environmental factors. These IgE are established with response to subjection of allergens in the air through pollen or any other source. The sensitization reaction arise during the initial exposure to the allergens that give rise to IgE antibodies that are specific to allergens and may get attached to the mast cell surface.

The emancipation of mediators of inflammation such as leukotrienes, prostaglandins, histamine etc. takes place when the successive exposure occurs and the allergen attaches to exterior of the mast cells which contains IgE antibodies specific to allergens. The activation of asthmatic attack is due to these mediators which are inflammatory and may also originate bronchospasm. The eosinophils, mast cells and T-helper cells wander into the airways if this infection or inflammation which causes asthma is not treated.[6]

The pathophysiology of this chronic inflammation may be explained by the following-

- Asthma- that affect the airways.
- Damage to the Epithelium.
- Excessive secretion of Mucus.
- Swelling or Edema.
- Spasm of the bronchi.
- Remodeling or the variation in the airways.

Asthma- that Affects the Airways

The parts of the lower respiratory tract which constitutes the trachea, bronchi and the bronchioles may get affected by this chronic inflammation-Asthma. It causes the constriction of bronchi and airways that get narrowed abnormally which may result in further pathophysiological conditions.

Damage to the Epithelium

The epithelial layer may get destructed or damaged. This may lead to the hyper responsiveness of airways and may ultimately cause the deprivation of the function of epithelium as a barrier.

This kind of airway hyper responsiveness may permit the entry of allergens, sensory nerve exposure that causes severe neural effects on the airways and the enzyme depletion which may help in breaking the mediators of inflammation in the disorder.

Excessive Secretion of Mucus

The mucus cells rapidly proliferate and grow and the glands of the mucus enlarge in Asthma. This may cause the excessive secretion of mucus and results in the emergence of plugs of mucus that obstructs the airways.

Swelling or Edema

This may occur when the dilation and leakage of the capillaries in the walls of airways takes place. This results in the secretion of airways in higher proportions and swelling occurs which imparts diminishing of airways and also abnormal degree of responsiveness.

Spasm of the Bronchi

This is known as bronchospasm. The narrowing of airways occurs due to the degranulation of substances from various cells and may also cause damage to the muscles.[3]

Remodeling or the Variation in the Airways

Asthma, if not controlled or prevented at certain level, there is affirmation that remodeling of airways may occur.[7]

Risk Factors or Causes of Asthma

Various factors including the environmental and the genetic factors accounts for the cause of Asthma.

- Premature birth
- Family Background of asthma.
- Tobacco smoke or if the women smokes during pregnancy
- Getting exposed to various toxic chemicals, industrial substances or plastics.
- Infants fed with soya based milk feeds.[8]
- Childhood bronchiolitis and children if exposed to Para influenza virus may show symptoms of breathing audibly and also illness.[6]

Few drugs may also precipitate the attack of asthma.[9] In most of the asthmatic patients, acute asthma is induced by the frequently used sanitizers like Sulfites and Sulfur dioxide.[10]

Prepubertal boys are more likely to get affected by the attack of asthma. Girls are likely to develop asthma during adolescence period. The way an individual acknowledges to the treatment is dependent upon the phenotype of that particular individual or patient.[11]

Signs and Symptoms Observed In Attack of Asthma

The signs and symptoms in asthma may become more and more severe and in many conditions it becomes fatal.

This includes the following symptoms

- Breathing out louder due to constriction of bronchi
- Shortness of breath,
- Coughing, because the airways which contain sensory nerves get stimulated.
- Tightness of the chest or pain in the chest, etc.[1]

Clinical Features of Asthma

The attack of asthma in an individual is triggered by various factors. These factors for the cause may differ in every individual having asthmatic attack. Few triggers that may lead to attack of asthma are as follows.

Clinical Features in which Asthma may likely to Attack are

- Hot or cold air exposure
- Due to the spread of allergens.
- Due to the use of few drugs like NSAID's
- Cold in common.
- Family background of asthma.
- A silent wheeze is heard on auscultation.
- Forced Expiratory Volume (FEV) becomes low in one second.
- Also due to various emotional feelings like anger, anxiety etc.[6]

When there are severe exacerbations in asthmatic attack, there is a severity in the blocking of airways and most of the common symptoms are not observed usually. Instead, other symptoms like feeling drowsiness, cyanosis or other emergency signs like the individual may not be able to speak easily due to the difficulty in breathing. These severe exacerbations are emergency cases in asthma.

Clinical Features in which the Extent of Attack of Asthma is lowered are

- Cardiac problems.
- Probable and continuous cough without difficulty in breathing that may be chronic at times.
- Dizziness.
- Disturbance in voice.
- Individual with the smoking history.
- Normal physical examination of chest.

Diagnosis for the Detection of Asthma

As it is known, that asthma is a result of various stimuli, the diagnosis and detection of this disorder can be done by few tests and this can be confirmed by the history of the patient and the response to corticosteroids and bronchodilators.

The skin testing is done so as to examine the presence of any stimuli of allergy. This monitors

the immune system and the IgE (Immunoglobulin-E) mediated reactions.

The obstruction of airways in asthma can be particularly evaluated by performing pulmonary function tests.

Individuals with greater and intermediate extent of asthmatic attack generally begin with the possible trials of the treatment and the outcome is evaluated by Spirometry. This spirometry has been proven to be the good detector of asthma attack which usually assesses the functioning of the lungs which may be further calculated by using the following parameters.

The ratio between the Forced Vital Capacity (FVC) and the Forced Expiratory Volume in one second (FEV_1) is taken to evaluate the functioning of lungs in asthma. This Spirometry test shows the probable accuracy among all the other tests for asthma.[1]

Other tests such as Peak expiratory flow, helps in the measurement of airway resistance.

Inhaled mannitol or methacholine, both of which are bronchospasm inducing drugs, are used in the diagnosis for the airway responsiveness evaluation. This type of test is usually done so as to distinguish asthma with other diseases that may be showing quite common symptoms as that of asthma and may be confusing. For example, diseases such as- rhinitis, failure of the heart, dysfunctioning of vocal cord etc.

Other tests which involves the eosinophils of sputum and the exhaled concentration of nitric acid (more than 25 ppb) i.e., the Non invasive testing is successfully used in the diagnosing asthma.[8]

The diagnosis of asthma is very essential to proceed for the probable management and treatment required based on the severity of the disorder.

Management or Control and a Novel Therapeutic Approach

Most of the people who are victims of asthma attack may not have control over their condition. Despite of many strategies applied by the researchers, asthma is still left uncontrolled due to various aspects.[11] Hence, to manage this, various control and therapeutic strategies have been developed.

- Rescue medicine is not needed
- Exercise or other physical activities are not limited.
- Lung functioning is normal.
- Few adverse effects from the drugs of medication.
- No exacerbations.[1]

The control of asthma is assessed periodically so as to achieve probable results. Apart from this various novel therapies have been designated recently in the management of asthma pharmacologically. Some of them are-

Corticosteroids

This has been considered effective in the treatment of asthma. The corticosteroids used in asthma treatment have anti-inflammatory effect.[13] Examples: Methylprednisolone, Hydrocortisone, Beclomethasone dipropionate (BDP), Triamcinolone acetonide (TAA) Flunisolide (FLN) etc.[14,15]

Anti Cholinergic Agents

Assessments have been made in the study of control of airways autonomically and the considerate advancement in the drug, Ipratromium bromide which is a derivative of atropine has shown therapeutic effect in asthma.[16]

Cromolyn Sodium (Disodium Cromoglycate)

This first line drug is very helpful in the control of chronic asthma. This drug does not show any bronchodilator effects and also is usually contraindicated when there is a severe attack of asthma.[17]

Theophylline

This drug helps widely in the safety and efficacy of the treatment and is prominently useful in the treatment of chronic asthma.[18]

Other drugs such as beta adrenergic receptor agonists (beta -2 is effective in asthma) also play

a very vital role in the treatment of acute asthma and also various other chronic diseases of airways.[19]

Also other novel therapeutic approaches such as Anti-IgE therapy, Anti IL-5 therapy, Thermal bronchoplasty, Antifungal therapy are widely used in the treatment of Asthma.[4]

Various Inhalation Devices also have proven the considerable therapeutic effect in asthma. Corticosteroids and beta agonists are usually administered through inhaled route. The drugs of bronchodilator administered through intermittent positive pressure breathing (IPPB), produced the similar effect than that of drugs administered through a nebulizer.[20]

CONCLUSION

As asthma is a widespread chronic inflammatory disorder which causes inflammation and obstruction of airways resulting in difficulty in breathing and sometimes also leading to fatal consequences, several attempts have been made in advancements of various therapies for treating severe exacerbations. However, the probability of various drugs and novel therapies has enhanced the control and management of the disorder. Furthermore, investigations are being carried out based on the safety, efficacy and economy of the drugs to manage severe consequences of this chronic disorder in foreseeable future.

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