

Review Article

BRONCHIAL ASTHMA AND ITS TREATMENT: A REVIEW

S.S. Bhandri*, M.P. Kabra, M.K. Vaishnav, R.B Gupta.

Department of Pharmacology, Kota College of Pharmacy, Kota (Rajasthan)

Corresponding Author's Email: bhandarisanjay001@gmail.com

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ABSTRACT

Bronchial Asthma is a chronic immunological disorder characterized by hyper-responsiveness to the bronchial smooth muscles to the various stimuli (Pollen, Gases, Chemicals etc.) resulting difficulty of breath. IgE immunoglobulin plays an important role in pathogenesis of Bronchial Asthma. Asthma has been traditionally divided into two basic types (Extrinsic Asthma, Intrinsic Asthma) according to the presence or absence of external precipitating factors. The principal aim of asthma treatment is to keep patient's symptom free and prevent deterioration in lung function. Sympathomimetic, Anti-cholinergic drugs, Methylxanthinederivatives and Corticosteroids are the principle drug category used in the treatment of Bronchial Asthma.

Key words: Bronchial Asthma, IgE immunoglobulin

BRONCHIAL ASTHMA:

The term asthma has been used clinically to refer to a disorder characterized by shortness of breath. It refers to a particular presentation of obstructive pulmonary disease with episodic wheezing and dyspnoea. The disease may begin at any time from early childhood until late adult life.

Asthma on a physiological basis as a condition with wide spread narrowing of the bronchial airways which changes its severity over short period of time either spontaneously or under treatment and is not due to cardiovascular disease. (**Ciba symposium, 1959**)

Asthma as a clinical syndrome characterized by increased responsiveness of the tracheobronchial tree to a variety of stimuli which is manifested physiologically by generalized airways obstruction which varies in severity over short periods of time either spontaneously or as a result of treatment and clinically by paroxysms of dyspnoea, wheeze and cough (**Thoracic Society(1987)**).

Asthma is common illness affecting around 5-10% of the total population in our country. Symptoms can appear at any age, but most commonly start in childhood till the age of

10 years and boys are affected twice as often as girls (Murthy, 1994).

CLASSIFICATION OF ASTHMA:

Asthma has been traditionally divided into two basic types according to the presence or absence of external precipitating factors.

1. Extrinsic asthma

a) Atopic asthma/ Allergic Asthma:

It is attributed to an immunologic response of the patient on exposure to an allergen, (a substance to which there is a specific hypersensitivity). It occurs in atopic subject who demonstrate immediate wheel and flare reaction it is due to type I (immediate) hypersensitivity reaction mediated by IgE. This type of asthma commonly starts in childhood and may resolve in early adult. There is often a family history of allergy like hay fever, asthma or eczema in the first degree relatives. Even the individual may give a history of infantile eczema, hay fever or rhinitis, increased serum IgE level and skin testing shows positive to several common allergens.

b) Non-Atopic asthma:

This asthma is noted in adults and environmental factors are active in its development. The constant exposure to a large amount of antigen is sufficient to

stimulate the appearance of antibodies. The antibodies combine with the inhaled allergens to form immune complexes, which fix and activate the complement and bring about type III reaction. The members of family may have asthma allergic rhinitis hay fever, urticaria and atopic dermatitis. The intracutaneous test gives late reaction to a single particular antigen to which they have been constantly exposed. A late reaction occurs 6 hours after bronchial challenge and it is associated with fever and leucocytosis. The response to bronchodilators is less satisfactory than type I asthma.

2. Intrinsic asthma

The intrinsic variety consists of patients in whom an extrinsic allergen can't be identified as the cause of symptoms. It occurs in middle aged adults. Often the attack may be precipitated from an episode of respiratory infection. The asthmatic attack may appear continuously. There may be a history of rhinitis, hyperplastic sinusitis or nasal polyposis.

Generally there is no family history of allergy, but it may exist probably by chance. Asthmatic attacks are not mediated through IgE though the same chemical mediators play a role. The skin tests show absence of immediate hypersensitivity to common

allergens and blood level of IgE not elevated. The condition shows less response to bronchodilators and death may occur within few years of onset of Conditions.

ETIOLOGY OF ASTHMA

Asthma includes a heterogeneous group of patients and attempts are made to find out a common denominator situations such as chronic inflammation of the airways, Allergy and psychogenic factors. But the unique common denominator has been shown to be hyper-reactive airways which manifest with variable airways obstruction (**Juniper et al, 1981**). It occurs in response to a wide variety of endogenous and exogenous stimuli. Variety of stimuli can precipitate an attack of asthma:

- 1) Air pollutants
- 2) Allergens
- 3) Bronchopulmonary aspergillosis
- 4) Emotional stress, happy and sad events
- 5) Exercise
- 6) Irritative dusts and fumes.
- 7) Menstruation
- 8) Occupational exposure
- 9) Oesophageal reflex
- 10) Sinus disease
- 11) Sleep
- 12) Food additives and preservatives
(Tartrazine, Met bisulphite)

- 13) Viral Infection
- 14) Pharmacological agents (Aspirin NSAID'S)
- 15) Environmental factors (cold air, wind, fog, ozone, Sulphur dioxide, cigarette smoke, Diesel fumes, House hold chemicals)

An environment history with special reference to the home is necessary to know about indoor allergens lie indoor allergens may be house dust mite, mammals, cockroach or molds.

The dust mite is an arthropod of 0-3 mm size. *Dermatophagoides farina* and *D. pteronyssinus* are common in temperate climate and *blomia tropicalis* is found in tropical climate (**Arlian, 1989**).

- Mammals such as cats, (dogs and rodents) can be sources of allergen in the home. Among them domestic cat (*Felis domesticus*) play a major role and its allergen is a glycoprotein small flakes of dander from the skin is the important sources of airborne cat allergen (**Morgenstern et al., 1991**). It remains airborne for a long period of time due to its size (3 μ) and is capable of reaching peripheral areas of lung. Further it can stick to walls, furnishings, carpets and clothing.

- Dogs (*Canis familiaris*) forms inhalant allergen and is found in dog saliva and dander which can sensitize a person (**De Groot, 1991**)
- Exposure to cockroach allergens found in kitchen cabinets and kitchen floor dust in heavily infested houses induced asthma. The excretory materials of cockroaches act as allergen.
- An important cause of seasonal asthma is due to exposure to high level of pollens. The major source of pollen allergens are trees, grasses, weeds and shrubs. They release large amount of pollen grains during early morning and remain airborne for long period in outdoor air currents.
- Molds and fungi encounter both indoor and outdoor environment

Airway hyperactivity is manifested by the propensity for widespread but reversible narrowing of the airways in response to diverse inciting factors. It is associated with constriction of airways smooth muscle, inflammation and mucosal edema, accumulation of mucus and an influx of inflammatory cells including neutrophils and eosinophils, there are many ways in which patients are heterogeneous. It includes

1. Factors responsible for precipitating an

attack (extrinsic with attack being precipitated by allergen immunoglobulin E (IgE) reaction, intrinsic or mixed.)

2. Location of airways obstruction (Large airways, small airways, or both)
3. Degree of reversibility of the airways obstruction (complete with a short or a prolonged round the clock treatment or incomplete)
4. Onset (Acute or chronic)
5. Frequency of asthmatic episodes once a year, 3 month, every month, every week, 2-3 days or daily.
6. Grade of severity
7. Duration of attack (short due to smooth muscle spasm, longer due to mucus plugging and edema).
8. Symptomatology: (cough central airways with abundant cough receptors, breathlessness smaller airways with sparse cough receptors, or both symptoms).
9. Response to therapy (Theophylline, beta-2 agonists or glucocorticoids).

TREATMENT:

The principal aim of asthma treatment is to keep patient's symptom free and prevent deterioration in lung function.

- Sympathomimetic treatment. It should

be used, as necessary all patients with asthma Symptoms.

- Rapid reversal of airways obstruction and relief symptoms is achieved by drugs that act as bronchodilator. These drugs are:

1. β_2 Agonist
2. Methyl Xanthines
3. Anticholinergic drugs

PROPHYLACTIC TREATMENT: The main aim to reduce risk of severe attacks, permanent airways inflammation and irreversible airflow obstruction, Asthma attacks can be prevented to a large extent by long-term administration of anti-inflammatory drugs.

1. Glucocorticoids
2. Sodium Cromoglycate
3. Ketotifen

CLINICALLY USED ANTI-ASTHMATIC AGENTS:

Drugs	Route of Administration	Adult dose
1. Sympathomimetics		
(α & β) specific effects		
Ephedrine	Oral	25-50mg.
Adrenaline	s.c.	0.2-0.5 ml.
($\beta_1+\beta_2$) effects		
Isoprenaline	Inhalation	2.5 mg
Specific β_2 effect		
Orciprenaline	Oral	10-20 mg
	Inhalation	650 mcg
Terbutaline	Oral	2.5-5 mg
	Inhalation	200 mcg
	i.v.	100-200 mcg
Salbutamol	Oral	2-4 mg
	Inhalation	90 mcg
	i.v.	100-200 mcg
Bitolterol	Inhalation	370 mcg
Fenoterol	Oral	5-15 mg
	Inhalation	200 mcg
Pirbuterol	Inhalation	200 mcg
Salmetrol	Inhalation	21 mcg
Formoterol	Inhalation	12 mcg
Bambuterol	Oral	20 mcg

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2. Anti-cholinergic drugs		
Ateropine	Oral	200-400mcg
Ipratopium	Inhalation	80 mcg
Oxiteropium		
3. Methylxanthinederivatices		
Aminophylline	Oral	200-400 mg.
Theophylline	Oral	65-500 mg,
Bamiphylline		
Enpropyhliline	Oral	
Doxophylline		
4. Anti-inflammatory Drugs		
Corticosteroids:		
Prednisone	Oral	5-10 mg.
Prediusolone	Oral	5-20 mg.
Melliyl Prednisolone	Oral	5-10mg,
Hydrocortisone	i.v.	2-4 mg,/kg/day
Fluticasone		
Beclomethasone	Inhalation	100-200 BID/QID mcg.
Triamcinolone	Inhalation	5-10 puff/day
Budesonide	Inhalation	100 mcg. BID/QID
Flunisolide	Inhalation	
5. Other drugs		
Cromoglycan Sodium	Inhalation	1 mg 2 puff QID
Nedocromil	Inhalation	4 mg. (2puffs) BID
Ketotifen	Oral	1-2 mg BID.

**INTERNATIONAL GUIDELINES FOR
ASTHMA MANAGEMENT: (Who
workshop report, 1995)**

1. Diagnosing asthma in infants below 5 years of age is, often difficult hence bronchodilators/anti-inflammatory medication may be helpful.
2. Infants and young children requiring symptomatic treatment more than two times per week should be given anti-inflammatory therapy daily. Metered dose inhalers (MDI'S) with spacers and attached face masks are as effective as nebulizers for delivery of drugs
3. Salmeterol is not recommended for treatment in children below the age of 4 years.
4. An expert panel report was that, the dose of inhaled steroids is always reducing gradually.

FOR ADULTS: (Takishima T *et. al*)

Step1:

1. Occasional use of relief bronchodilators.
2. Inhaled short acting β_2 agonist as required for symptom relief are acceptable. But not given more than once daily.

Step 2:

1. Regular inhaled antiinflammatory agents
2. Inhaled short acting β_2 agonist plus inhaled steroid preferred. Inhaled Cromoglycan Sodium/ Nedocromil sodium use alternatively
3. Budesonide/Beclomethasone 100-400 mcg twice a day
Fluticasone 50-200 mcg BID
4. Sustained release theophylline may be substituted to avoid side effects of high dose inhaled steroids.

Step 3:

1. High dose inhaled steroids or low dose inhaled steroids plus long acting inhaled β_2 agonist
2. Budesonide/Beclomethasone 800-2000 mcg/day OR
3. Budesonide/Beclomethasone 100-400 mcg twice a day OR
4. Budesonide/Beclomethasone 100-400 mcg twice/day OR
5. Fluticasone 50-200 mcg twice/day + Salmeterol 50 mcg twice/day.

Step 4:

High dose inhaled Steroids and regular Bronchodilators.

Inhaled short acting β_2 agonists as required with inhaled Beclomethasone/Budesonide

800-2000 mcg/day or Fluticasone 400-1000 mcg/day plus

- A sequential therapeutic trial of one or more of
- Inhaled long acting β agonists
- Sustained release Theophylline
- Inhaled Ipratropium /Oxipropium
- Long acting β agonist tablets
- High dose Inhaled bronchodilators Cromoglycate or Nedocromil

Step-5:

Addition of regular steroid tablets:

1. Inhaled short acting β agonist as required with inhaled beclomethasone/ Budesonide 800 – 2000 mcg/day or
2. Fluticasone 400-1000/day + Long acting bronchodilators + Single dose Prednisolone tablet.

STEPPING DOWN:

Treat every 3-6 months, if control is achieved a stepwise reduction in treatment may be possible. In patients whose treatment was recently started at step 4 or 5 or included steroid tablet for gaining control of asthma, this reduction may take place after a short interval. Other patients with chronic asthma a three to six month period of stability should be shown before few

stepwise reductions are undertaken.

FOR CHILDREN:

Step 1: Occasional use of bronchodilators:

Short acting β_2 agonist "as required" for symptoms relief but not more than once daily. **(De monechy J.G.R et. al)**

Step 2: Regular inhaled preventer therapy:

Inhaled short acting β agonist as required + Cromoglycate powder 10-20 mg 3-4 times/day + Budesonide/Beclomethasone up to 400 mcg/day OR

Fluticasone upto 200 mcg/day.

Consider a 5 day course of soluble prednisolone to be given.

Step3: Increase the dose of inhaled steroids:

Inhaled short acting β agonist as required + Beclomethasone/ Budesonide up to 800 mcg/Daly OR

Flutiscsone upto 500 mg/ Day

Consider Prednisolone or slow release Xanthines or consider adding regular twice daily long acting β agonist to be given.

Step 4: High dose inhaled steroids and Bronchodilators:

Inhaled steroids (up to 2 mg/Day) and other treatment as in step 3, slow release Xanthines or nebulised β agonist. **(Henry RL et.al)**

CONCLUSION: There are various pathological origin of Bronchial Asthma therefore no single medicine which relief from the symptoms of Bronchial Asthma. In the name of the treatment only the symptomatic treatment is available. Drugs like Bronchodilators, Corticosteroids, Anti-histaminic are used in combination of different dosage for better symptomatic relief and minimize the disease progress.

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