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ब्रोंकाइल अस्थमा

BRONCHIAL ASTHMA

सत्यमेव जयते

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DRAFT DG MEMORANDUM FOR BRONCHIAL ASTHMA–180

Definition

1. Asthma is a common disorder that has significant genetic and environmental components, and is described as "*a chronic inflammatory disorder of airway hyper responsiveness that leads to recurrent episodes of wheezing, breathlessness, chest tightness and coughing, particularly at night or in the early morning. These episodes are usually associated with widespread, but variable, airflow obstruction within the lung that is often reversible either spontaneously or with treatment.*"

Diagnosis

2. **History**: Symptoms such as episodic breathlessness, wheezing, cough and chest tightness prompt a diagnosis of Asthma. History of nocturnal exacerbations, variability (particularly seasonal variability), trigger factors (like pollens, dusts, fumes, strong smells, exercise, etc.) or a positive family history strengthens the clinical suspicion. Asthma is often associated with other manifestations of atopy like allergic rhinitis, conjunctivitis or dermatitis. Response to appropriate asthma therapy is another factor that strongly suggests asthma.

3. Atypical presentations like *cough-variant asthma*, where chronic cough is the principal symptom, if not the only symptom and *exercise-induced asthma*, where patients experience typical asthma symptoms or sometimes troublesome cough 5-10 minutes after completing exercise, more so in a dry and cold atmosphere, also have to be considered as variants of asthma and investigated accordingly.

4. **Physical examination**: Since asthma is defined by the variability of its manifestations, the physical examination may be normal during the asymptomatic phases. The most common abnormal finding is that of diffuse polyphonic wheeze.

5. **Investigations**: Two methods must be employed for assessment of airflow limitation - Spirometry and Peak Expiratory Flow (PEF) measurement.

   (a) **Spirometry** -If FEV1/FVC is less than 70% (normally more than 75-80%), it is indicative of airflow obstruction. Improvement

in FEV_1 of more than 12% and 200 mL after bronchodilator treatment indicates reversible airflow obstruction and is suggestive of asthma. A characteristic flow-volume loop is created with scooping of the expiratory loop consistent with airflow limitation (Fig 1).

Fig 1: Flow-volume loops in asthma. A, The typical scooped appearance of the flow-volume loop in asthma is shown as the solid line. The predicted normal flow-volume loop is shown by the dashed line. B, The scooped appearance of the initial flow-volume loop may show complete reversal following use of a bronchodilator. C, in some cases, the reversal of the scooped appearance following use of a bronchodilator is incomplete.

(b) **Peak Expiratory Flow (PEF)** - It is measured using a Peak Flow Meter and is an important aid in both diagnosis and monitoring of Asthma. It should ideally be measured first thing in the morning, before treatment is taken (when the values are generally lowest) and the last thing at night (when the recordings are generally highest). PEF variability can be measured by calculating the amplitude (the difference between maximum and minimum readings for the day), expressed as a percentage of the mean daily PEF value, and averaged over 1-2 weeks. A 60L/min (or 20% or more of prebronchodilator PEF) improvement after inhalation of a bronchodilator, or diurnal variability of more than 20% suggests a diagnosis of Asthma. PEF is also a useful tool to monitor the course of the disease and thus to titrate the doses of medications from time to time.

(c) **Measurements of airway responsiveness** can be done at a respiratory centre using direct airway challenges such as inhaled

methacholine and histamine or indirect challenges like inhaled mannitol. Exercise testing (fall in FEV1 by more than 20% after exercise) can be used to demonstrate airway hyper responsiveness in some patients. All these tests are suggestive but not exclusive to Asthma, and are positive in many patients of allergic rhinitis, cystic fibrosis, bronchiectasis and even COPD.

(d) **Eosinophilia**: Peripheral blood eosinophilia (greater than 4 percent or 300 to 400 /c mm) may be seen in both allergic and nonallergic asthmatics. When present, eosinophilia may be used to support a diagnosis of asthma; however, its absence is of no value in excluding asthma. Unusually high eosinophil counts (greater than 800 /c mm) suggest the presence of other disorders, such as allergic bronchopulmonary aspergillosis, Churg-Strauss syndrome, tropical eosinophilia, and Loeffler's syndrome. It should be noted that eosinophilia may not be present if the patient is taking corticosteroids.

6. Other alternative diagnoses that must be excluded are—

(a) Cardiac disorders leading to similar symptoms due to left ventricular failure

(b) Other obstructive airway diseases like COPD

(c) Diffuse parenchyma lung diseases

(d) Upper airway obstruction and inhaled foreign bodies

(e) Hyperventilation syndrome and panic attacks

(f) Vocal cord dysfunction

7. **Asthma Severity**: Conventional assessments of asthma severity have combined assessments of symptoms, amounts of β2-agonist used to treat symptoms, and lung function. Based on the level of airflow limitation and its variability, asthma can be subdivided by severity into four types or steps: Intermittent, Mild Persistent, Moderate Persistent, and Severe Persistent (Table 1). This classification is useful in guiding management.

Table 1. Classification of Asthma severity by Clinical features/ flow limitation (Before treatment)

STEP 1: Intermittent	STEP 2: Mild Persistent
Symptoms less than once a week Brief exacerbations Nocturnal symptoms not more than twice a month ●FEV1 or PEF ≥ 80% predicted ●PEF or FEV1 variability < 20%	Symptoms more than once a week but less than once a day Exacerbations may affect activity and sleep Nocturnal symptoms more than twice a month ●FEV1 or PEF ≤ 60% predicted ●PEF or FEV1 variability 20-30%
STEP 3: Moderate Persistent	**STEP 4: Severe Persistent**
Symptoms daily Exacerbations may affect activity and sleep Nocturnal symptoms more than once a week Daily use of inhaled short-acting β2-against ●FEV1 or PEF 60–80% predicted ●PEF or FEV1 variability > 30%	Symptoms daily Frequent exacerbations Frequent nocturnal asthma symptoms Limitation of physical activities ●FEV1 or PEF ≤ 60% predicted ●PEF or FEV1 variability > 30%

8. **Asthma Control**: The aim of treatment should be to achieve and maintain control of symptoms for prolonged periods with due regard to safety of treatment and potential for adverse effects. Classification of control is given at table-2.

Table 2. Types of asthma control

Assessment of clinical control of Asthma (preferably over 4 weeks)

Characteristic	Controlled (All of the following should be present)	Partly Controlled (Any measure present)	Uncontrolled
Day time symptoms	Do not occur or only occasional (twice or less/week)	Occur sometimes (more than twice/ week)	Three or more features of partly controlled Asthma An exacerbation in any week makes
Limitation of activities	Normal activity	Limitation of normal activity	

Nocturnal symptoms/awakening	No symptoms at night	Sleep interrupted night symptoms	that an uncontrolled asthma week.
Need for reliever/ rescue treatment	No need for reliever puffs (twice or less/week)	Need reliever puffs more than twice/ week	
Lung Function (PEFR or FEV1)— without administration of bronchodilator	Normal	<80% of predicted or personal best (if known)	

Management

9. Pharmacologic therapy for asthma is subdivided into acute, **short-term** "reliever" medications and **long term** "controller" medications. Reliever medications are bronchodilators such as inhaled salbutamol and ipratropium bromide and oral/intravenous theophylline. The most widely used controller medications are inhaled corticosteroids, which have a localized anti-inflammatory effect.

10. **Route of administration**: Inhaled medications for asthma are available as pressurized metered-dose inhalers (MDIs), breath-actuated MDIs, dry powder inhalers (DPIs), soft mist inhalers, and nebulized aerosols. Individual patient preference, convenience, and ease of use may influence not only the efficiency of drug delivery but also patient adherence to treatment and long-term control. Pressurized MDIs (pMDIs) require training and skill to co-ordinate the actuation of the inhaler and inhalation. Use of a holding chamber (spacer) not only makes pMDIs easier to use but also improves drug delivery and reduces oro-pharyngeal deposition and thus reduces local and systemic side effects. Breath-actuated pMDIs may be used by patients who are not able to use pMDIs in a coordinated way.

11. **Controller medications** :

(a) **Inhaled corticosteroids** : Inhaled corticosteroids (ICS) are the most effective treatment available for persistent asthma (Table-3). They effectively reduce asthma symptoms, improve quality of life, improve lung function, decrease airway hyper responsiveness, control airway inflammation, reduce frequency and severity of exacerbations and reduce asthma mortality.

Drug	Low daily dose (μg)	Medium daily dose (μg)	High daily dose (μg)
Beclomethasone dipropionate	200 - 500	> 500 - 1000	> 1000 - 2000
Budesonide	200 - 400	> 400 - 800	> 800 - 1600
Ciclesonide	80 - 160	> 160 - 320	> 320 - 1280
Fluticasone propionate	100 - 250	> 250 - 500	> 500 - 1000
Mometasone furoate	200	≥ 400	≥ 800

Ciclesonide and Budesonide can be used for once daily dosing in mild patients.

Local adverse effects from inhaled glucocorticosteroids include oropharyngeal candidiasis, dysphonia, and coughing from upper airway irritation. There is no evidence that use of inhaled steroids increases the risk of pulmonary infections, and they are not contraindicated in patients with active Tuberculosis.

(b) **Leukotriene modifiers**—This subset includes cysteinyl-leukotriene 1 (CysLT1) receptor antagonists (like montelukast) and a 5-lipoxygenase inhibitor (zileuton). Thus they can be used for their steroid sparing effect and are also very effective in some cases of Aspirin-sensitive asthma.

(c) **Long acting inhaled β2-agonists** (LABA)—These drugs should always be used in combination with inhaled corticosteroids, never as monotherapy.

(d) **Theophylline**—It is a bronchodilator and, when given in a lower dose, has modest anti-inflammatory properties. It is available in sustained release formulations that are suitable for once-or-twice daily dosing. It is a useful adjunct to conventional treatment when the control is not satisfactory.

(e) **Cromones**—Sodium cromoglycate and nedocromil sodium - The role of these drugs in long term management of Asthma is limited.

(f) **Long-acting anticholinergics**—Recent evidence has shown that long acting inhaled anticholinergics (Tiotropium) have a significantly favorable action for long term control of asthma, though they are inferior to LABA.

(g) **Anti-IgE (Omalizumab)**—This treatment option is limited to patients with elevated levels of serum IgE.

(h) **Systemic glucocorticosteroids**—Long-term oral glucocorticosteroid therapy (that is, for periods longer than two weeks as a steroid "burst") may be required for severely uncontrolled asthma, but its use is limited by significant side effects.

12. **Reliever Medications**

(a) **Rapid-acting inhaled β2-agonists**—These are the agents of choice for immediate relief of bronchospasm during acute episodes and also for pre-treatment to prevent asthma in cases of exercise-induced asthma. Commonly available agents include salbutamol and levo-salbutamol.

(b) **Anticholinergics**—Inhaled anticholinergics like Ipratropium bromide, though not as effective as β2-agonists, still have add on effect when used along with β2-agonists during acute episodes of asthma.

(c) **Theophylline**—Role of short acting theophylline for relief in acute episodes of asthma is considered controversial. It may not provide added bronchodilation but may enhance respiratory drive.

13. **Management protocols**

The goals for successful asthma management are:

(a) Achieve and maintain control of symptoms

(b) Maintain normal activity levels, including exercise

(c) Maintain pulmonary function as close to normal as possible

(d) Prevent asthma exacerbations

(e) Avoid adverse effects from asthma medications

(f) Prevent asthma mortality

14. **Prevention of symptoms and exacerbations**: Every asthma patient should be encouraged to identify one's own trigger factors, and attempts must be made to avoid exposure to such factors. Cigarette smoking and also exposure to second hand smoke must be completely avoided. Other commonly identified triggers like fumes, dust, pollens, strong smells, etc should be avoided. Living environment should be kept clean, dust free and attempts must be made to make it free of mites, cockroaches and fungus. Food items

and additives that have been identified to trigger symptoms must be avoided. Some drugs that can exacerbate the symptoms of asthma like Aspirin and β-blockers should be avoided. Patients with severe asthma should be given influenza vaccination annually. Obesity and emotional stress are known to trigger asthma symptoms and these factors must be actively controlled in known cases of asthma.

Rhinitis, sinusitis, and polyposis are frequently associated with asthma and need to be treated for adequate control of asthma. Gastro-esophageal reflux can exacerbate asthma, and asthma sometimes improves when the reflux is corrected.

15. **Assessment, treatment and monitoring**: A scheme to assist physicians in making decisions on step up and step down of treatment is shown in Fig 2. Step 2 is the initial treatment for most treatment-naive patients with persistent asthma symptoms. Treatment may be started at step 3 if the asthma is severely uncontrolled at presentation.

16. After initiating treatment, clinical improvement starts within days of starting treatment, but full effect may take 3-4 months. It is recommended that the treatment should be maximized initially to ensure adequate control and in most cases it would be possible to step the treatment down after a period of time. When inhaled glucocorticosteroids alone are used in medium—to-high doses, a 50% reduction in dose should be attempted at 3 month intervals. When control is achieved at a low-dose of ICS alone, in most patients treatment may be switched to once daily dosing (Ciclesonide or Budesonide). When asthma is controlled with a combination of LABA and ICS, the preferred approach is to first reduce the dose of the ICS component gradually to a low dose and then discontinue the LABA component if the disease remains in control.

17. **Difficult to treat Asthma**: Majority of patients can achieve the targeted control with the principles mentioned above. A small subset remains uncontrolled or partially controlled even at step 4. Such patients may have steroid resistance or steroid dependence and should be offered higher doses of steroids. However, if the control remains sub-optimal beyond six months, the doses should be tapered to the lowest level at which the maximal possible control is maintained. All such patients should also be investigated for alternative diagnosis and should be referred to respiratory centre for evaluation.

18. **Management of Acute Exacerbations**: The primary therapies for exacerbations include repetitive administration of rapid-acting inhaled bronchodilators, early introduction of systemic steroids, and oxygen supplementation. The aim of treatment is to relieve airflow obstruction and hypoxemia as early as possible. Management of exacerbations is dependent on the severity of the episode. The severity can be broadly classified as in Table 4. All patients with acute exacerbation should be admitted to a hospital. The treatment algorithm for exacerbations is given in Figure-3.

19. **Disposal of cases diagnosed to have Asthma.**

(a) Initially all patients with bronchial asthma will be placed in medical category P3 (T-24). All service personnel will be issued a Peak Flow Rate Meter, and will be required to maintain a PEFR diary. This diary may be checked by AMAs on a monthly basis. All cases will be advised sheltered appointments required to avoid exposure to known triggering factors.

(b) After six months, if controlled (Table-2), they will be placed in medical category P2(perm). If partially controlled, then will be placed in medical category P3 (perm) with monthly review by medical specialist. The diary will be checked during every review by the specialist to take decision on optimization of treatment.

(c) **Severe persistent cases who do not achieve optimum control** and have frequent exacerbations requiring hospitalization will be evaluated at respiratory center to consider invalidment from service.

(d) Patients with 'intermittent asthma' who have been documented to be asymptomatic for two year in medical/respiratory OPD can be considered for upgradation to P1 by senior adviser (Respiratory Medicine) or Consultant (Medicine).

Table 4

Severity of Asthma Exacerbation

	Mild	Moderate	Severe	Respiratory arrest imminent
Breathless	Walking, can lie down	Talking, prefers sitting	At rest, hunched forward	

	Mild	Moderate	Severe	Respiratory arrest imminent
Talks in	Sentences	Phrases	Words	
Alertness	May be agitated	Usually agitated	Usually agitated	Drowsy or confused
Respiratory rate	Increased	Increased	Often > 30/min	
Accessory muscles and suprasternal retractions	Usually not	Usually	Usually	Paradoxical thoraco-abdominal movement
Wheeze	Moderate, often only end-expiratory	Loud	Usually loud	Absence of wheeze
Pulse (/min)	<100	100–120	>120	Bradycardia
Pulsusparadoxus	Absent <10mmHg	May be present 10–25 mmHg	Often present >25mmHg	Absence suggests respiratory muscle fatigue
PEF after initial bronchodilator %predicted or % personal best	Over 80%	Approx. 60–80%	<60% (<100L/min) or response lasts <2hrs	
PaO_2 (on air)	Normal	>60mmHg	<60 mmHg possible cyanosis	
$PaCO_2$	<45 mmHg	<45 mmHg	>45 mmHg	
SaO_2% (on air)	>95%	91–95%	<90%	

The presence of several parameters, but not necessarily all, indicates the general classification of the exacerbation.

Figure-3

Stepwise approach to management of bronchial asthma

Initial Assessment

- History, physical examination, PEF measurement, Oxygen saturation, arterial blood, chest X-ray if required

Initial Treatment

- Oxygen to achieve saturation > 90%
- Inhaled rapid acting β2-agonist continuously for one hour
- Systemic glucocorticosteroids if no immediate response, or if patient recently took oral glucocorticoids, or if exacerbation is severe.
- Sedation is contraindicated

Reassess after 1 hour

Moderate Episode

- Oxygen
- Inhaled rapid acting β2-agonist and inhaled anticholinergic every 60 min
- Oral glucocorticosteroids
- Continue treatment for 1-3 hours, provided there is improvement

Severe Episode

- Oxygen
- Inhaled rapid acting β2-agonist and inhaled anticholinergic every 60 min
- Oral glucocorticosteroids
- IV Magnesium sulphate

Reassess after 1-2 hours

Good response

-Response sustained 60 min after last treatment
-Physical examination normal-no distress
-PEF > 70%
-O2 Saturation > 90%

Incomplete response

-Risk factors for near fatal asthma
-Physical examination-mild to moderate signs
-PEF < 60%
-O2 Saturation < 90%

Acute Care Setting

-Oxygen
-Inhaled rapid acting β2-agonist ± anticholinergic
-Systemic Glucocorticosteroid
-IV Magnesium sulphate

Poor response

-Risk factors for near fatal asthma
-Physical examination-severe symptoms, drowsiness, confusion
-PEF <30%; PO2<60mmHg
-PCO2>45mmHg

Intensive care

-Oxygen
-Inhaled rapid acting β-2 agonist ± anticholinergic
-Intravenous Glucocorticosteroid
-Consider intravenous theophylline or intravenous β2-agonist
-Possible intubation and mechanical ventilation

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