MANAGEMENT OF AN ACUTE EPISODE OF ASTHMA IN CHILDREN

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Abstract: Bronchial asthma involves inflammation of the bronchioles resulting in respiratory symptoms, the most prominent of which are wheeze and difficulty in breathing. There can be exacerbation of the symptoms of asthma due to various triggering factors and these episodes may seriously impair the functional capacity of the child. Identification of the problem and prompt optimal treatment can lead to favorable outcomes in most cases. Short acting beta agonists and corticosteroids are the mainstay of treatment of exacerbations of asthma. Severe exacerbation may be fatal if not managed appropriately. Frequent and regular assessment of response after each intervention is an important part of optimal management.

Abbreviations: ED- Emergency department, MDI – Metered dose inhaler, LABA – Long acting beta agonist, SABA – Short-acting beta agonist, SpO2 - peripheral capillary oxygen saturation, V/Q mismatch – ventilation/perfusion mismatch

Introduction

It is estimated that approximately 235 million people of all ages and ethnic backgrounds have asthma worldwide.¹The pathophysiology of asthma involves inflammation of the bronchioles which is characterised by recurrent exacerbations. These exacerbations often affect the daily activities and functional capacity of the individual. The World Health Organisation estimates that 15 million disability-adjusted life-years (DALYs) are lost annually from asthma.²

Acute exacerbations of asthma can also be life-threatening. It is estimated that 1 in every 125 deaths worldwide is due to asthma and most of these deaths are preventable.² There are several triggering factors that can precipitate an acute exacerbation of the ongoing inflammatory process – climate change, viral infections, food allergy etc. The article focuses on management of an acute asthma episode in children in the setting of a hospital or clinic.

Key points

- Short acting beta agonists and corticosteroids form the mainstay of management.
- Humidified oxygen by mask must target an SpO2 of 92-94%. Avoid hyper-oxygenation.
- Nebulization of salbutamol should be performed only through high flow oxygen and not through electronic nebulisers.
- It is very important to assess the vital parameters and response to treatment regularly and after every intervention.
- Endotracheal intubation can complicate the management and is to be avoided as far as possible. Non-invasive ventilation may be carried out if necessary.
- Nebulization of child with respiratory distress due to pneumonia or cardiac failure without treating primary cause is ineffective and is often detrimental.
- Arterial blood gas (ABG) analysis has little role in guiding management, clinical status is more important.

Triggers for exacerbation of asthma³

Asthma triggers are factors that can instigate an exacerbation of symptoms in a person who has a tendency to asthma. These triggers may either irritate and constrict the bronchioles or increase the underlying inflammation. Some of the common triggers are:

- infections, usually of viral origin
- allergens, most commonly from house dust mites, pets or pollen
- exercise, especially in cold weather
- emotions such as excitement, fear or anger
- irritants in the air cigarette smoke, diesel exhaust, perfume or other strong scents, household sprays, sulphur dioxide, grain or flour dust, sawdust
- changes in the weather (e.g. cold weather)
- food additives such as tartrazine (an artificial food colouring), or food allergens, such as peanuts
- Medications which a person is allergic to (e.g. aspirin).

Risk factors for asthma exacerbations

Some of the factors that increase the incidence of acute asthma exacerbations are given below:

- Previous near-fatal asthma
- Previous admission for asthma especially if in the last year
- Repeated attendances at emergency department (ED) for asthma care
- Requiring two or more classes of asthma medication
- "Brittle" asthma where there is a wide variation in peak expiratory flows despite of optimum medications.
- Exacerbations precipitated by food
- Use of more than two beta-agonist metered-dose inhaler (MDI) canisters per month
- Insufficient controller therapy or poor adherence to controller therapy
- Denial of, or failure to appreciate the severity of illness
- Associated depression or other psychiatric disorder
- Exacerbations precipitated by food
- Use of more than two beta-agonist MDI canisters per month
- Insufficient controller therapy or poor adherence to controller therapy
- Failure to appreciate the severity of illness
- Associated depression or other psychiatric disorder

Assessment of severity

Several clinical asthma severity scores have been designed for use in the acute care setting to evaluate initial exacerbation severity, assess response to treatment, and help determine if hospitalization is necessary. It is important that children with exacerbations are assessed repeatedly. A number of clinical tools exist, no single tool being proven to be superior. The same tool must be used each time to reassess the progress. Two of the commonly used scores are the BECKER Asthma Score and the Pulmonary Index Score (PIS).⁴ These scores however are not uniformly used and clinical assessment of severity is what is commonly practised. Based on clinical criteria, severity may be classified into several types (Box 1).

MANAGEMENT OF ACUTE EXACERBATION OF ASTHMA IN CHILDREN

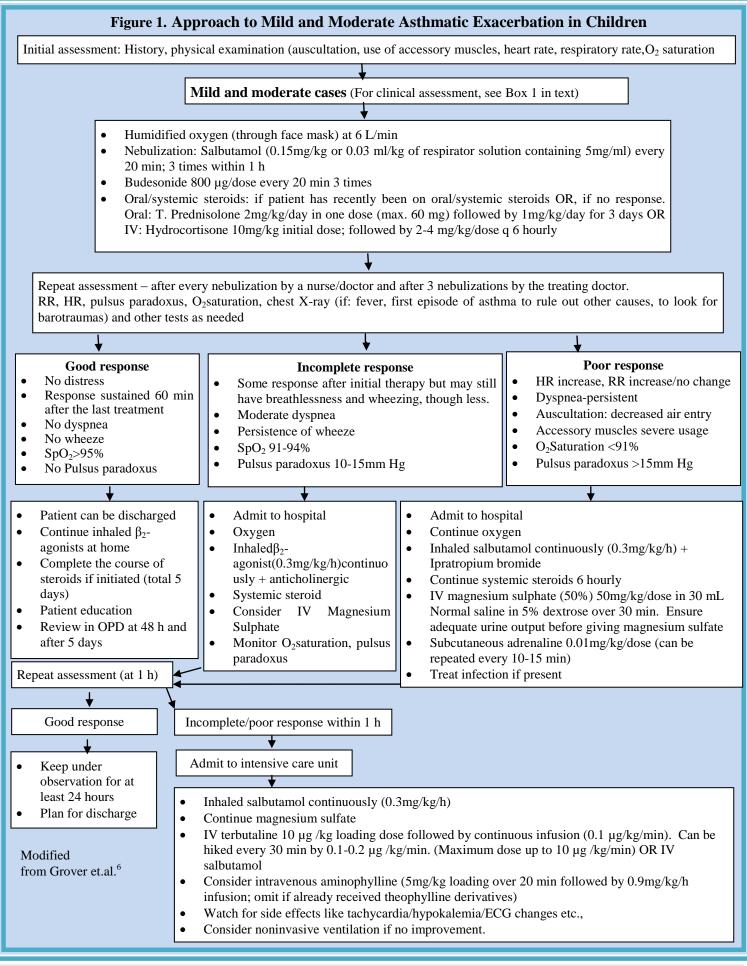
In the setting of a mild to moderate acute exacerbation, primary care can be given by the parents or at a small medical centre. Short acting Beta Agonists(SABA)are the mainstay of management (See following pages for dosage and administration). Regular and repeated assessment of response after every intervention is vital because a poor responder may require a change in strategy, without which the condition may worsen.

Transfer to a higher center should be considered in:

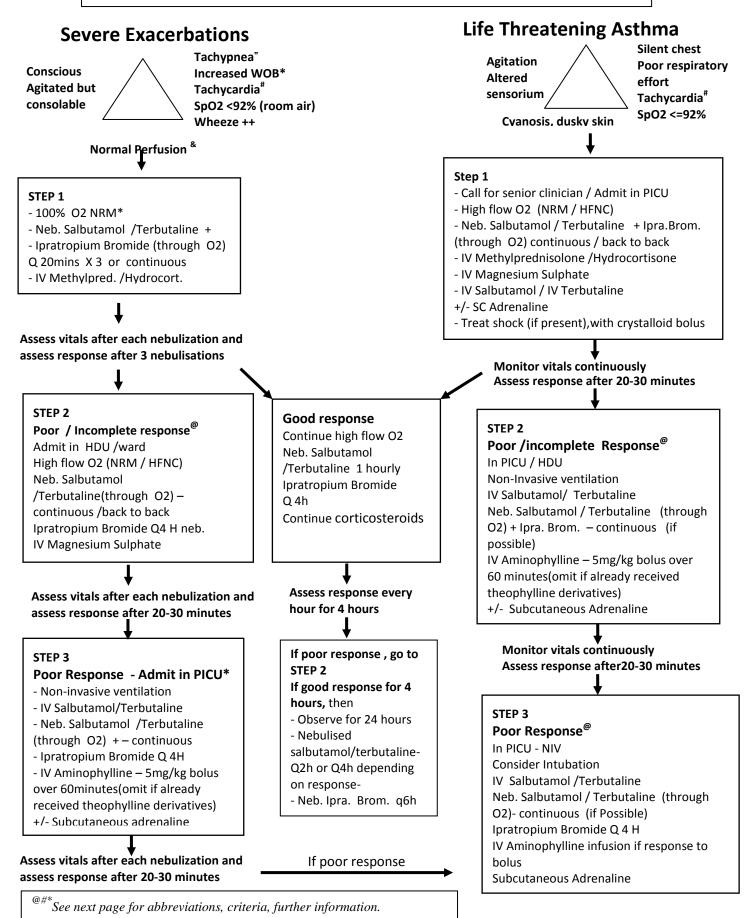
- Moderately to severely ill patient not responding to initial management with beta agonist
- Persistent hypoxia (Oxygen saturation <94% on room air)
- Relapse of symptoms within 4 hours

Good communication is crucial to ensure that treatments ordered in the first centre are not missed or duplicated during the transfer of care. Transfer is preferred in an Ambulance with Nebuliser and oxygen. It is important to educate the parents about the danger signs before transfer.

The algorithmic approach to management of mild, moderate and severe exacerbations of asthma in children are shown in Figures 1 and 2.



Acute Care Management of Severe Asthma in Children



 Assessment of severity is th Re-assessment after each in Aminophylline is NOT recon All that wheezes is NOT astl Anticipate worsening of hyp salbutamol nebulization Rapid deterioration during severation 	AVOID INTUBATION if Possible <u>Absolute Indications (for Intubation)</u> Respiratory Arrest Cardiac Arrest Severe Exhaustion Rapid deterioration of Mental status	
 consider non-asthmatic etic Physician / SPO2 monitoring 	@ Incomplete /Poor Response Tachycardia/ tachypnea	
# Tachypnoea RR >50/min (2-5 years) RR >30/min (>5 years)	*WOB:Work of Breathing *NRM:Non Rebreathing Mask *HFNC:High Flow NasalCannula	Persistent dyspnea / WOB Wheeze persistent Decreased air entry / Silent Chest on auscultation SPO2 < 92% (on high flow O2)
RR >60/min (<2 years) # Tachycardia HR >130/min (2-5 years) HR > 120/min (>5 years	*Normal perfusion Capillary refill time < 2 secs Pink colour – nail beds	PulsusParadoxus 10-15mmHg or>15mmHg Bradycardia and bradypnea – ominous signs indicating late respiratory failure

Warm extremities

Dosages of common medications

HR > 120/min (>5 years

	Drugs	Route	Dose	Remarks
1.	Salbutamol	Nebulized	0.05 -0.1mg/kg Or 2.5mg (2-5 yrs.) 5mg (>5 yrs.) Diluted in 3-4 ml Normal saline ONLY & O2 flow rate 6-8ml/min	Worsens hypoxia in hypoxic asthmatics (if given without O2) Tremors, tachycardia,arrhythmias
			Respirator solution 5mg/ml	
2.	Ipratropium Bromide	Nebulized	250-500 mcg Q4 -6Hrly	Peak response develops after 30- 90mins
3.	Terbutaline	IV -Infusion	0.1 to 10 mcg/kg/min 3mg/kg in 50ml NS – 1ml =1mcg/kg/min	
4.	Methyl Prednisolone	IV	0.5 to 1mg/k/dose Q6H	Hypertension /Hyperlycemia
5.	Hydrocortisone	IV	2-4mg/kg /dose Q6 hourly	Hypertension /Hyperlycemia
6.	Magnesium Sulphate	IV	25-50mg/kg/dose over 20-30min.	Hypotension, muscle weakness, areflexia, respiratory depression
7.	Aminophylline	IV	Loading dose: 5mg/kg/dose over 30min <6mo: 0.5mg/kg/hr 0.5-1 yr : 0.85 -1mg/kg/hr 1-9yrs: 1mg/kg/hr >9 yrs.: 0.75mg/kg/hr	AVOID if the child is on theophylline derivatives EXTREMELY narrow therapeutic index Decrease dose in patients with hepatic and cardiovascular dysfunction
8.	Adrenaline	Subcutaneous	0.1ml/kg (1:10000)	In Life threatening or Near fatal asthma Tachycardia / Hypertension
9.	Prednisolone	Oral	10mg (<2 years) 20mgm stat (2-5 yrs) 30-40mg >5 yrs	Early in the management of Acute Asthma

Severe asthma

Box 1: Clinical assessment of severity of asthma

Mild asthma⁵ Normal mental state Subtle or no increased work of breathing, accessory muscle use/ recession. Able to talk normally, wheeze +

Conscious, Irritable but consolable Tachypnea[#], increased work of breathing Tachycardia[#] SpO2 <92% (Room air) Wheeze ++

Moderate asthma⁵

Normal mental state		
Some increased work of		
breathing accessory muscle		
use/recession	I	
Tachycardia		
Some limitation of ability to		
talk, wheeze +		
# - See management algorithms		

Life-threatening asthma Agitation, fighting the mask, Altered sensorium Silent chest Poor respiratory effort Tachycardia SpO2 <=92%

Management in the emergency room

Goals of management in the emergency room

- Rapid reversal of airflow obstruction by administration of inhaled bronchodilators and early institution of systemic glucocorticoids
- Correction of hypoxemia and severe hypercapnia
- Reduction of likelihood of recurrence by ensuring adequate baseline controller therapy when indicated

Oxygen

Hypoxemia, if present, is alleviated by administration of supplemental oxygen (hypercapnia usually improves with reversal of airflow obstruction).Humidified Oxygen should be given to maintain the SpO2 around 92-94%. It is advisable not to target a higher SpO2 (>94%) as, this may worsen the physiological vasomotor response to hypoxia and lead to a ventilation/perfusion (V/Q) mismatch.

Investigations

The role of investigations is limited and indicated only in specific settings.

Chest X-Ray - In the management of children with acute exacerbation of asthma chest radiographs (CXRs) are not very useful in guiding therapy.

Consider a chest x-ray in case of

• Acute worsening of clinical status

- Lack of response to asthma therapy
- Focal clinical findings, fever, severe disease
- To rule out an asthma mimic or an underlying pneumonia as a cause of acute exacerbation

Arterial blood gas (ABG) analysis- Child's clinical state is more important in guiding therapy. ABG has little role.

ADMISSION

Admission is considered for

- Patients who were moderately to severely ill on arrival and who have little improvement after initial therapy
- Patients who required beta-agonist therapy more often than four hours
- Patients requiring supplemental oxygen or with low oxygen saturation on pulse oximetry ,an hour or more after commencement of initial therapy
- A history of rapid progression of severity in past exacerbations.
- Poor adherence with outpatient medication regimen
- Inadequate access to medical care.
- Inability of the caregiver(s) to provide medical care and supervision at home.

Patients who require treatment more often than every two hours may need to be admitted to an intensive care unit (ICU)

Inhaled bronchodilator therapy

SABA is the cornerstone in management in the ED as well. As mentioned earlier, MDIs are equally effective, if given at the right dose.^{6,7}Salbutamol is most commonly prescribed. Terbutaline nebulisation is equally effective and safe.

Short acting beta agonists

SABAs relax airway smooth muscles and lead to a prompt increase in airflow. They provide rapid relief of acute asthma symptoms (eg. coughing, wheezing, chest tightness, and shortness of breath). The onset of action for SABAs is less than 5 minutes; with a time to onset of action of about 10 to 15 minutes and peak effect beginning within 30 minutes.

These can be administered as nebulisation or with a MDI with spacer. There is good evidence that pressurised MDI with spacer is at least as effective as, and possibly superior to delivery of medication by jet nebulizer for reversing acute bronchospasm in infants

and children.^{5,6} The child is reassessed every 10-20 minutes and doses are repeated if required, every 20 minutes.

If symptoms such as wheezing and dyspnea resolve and peak flow measurements improve (if following peak flow) after one to two beta agonist treatments and do not return

within four hours, then the patient may safely continue at-home treatment with a SABA given every four to six hours as needed. However, SABAs should not be prescribed on a regular schedule because of concerns about a possible relationship between the frequent use of these agents and deteriorating asthma control.

Points to note with SABA therapy

- It is to be noted that Salbutamol may inhibit the physiological hypoxia-induced pulmonary vasoconstriction (this beneficial reflex phenomena diverts blood flow to well ventilated areas). Therapy may lead to increased blood flow to the hypoxic alveolus aggravating the ventilationperfusion mismatch and worsening hypoxia in the already compromised child. It is therefore, not uncommon for a hypoxic child to deteriorate during salbutamol nebulizer therapy. Hence, close physician monitoring is essential during nebulization.
- Nebulization of salbutamol should therefore be performed only through high flow oxygen and not through electronic nebulisers. Pulse oximetry and resuscitation equipment should also be close at hand when nebulizing a child with life-threatening or near fatal asthma.
- Prefilled epinephrine syringe (0.1 ml/kg of 1:10,000) must also be available close at hand.

Dose of Salbutamol¹⁰

- 0.15 mg/kg of Salbutamol is given as nebulisations
- MDI dosage (given below)

WEIGHT	DOSE
5-10 kg	4 puff
10-20 kg	6 puff
>20 kg	8 puff

Nebulization of salbutamol should therefore be performed only through high flow oxygen and not through electronic nebulisers. **Continuous nebuliser therapy:** may be considered when the exacerbation is life threatening, not responding to one hour of therapy or requiring nebulisations more frequently than hourly. It is equally efficient and safe and is believed to abolish the reflex bronchoconstriction after intermittent

nebulisations.

Dose:0.5 mg/kg/h up to a maximum of15 mg/h.

Alternatively very frequent nebulisations (every 10-15 minutes) can be given. In such conditions, cardiac monitoring is important and serial electrolyte monitoring (serum potassium) is recommended.

Anti-cholinergics

In near fatal asthma, the large and medium bronchioles are constricted. These are supplied by parasympathetics, and anti-cholinergic medications play an effective role in relieving the spasm. They also relieve mucosal edema and secretions.

Dose of Ipratropium bromide¹⁰

- MDIs 4-8 puffs
- Nebulisations (Dose given below)

WEIGHT	DOSE
<20 kg	250 mcg
>20 kg	500 mcg

Corticosteroids

The cascade of inflammation needs to be inhibited in exacerbations and corticosteroids are a vital part of management. There is strong evidence to suggest that administration of corticosteroids with an hour of presentation, rapidly relieves airflow obstruction, decreases relapse rate, a may reduce hospitalizations. Systemic glucocorticoids are not indicated in children with mild exacerbations.

In acute severe asthma, the administration of glucocorticoids enhances the bronchodilator response to beta agonists by reversing desensitization and down-regulation of beta receptors. The effects are noted within two to four hours of administration. Administer systemic glucocorticoids as soon as possible if indicated. Oral administration is suitable for most patients, provided there is no vomiting and gut function is good.

Dose:

- Oral Prednisolone 1-2 mg/kg /day as a single dose • (max. 60mg). Continue 1 mg/kg/day for 3 days
- IM Dexamethasone 0.15 -0.3mg/kg/dose 12h
- IV Hydrocortisone 2-4 mg/kg/dose q6h ٠
- IV Methyl Prednisolone 0.5 -1 mg /kg/doseq6h

If the patient is already on inhaled steroids, it may be continued, although inhaled steroids alone in an acute setting has poor evidence of benefit. The dose is tapered if it is being required for more than 10 days. Decreasing by 50% per day is a suitable method.

Antibiotics

Routine antibiotic administration has no benefit in acute asthma exacerbations. They are necessary to treat comorbid infections.

RE-EVALUATION

After every step of management, the child is reassessed. In severe and life-threatening asthma, assessment of vital parameters (heart rate, respiratory rate, blood pressure, sensorium) must be done every 15-20 minutes or ideally continuously in an ICU setting. The decision to go to the next step of management is based on the response to treatment. Continuing to treat based on initial assessment of severity without reassessment is detrimental and is to be avoided. Treatment must therefore be guided by repeated assessments.

Subcutaneous Terbutaline/ adrenaline

Subcutaneous or intramuscular administration of betaagonists may be superior to inhaled beta-agonists in these situations:

- children with severe exacerbations and poor • inspiratory flow
- anxious, young children who are uncooperative •
- children with suboptimal response to initial ٠ aerosolized therapy.

Typically, subcutaneous therapy is given within minutes of arrival to a severely ill patient in the situations mentioned. Adrenaline and Terbutaline are equally efficient.

Dose

Terbutaline 0.01 mg/kg/dose (0.01 mL/kg of a 1 mg/mL)

After every step of management, the child is reassessed.

Treatment must therefore be guided by repeated assessments.

solution), with a maximum dose of 0.4 mg (0.4 mg)mL) S/C

Adrenaline 0.01 mg/kg (0.01 mL/kg of 1:1000 solution [1 mg/mL]), with a maximum dose of 0.4 mL (0.4 mg) S/C

Intravenous Terbutaline

It is used commonly in intensive care setting and in severe exacerbations, not responding to inhaled and subcutaneous bronchodilators and steroids. **Dose** :

- 0.4 mcg/kg/min to 4 mcg /kg/min (maximum dose: 10 mcg/kg/min).
- Increase the dose every 30minutes by 0.1 to 1 mcg/kg/min titrating according to the clinical response and side effects

Anticipated side effects: tachycardia, arrythmias, hypotension and electrolyte disturbance. A few fluid boluses appropriate for weight, will help in blunting the tachycardia.

Magnesium sulphate

Magnesium sulphate is a directly acting smooth muscle relaxant that may be considered for administration in severe exacerbations unresponsive to initial treatments after one hour and as add-on therapy for life-threatening exacerbations. Magnesium sulphate is inexpensive and available widely; its use is also associated with minimal adverse effects.

Dose:

- 25-75 mg/kg(max 2 g) over 20 minutes or
- 10-20 mg/kg /hr for 4 has a short infusion. ٠

Common side effects are hypotension and hypotonia and hence warrants close monitoring. There is insufficient evidence regarding the benefit from continuous infusion of magnesium sulphate.

Theophylline

Theophylline is another good drug for rescue therapy. It is a potent bronchodilator and may also exhibit anti-inflammatory and immunomodulatory actions. improve respiratory muscle function, hasten mucociliary clearance, and act centrally to stimulate respiration. Once very popular, the drug is now less preferred to other

agents with better clinical profiles. However, it is effective in life threatening asthma not responding to maximal doses of bronchodilators and steroids.

Dose:

- 4-6 mg/kg as bolus dose over one hour followed by 0.8-1.2 mg/kg as infusion. Bolus is avoided if patient has received any recent deriphylline derivative.
- 10-20mcg/ml is the therapeutic level

Patients should receive cardiac monitoring during this period, as they are prone to arrhythmias and should remain in "line of sight" of nursing staff.

VENTILATORY SUPPORT

In patients continuing to worsen, endotracheal intubation is often not the answer, and is to be avoided as far as possible. Endotracheal intubation and mechanical ventilation can worsen the situation if not used judiciously. All measures must therefore be taken to manage with pharmacotherapy and non-invasive positive pressure mechanical ventilation (NIPPV) may be considered if necessary. It may buy time for the administered drugs to act. A continuous positive airway pressure (CPAP) or bi-level positive airway pressure (Bi-PAP) machine may also be used.

Indications for Intubation:

Refractory Hypoxemia Impending Respiratory failure, Cardiac arrest Rapidly worsening sensorium

DISCHARGE ADVICE

A child who shows good response to 1-2 doses of bronchodilators and steroids within 2 h of therapy and not requiring further doses can be discharged. All patients seen for an acute asthma exacerbation should have an inhaled short-acting beta-agonist (SABA) available for treatment of symptoms. If the patient has received a dose of steroid, a short course of oral glucocorticoids may be given. The action plan and review date must be clearly explained to the parents. They should be advised to bring back the child immediately in case of any worsening.

COMMON ERRORS TO AVOID

• Nebulization using the electrical nebulizer and not using high flow oxygen can worsen the already compromised oxygenation due to V/Q mismatch.

- Nebulization of child with respiratory distress due to pneumonia or cardiac failure without treating primary cause is ineffective and is often detrimental.
- Continuing to treat based on initial assessment of severity without reassessment is to be avoided. Treatment is guided by repeated assessments.

TAKE HOME MESSAGES

- Recognize asthma correctly since "all that wheezes is not asthma".
- Salbutamol can precipitate hypoxia in children with respiratory distress and wheeze due to asthma mimics. Nebulisations are to be given only with high flow oxygen.
- Determine severity of the asthmatic exacerbation on arrival.
- Every intervention should be followed by a rapid cardiopulmonary assessment to determine the next step in the protocol.

References

1. "World Health Organization Fact Sheet Fact sheet No 307: Asthma". 2011.

2. Matthew Mazola, Denise Fabian et. al., Global burden of asthma, GINA Report 2015

3. Causes of asthma and trigger factors, GINA 2015, http://www.ginasthma.org

4. Controlled trial of oral prednisone in the emergency department treatment of children with acute asthma.Scarfone RJ, Fuchs SM, Nager AL, Shane SA Pediatrics. 1993;92(4):513PIS

5. The Royal Children's Hospital Melbourne guidelines available

 $athttp://www.rch.org.au/clinicalguide/guideline_index/Asthm a_Acute/$

6. Beta-agonists through metered-dose inhaler with valved holding chamber versus nebulizer for acute exacerbation of wheezing or asthma in children under 5 years of age: a systematic review with meta-analysis.AUCastro-Rodriguez JA, Rodrigo GJPediatr. 2004;145(2):172.

7. Acute Bronchial Asthma; Grover S, Jindal A, Bansal A, Singhi S C; Indian J Pediatr May 2011

8. British Thoracic Guidelines 2009

9.Pediatric Emergency Care -2009 ;25(10):687-82

10. Royal Children's Hospital, Melbourne guidelines.