

It has been shown beyond doubt that the backbone of asthma pharmacotherapy is inhalation therapy. All national and international guidelines advocate inhaled medication during acute exacerbations and for the long-term management of asthma severity of all grades.

Devices used to administer inhalation therapy are pressurized metered dose inhalers (pMDIs), dry powder inhalers (DPIs), breath actuated inhalers (BAIs) and nebulizers. Whereas the use of nebulizers is best restricted to the management of acute exacerbations, the other devices can be used both for chronic stable asthma and for acute exacerbations.



According to the Global Initiative for Asthma 2011 guidelines for children of all age groups, the recommended inhaler device is a pressurized metered dose inhaler (pMDI) + spacer, and for children younger than 4 years, pMDI + spacer + mask. Several studies have shown that a pMDI along with a spacer is as therapeutically effective as a nebulizer for controlling moderate to severe exacerbations.

Nebulizers are used and abused in clinical practice. This article highlights the advantages and limitations of nebulizer therapy in clinical practice.

### Basics of nebulizer

A nebulizer aerosolizes the drug in liquid form, using compressed air or oxygen, vibrations from an ultrasonic energy source or, more recently, a vibrating mesh. The liquid drug is put in the nebulization chamber, which is then attached to the compressor with the help of a connecting tube. A mask or a mouthpiece attached to the chamber facilitates inhalation.

A nebulizer is best used by children and adults suffering from acute exacerbations of asthma. It is also useful in very young children and elderly subjects with chronic persistent asthma, who can not use any other inhaler device for want of sufficient inspiratory flow or can not hold their breath for more than a few seconds.

### Nebulizer drugs

The liquid used for nebulization may be of two types:

- Solutions containing a drug, which is

homogeneously dissolved in saline or another respirable liquid.

- Suspensions containing small particles of insoluble drugs suspended in liquid. Currently, bronchodilators, steroids, mucolytics and antibiotics are available for nebulization.

### Nebulization during acute asthma

During an acute exacerbation of asthma, depending upon the severity, we can use a pMDI + spacer or a nebulizer to deliver a bronchodilator. It is preferable to nebulize, if SpO<sub>2</sub> is below 92%. In such a case, it is preferable to connect the nebulization chamber to oxygen supply at a rate of 6-8 litres per minute so that the bronchodilator is delivered along with oxygen.

**Note:** When managing a COPD exacerbation, never connect the nebulizer to the oxygen source. Oxygen should always be given at a low flow rate of 1-2 litres per minute in COPD. This flow rate is insufficient to generate sufficient aerosol for nebulization.

To nebulize, break one respule of Salbutamol or Salbutamol + Ipratropium combination.

Add contents to the nebulization chamber. Add 2 cc of normal saline to the chamber to achieve the fill volume and nebulize for at least 15 minutes. If there is no improvement in condition, repeat not more than twice more within one hour, along with other recommended treatment.

Monitor SpO<sub>2</sub>, pulse, BP and RR. We should be particularly vigilant for arrhythmias and hypokalemia while nebulizing with bronchodilators.

### Practical tips

- The volume of drug solution must not exceed the maximum fill volume. Fill volume (optimal volume of the drug to be put in the nebulization chamber) differs from nebulizer to nebulizer and ranges from 2 ml to 4 ml.
- A respule contains prediluted drug ready for use. Break the respule and pour the liquid drug into the nebulization chamber.
- A respiratory solution contains the drug in concentrated form. It must be diluted in the ratio of one part of drug solution to three parts of normal saline, without exceeding the fill volume.

DRUGS AVAILABLE FOR NEBULIZER		
Drug	Drugs available as	Dose
<b>Bronchodilators</b>		
<b>β<sub>2</sub> Agonists</b>		
Salbutamol/Albuterol	Respules	1 mg/ml (2.5 ml and 5 ml)
	Respirator solutions	1mg/ml, 2mg/ml, 5mg/ml, 5mg/2.5 ml
Levosalmotamol	Respules	0.31 mg/ 3 ml, 0.63 mg/ 3 ml, 1.25 mg/ 3 ml
Arformoterol	Respules	15mcg/2ml
<b>Anticholinergics</b>		
Ipratropium	Respules	250 mcg/ml and 500 mcg/ml
	Respirator solutions	250 mcg/ml and 500 mcg/2.5 ml
<b>Corticosteroids</b>		
Fluticasone propionate	Respules	0.25 mg/ml
Budesonide	Respules	250 mcg and 500 mcg per ml ( 2 ml vials)
<b>Mast Cell Stabilizer</b>		
Cromolyn Sodium	Respirator solutions	10 mg/2 ml
<b>Combinations</b>		
Salbutamol + Budesonide	Respules	Salbutamol sulphate 2.5 mg, Budesonide 0.5 mg/2.5 ml and Salbutamol sulphate 2.5 mg, Budesonide 1 mg/ 2.5 ml
Levosalmotamol + Ipratropium	Respules	Ipratropium bromide 500 mcg, Levosalmotamol 1.25 mg/2.5 mL.
Salbutamol + Ipratropium	Respules	Salbutamol 2.5 mg + Ipratropium 0.5 mg/ 2.5 ml
<b>Mucolytics</b>		
Ambroxol	Respules	7.5 mg/ml
N-Acetylcysteine	Respules	20% w/v 2 ml and 5 ml
<b>Antibiotics</b>		
Tobramycin	Respules	300 mg / 5 ml
Colistimethate sodium	Vial	1 million units powder to be reconstituted with 2-4 ml of 0.9% normal saline

- Maintain optimal driving gas flow rate for nebulization at 6–8 litres per minute.
- The ideal duration of nebulization is 15 minutes.
- There is a spluttering sound when the volume of the liquid drops. Continue to nebulize for about a minute after the spluttering begins. Tap the nebulization chamber to increase the mist output.
- Residual volume is the volume of liquid drug remaining in the nebulization chamber after nebulization. Lower the residual volume of a nebulizer, lesser is the fill volume required. If the residual volume is less than 1 ml, a fill volume of 2–2.5 ml may be adequate. Nebulizers with residual volumes of more than 1ml generally require fill volumes of 4 ml.
- It is preferable to use a mouthpiece instead of a facemask. With the mask, the drug is more likely to leak and enter the eyes or remain on the facial skin
- A facemask should be preferred for children too young to use a mouthpiece, or if the patient is too unwell or can not co-operate.
- Do not use a nose clip while using the mouthpiece. It is inconvenient and uncomfortable. There is no strong evidence to support the use of a nose clip.
- Watch out for adverse effects after nebulization:
  - Nebulized ipratropium can cause ocular complications if it enters in the eye.
  - Nebulized steroids can cause bruising, hoarseness and candidiasis of the mouth and throat (thrush) in some patients.
- Advise patient to wash face and rinse mouth with water after nebulization.

### Cleaning the nebulizer

Nebulizers must be cleaned regularly to avoid crystallization and the growth of microorganisms in the residual liquid in the nebulizer, which could lead to cross infections.

Do the cleaning in a dust- and smoke-free area away from open windows.

1. After each treatment, rinse the nebulizer cup with warm water, shake off excess water and let it air dry.
2. At the end of each day, wash the nebulizer cup and mask(or mouthpiece) in warm, soapy water using a mild detergent. Rinse thoroughly and allow to air dry.
3. There is no need to clean the tube that connects the nebulizer to the air compressor.
4. Every third day, disinfect the equipment after washing it.

### Disinfecting the nebulizer

The Cystic Fibrosis Foundation Consensus Conference on Infection Control (*Nebulizer use and maintenance by cystic fibrosis patients: a survey study. Respiratory care; December 2004, Vol 49, No 12*) mentions various methods for disinfection:

- Soak the nebulizer in a mixture of 1 part bleach to 50 parts water for 3 minutes
- Soak the nebulizer in 70% isopropyl alcohol for 5 minutes
- Soak the nebulizer in 3% hydrogen peroxide for 30 minutes.



However, the most common method propagated by equipment manufacturers is to use vinegar solution for disinfection. (Mix ½ cup white vinegar with 1½ cups of water. Soak the equipment for 30 minutes and rinse well under a steady stream of water. Shake off the excess water and allow to air dry on a paper towel).



The Guideline for Disinfection and Sterilization in Healthcare Facilities, Issued by the Centre for Disease Control, USA in 2008 also suggests Glutaraldehyde 2% solution for 20 minutes as an effective disinfection procedure which we follow at CRF.

The latest agent that is being studied as an effective disinfectant is Squamaline which promises to be an easy to use and highly effective method for disinfection of nebulizers in future. (*Ref. Soluble squalamine tablets for the rapid disinfection of home nebulizers of cystic fibrosis patients. Djouhri-Bouktab L, et al, J Cyst Fibros. 2012 Jun 22. [Epub Ahead of print]* )

Always allow the equipment to completely dry before storing in a plastic, zipper storage bag.

The nebulizer should be run empty for sometime before the next use after cleaning.

### COMPRESSOR CARE

1. Cover the compressor with a clean cloth when not in use. Wipe it with a clean, damp cloth, when necessary.
2. Do not put the air compressor on the floor either for treatment or for storage.
3. Check the air compressor's filter as directed. Replace or clean according to the directions from the equipment supplier.
4. Always keep an extra nebulizer cup and mask or mouthpiece.
5. Store medicines in a cool, dry place. Check them often. If they have changed colour or formed crystals, discard and replace with new stock.

### Home nebulization - The double edged sword

Keeping a nebulizer at home has become a bit of a fashion these days. More so in families with children, who have attacks of breathlessness or wheeze for which their pediatricians nebulize them with bronchodilators in the clinic, without initiating controller therapy with inhaled corticosteroids.

After repeated visits to such a pediatrician, the parents make a “smart” decision to buy a nebulizer to treat their child's breathlessness conveniently at home. Some pediatricians advise the parents, in good faith, to purchase a nebulizer and keep it at home.

But, do parents realize the harm they are doing to the child by bringing a nebulizer home?

Murphy and Holgate reported in 1989 that though most patients think that they benefit greatly from using nebulizer treatment at home, there is a need for better selection of patients along with regular monitoring of their treatment. Almost 34% of patients reported that in case of treatment failure, they would still continue to take nebulizations as many did not have any help at home in case of any emergency. Almost 15% admitted to exceeding the recommended dose. (*The use and misuse of domiciliary nebulizer therapy on the Isle of Wight. Murphy D, Holgate ST. Respir Med. 1989 Jul;83(4):349-52.*)

### Hazards of home nebulization

- Nebulizers deliver unnecessarily high doses of the drug. A pMDI + spacer delivers a much lower dose but still achieves the same result.
- Drug wastage is high.
- There is increased chance of ocular side effects if short acting anti-muscarinic agents like ipratropium are used with a mask.
- Nebulized steroids when delivered using a mask may lead to thinning of the skin.
- Nebulizers give parents a false sense of security that they are well equipped to handle any emergency.
- Most importantly, repeated attacks of asthma with uncontrolled airway inflammation leads to airways remodeling. Over a period, this will render the child's bronchoconstriction non-responsive to the conventional method of treatment. The child may grow up into an adult with severe asthma.

In conclusion, we would like to reiterate that nebulizers are very good devices to deliver inhaled bronchodilators in cases of emergency but day-to-day use of nebulizer at home by patients should be strongly discouraged. **In fact, the goal of asthma management should be to control the child's asthma so well that there should be no need to use a nebulizer.**