
*THE MALAYSIAN THORACIC SOCIETY*

# The Malaysian Thoracic Society Recommendations on Inhalational Therapy During the COVID-19 Pandemic

5 April 2020

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## Introduction

- Nebulisation therapy is commonly prescribed when patients present to the emergency department (ER)/clinic with acute exacerbation of obstructive airway diseases (e.g. asthma, COPD, bronchiectasis, etc)
- Aerosols generated during this procedure will disperse to the surrounding environment.
- This increases the risk of spreading airborne/droplet-mediated infectious diseases, e.g. COVID-19, SARS, MERS, etc.
- Therefore, nebulisation should be avoided, particularly in healthcare facilities during a pandemic

## Objectives

- To provide alternative approaches of inhalational therapy for patients with acute exacerbation of obstructive airway diseases, e.g. asthma, COPD, etc.
- To provide scientific evidence supporting these alternative approaches
- To provide practical steps in implementing these alternative approaches

## What are the alternatives to nebuliser?

### i. Use pMDI/DPI alone (without a spacer)

- For patients with *satisfactory inhaler technique*, they should be instructed to use their pressurised metered-dose inhaler (pMDI)/dry-powder inhaler (DPI) prescribed.
- Dosage recommendations:
  - Ask the patient to inhale 2 puffs of a bronchodilator (salbutamol/terbutaline or fenoterol + ipratropium bromide) initially

- If the response is inadequate, the patient can be instructed to repeat the same dose every 2 minutes until a satisfactory response is reached or until 6 - 10 puffs of the bronchodilator have been administered.
- If the condition is still not controlled at the end of this "first-round" therapy, repeat the above treatment steps and consider admitting this patient.
- If the condition is better controlled, the patient can be instructed to use 2 puffs of the bronchodilator every 20 minutes for another hour before discharge from the clinic.
- After that, the patient should be instructed to take 2 puffs of the bronchodilator every 4 - 6 hours for another 2 - 3 days before going back to their regular reliever dose and controller medication(s).

**Remarks:**

- In addition to the bronchodilator, patients should be prescribed a course of oral *prednisolone* (0.6 mg/kg, max. 50 mg od) for another 5 - 10 days.
- In severely breathless patients, supplementary oxygen should be given via nasal prongs while inhaled bronchodilators are administered

**ii. Use pMDI with a spacer**

- For those who *cannot use pMDI alone*, either because of poor inhaler technique, severe dyspnoea or any other reasons, they should be instructed to use **pMDI with a spacer**

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**Evidence supporting this alternative approach**

1. In a systematic review with meta-analysis performed by *Jose et al.* children under 5 years of age who presented with acute exacerbation of asthma or wheezing did better when they received $\beta$ 2-agonist via the pMDI + VHC compared to the control group who received the same drug via nebulisers. Those in the MDI + VHC group were less likely to require hospitalisation (OR 0.42, 95% CI 0.24-0.72, P=0.02) and had improved clinical score (standardiSed mean difference, 0.44; 95% CI, 0.68 to 0.20; P = .0003)

2. In a Cochrane review by *Cates et al.*, where 2295 children and 614 adults were drawn from 27 trials which included patients from the emergency room and community settings, methods of $\beta$ 2-agonist delivery (either pMDI + VHC or

nebuliser) did not appear to affect hospital admission rates. Length of stay in the ER for children was significantly shorter when the VHC was used, with a mean difference of - 0.53 hours (95% CI: -0.62 to -0.44 hours).

3. Compared with nebulised therapy, *Hendeles et al* showed that pMDI + VHC offered practical advantages over nebulised therapy, including the capacity for home use by the patient, portability, less setup time, and required less maintenance (no need for daily disinfection).

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**Types of spacers**

A spacer is a tube/extension device that adds space or volume between the inhaler and the mouth to overcome poor *hand-breath coordination*.

**Valved- or Non-valved Spacer**

They can be divided into 2 main types:

*i.* *Non-valved Spacer*

- It is a simple tube which adds space and volume between the pMDI and mouth
- There is **no** one-way valve to contain the aerosol plume after pMDI actuation
- The volume for this type of spacer is typically about 100 ml
- As a result of this, only the *single-breath manoeuvre* technique should be used

*ii.* *Valved-Spacer or Valve-Holding Chamber (VHC)*

- It is a spacer with a **one-way valve** incorporated in the mouthpiece/mask
- This allows the aerosols to be inhaled and not exhaled into the spacer
- The volume for this type of spacer is typically between 100 - 700 ml
- This design allows the aerosols to be delivered with the *tidal-volume manoeuvre* as well as the *single-breath manoeuvre*

**Volumes of Spacer**

iii. The volumes of commercially-made spacers are typically between 100 - 700 ml and a distance of ≥ 10 cm is kept between the pMDI and the patient's mouth.

iv. Arbitrarily, the volumes of the spacers can be divided into the following categories:

- Small-volume Spacers (≤ 100 ml)
  - They are usually used for small-sized children with a valve-incorporated at the facemask (VHC).
  - If non-valved spacers are used, small volume spacers are recommended (where the *single-breath manoeuvre* can be more effectively deployed).
- Small to Medium-volume Spacers (100 - 350 ml)
  - These spacers usually incorporate a unidirectional valve at its mouthpiece
  - They are recommended for older children
- Medium to Large-volume Spacers (350 - 700 ml)
  - These spacers usually incorporate a unidirectional valve at its mouthpiece
  - They are recommended for older children or adults
- Very Large-volume Spacers (> 700 ml)
  - They are bulky and hence less portable.
  - As a result, these spacers are getting less popular.

**Interfaces of Spacer**

- There are 2 types of interface for the spacers

i. Face Mask/Oro-nasal mask

- This type of interface is recommended for young children and sometimes older children/adults who prefer this interface
- The mask chosen should cover the nose and mouth completely, but should not be too big (*to reduce the anatomical dead space)

ii. Mouthpiece

- Appropriate for children older than 5 years old and adults

## Materials of Spacer

They can be divided into 2 categories:

i. ***Non-conducting*** materials, e.g. plastic, polycarbonate and polymer

- They are susceptible to electrostatic charging of their inner surface which attracts the aerosols and reduces the dosage delivered to the patient.
- Hence, priming of new spacers made from these materials is required. Besides, the inner surface should not be rubbed during cleaning
- Some commercially-made spacers are coated with an antistatic inner lining to reduce the electrostatic charges

ii. ***Conducting*** materials, e.g. aluminium and steel

- The electrostatic charges generated can be discharged quickly by touching the wall of these spacers
- Therefore, priming of inhaled drugs is not required
- Besides, cleaning can be made with a brush or cloth

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## Dosages Recommendations (for pMDI + Spacer)

- For new spacers, prime them with 4 puffs of a bronchodilator to reduce the effect of electrostatic charge on the inner wall
- After that, the patient is asked to inhale the bronchodilator with his/her mouth via the spacer's mouth nozzle/oro-nasal mask attached to the spacer.
- Actuate one puff of a bronchodilator (salbutamol/terbutaline/fenoterol ± ipratropium bromide) at a time, followed by another puff after an interval of 15 - 30 seconds.
- If the response is inadequate, repeat the above sequence every 2 minutes until a satisfactory response is reached or until 6 - 10 puffs of bronchodilator have been administered.
- If the condition is still not controlled at the end of this "first-round" therapy, repeat the above treatment steps and consider admitting this patient.

- If the condition is better controlled, the patient should be instructed to use 2 puffs of bronchodilator every 20 minutes for another hour before discharge from the clinic.
- After that, the patient should be instructed to take 2 puffs of the bronchodilator every 4 - 6 hours for another 2 - 3 days before going back to their regular reliever dose and controller medication.

  **Remarks:**

  - In addition to bronchodilator, patients should be prescribed a course of oral prednisolone (0.6 mg/kg, max. 50 mg od) for another 5 - 10 days.
  - In severely breathless patients, supplementary oxygen should be given via nasal prongs while inhaled bronchodilators are administered

**Dose conversion: Nebulisers versus Spacers**

- Equivalent dose conversions from *conventional nebuliser* to *pMDI + Spacer* are proposed in the table below as a general guide. The actual delivered dose may vary depending on the pMDI and type of spacer used.

**Table 1: Equivalent dose conversions**

| Medication | Dosage for Nebuliser Solution | MDI equivalent dose (with spacer) |
|---|---|---|
| Salbutamol | 2.5 mg | 3 - 5 puffs |
| | 5.0 mg | 5 - 10 puffs |
| Ipratropium bromide | 0.25 mg | 2 puffs |
| | 0.50 mg | 4 puffs |
| Budesonide | 0.25 mg | Fluticasone (125µg) 2 puffs |
| | 0.50 mg | Fluticasone (125µg) 4 puffs |

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**How to use the spacer with the pMDI?**

- Before using the spacer with the pMDI, there are two matters to decide:

i. What interface to use? (mouthpiece or oro-nasal mask?)

   a. If the mouthpiece is used, place the mouthpiece between the teeth and seal with the lips

   b. If the oro-nasal mask is used, place the mask over the face to cover the nose and mouth firmly

ii. Which manoeuvre to use? (tidal-volume manoeuvre or single-breath manoeuvre?)

   a. If valved-spacer (VHC) is used - either the *tidal-volume manoeuvre* or the *single-breath manoeuvre* can be used

   b. If non-valved spacer is used - only the *single-breath manoeuvre* should be adopted

- The following steps are recommended when pMDI is used with a spacer:

**Table 2: Steps when pMDI is used with a Spacer**

| | Common initial steps |
|---|---|
| 1. | Shake the inhaler |
| 2. | Remove the inhaler cap |
| 3. | Assemble the inhaler nozzle to the MDI receptacle of the spacer |
| 4. | Prime the spacer with 4 puffs of drugs if the spacer is new or after cleaning.<br><br>(**Note:** Priming is only required for spacers made from non-conducting materials. It is not required for spacers with conducting wall) |
| 5. | Ask the patient to sit upright |
| 6. | Ask the patient to exhale as much as he/she can comfortably do so<br><br>*Subsequent steps depend on the manoeuvre used: |
| | For the single-breath manoeuvre: |
| i. | Actuate the inhaler (1 puff at a time) and ask the patient to breathe in |

| | |
|---|---|
| | slowly (4 - 5 seconds) without producing any whistling sound |
| ii. | Hold the breath for 10 seconds |
| iii. | Deliver the 2nd and subsequent doses of the drug (as prescribed) by repeating the same sequence after an interval of 15 - 30 seconds |
| | **Remarks:**<br>● *Do not actuate multiple doses* together into the spacer and inhale them all at once.<br>● *Rinse the mouth if inhaled corticosteroid* is used |
| | For the *tidal-volume manoeuvre*: |
| i. | Actuate the inhaler (1 puff at a time) and ask the patient to breathe in and out through the interface without producing any whistling sound |
| ii. | Keep the mask over the face and ask the patient to breathe in and out for 5 breaths before removing the mask. |
| iii. | Deliver the 2nd and subsequent doses of the drug (as prescribed) by repeating the same sequence after an interval of 15 - 30 seconds |
| | **Remarks:**<br>● *Do not actuate multiple doses* together into the spacer and inhale them all at once.<br>● *Rinse the mouth if inhaled corticosteroid* is used |

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## Frequently-Asked Questions (FAQs)

### Can spacers be shared?

- We recommend that spacers **should not** be shared
- There is a potential risk of spreading infection from one user to other users, even with disinfection
- In situations where spacers need to be shared as a result of scarce resources, a stricter and higher standard of disinfection should be embraced (refer to the section on "*How to clean and disinfect the spacers*" below)

**Can inhalers be shared?**

- We recommend that inhalers should not be shared
- In situations where sharing of inhaler become unavoidable, proper disinfection should be adopted (refer to the section on "*How to clean and disinfect the inhaler*" below)

**What if my patient cannot afford the commercial spacer?**

- Options may include home-made/custom-made spacers with plastic bottles/toilet roll
    - These devices may still serve the purpose of providing a space between the pMDI and mouth to overcome poor hand-breath coordination
    - However, their performance is **highly variable**:
        - The size and shape of these bottles have not been tested with a particular type of inhaler to identify the ideal combination.
        - Besides, the electrostatic charge on the device wall will reduce the dose of the inhaled aerosols delivered to the patient
        - The absence of a one-way valve in the bottle cannot ensure the flow of aerosols only happens in one direction. Rebreathing via this spacer leads to contamination of the spacer's wall with moisture in the breath
        - Therefore, only the *single-breath manoeuvre* should be used when these spacers are used
- **Remark:** They should not be considered an equivalent replacement of the commercially manufactured spacers and should only be used when there is no suitable option available.

**What is the best valved-spacer (VHC)?**

- As VHC design has become more sophisticated and understanding of clinically relevant testing conditions has evolved, emphasis has shifted from the size and shape of the spacers to other aspects of performance, such as consistency of drug delivery under a variety of test conditions, the influence of conducting or charge dissipative materials, and the factors influencing facemask performance

**How to clean and disinfect spacers?**

- Commercially-made spacers should be cleaned and disinfected according to the manufacturer recommendations. The following outline the general principles involved:
- *Cleaning of spacers*
    - Cleaning alone is adequate if the spacer is not going to be shared
    - Steps involved:
        i. Disassemble the spacer before cleaning.
        ii. Wash the separate components with warm soapy water.
        iii. Soak them in clean water for 15 minutes.
        iv. Rinse them thoroughly with sterile water and air-dry prior to reassembly.
        v. (Note: *sterile water* includes water that is manufactured commercially or water that has been boiled for five minutes).
- In situations where sharing of spacers becomes unavoidable due to the lack of resources, a higher standard of disinfection than that recommended by the product brochures should be embraced.
- There is inadequate data to suggest what is the best high-level disinfection. The following disinfection techniques have been reported in the literature:
- *Disinfection of spacers*
    - In this situation, apart from cleaning the disassembled components with warm soapy water, they should be disinfected with one of the following methods:
        i. Soak the components for 5 minutes in ViruSolve + EDS solution for 5 minutes; rinse with sterile water and air dry after that
        ii. Dishwasher with a heat cycle of 158 $^{0}$F/ 70 $^{0}$C for 30 minutes; air dry after that
        iii. Soak in 3 percent hydrogen peroxide for 30 minutes; rinse with sterile water; air dry after that

- For spacers made of **metallic materials**, 2 additional disinfection techniques can be used:
    i. Rolling boil for five minutes (set timer when boil starts); air dry after that
    ii. Countertop baby bottle steriliser. No need to rinse with sterile water; air dry after that
- **Remark:** For patients who are on isolation precautions, their spacers must never be shared.

**How to clean and disinfect inhalers?**

- We recommend that individual inhaler should not be shared
- However, in situations where sharing of inhalers becomes unavoidable, proper disinfection should be adopted.
- The inhaler consists of 2 components: the plastic body with nozzle and the canister containing the drug
- We recommend that the inhaler nozzle and the canister be wiped with an alcohol swab/pad before and after each usage.
- **Remark:** For patients who are on isolation precautions, their inhaler devices must never be shared.

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**Can I administer inhaled drugs to patients on endotracheal intubation?**

- In order to prevent the dispersion of aerosols to the environment, ventilation of all intubated patients should be performed in a closed-circuit system.
- Inhalational drugs can be delivered via this system with some adaptation of the circuit.

**Can I administer inhaled drugs to patients on non-invasive ventilation (NIV)?**

- We recommend that NIV should be performed in an isolation room, preferably with a negative-pressure set-up during the pandemic

- For patients who require inhaled bronchodilator therapy during NIV, the latter can be interrupted temporarily, be supplemented with nasal oxygen, while the inhaled drug is delivered with a pMDI + a spacer.

**What if nebulisation cannot be avoided?**

- Acute exacerbations of asthma, COPD, bronchiectasis, etc often result in airway obstruction requiring nebulised bronchodilator therapy.
- However, nebulisation results in the generation of aerosols, with the risk of spreading SARS-CoV-2 virus
- Thus, we should **AVOID** nebulisation for any patient in the ER/clinics/wards, particularly in the non-isolation room
- In situations where nebulisation cannot be avoided, it SHOULD ONLY be carried out in a single-isolation room, preferably that with a negative-pressure setting
- In order to reduce transmission, the patient should be instructed to use the nebuliser after the healthcare worker has left the room
- Before healthcare providers enter the single-isolation room, they should wear personal protective equipment.

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**Contributors**

- Pang Yong Kek
- Asiah Kassim
- Wong Jyi Lin
- Kuan Yeh Chunn
- Hilmi Lockman
- Hooi Lai Ngoh
- Tie Siew Teck
- Jessie Anne De Bruyne
- Roslina Manap
- Liam Chong Kin
- Nurhayati Mohd Marzuki
- Ong Choo Khoon
- How Soon Hin
- Helmy Nadine Haja Mydin
- Lem Li Khen
- Norhaya Mohd Razali
- Kumaresh Raj Lachmanan

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