

# PALLIATIVE PEARLS

BY ENCLARA PHARMACIA

## Inhaled Therapy Case: Selecting the Best Device & Mixing Nebs

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### Patient Case

DP is a 72 year old female with a primary diagnosis of COPD and comorbidities of CHF, hypertension, obstructive sleep apnea, seizures, depression and neuropathic pain. Allergies include anaphylactic reaction to amitriptyline, bee venom and diphenhydramine and skin rash with sulfa drugs. Current medications pertinent in managing COPD and respiratory congestion:

- Albuterol 0.083%; 1 vial via nebulizer inhaled Q.I.D. as needed for shortness of breath
- Atropine 10mg/ml oral compounded suspension; 2 drops SL every 4 hours as needed for excess secretions
- Budesonide 0.25mg/2ml; 1 vial via nebulizer inhaled BID for shortness of breath
- Combivent Respimat® (albuterol-ipratropium); Inh 1 puff Q.I.D. for shortness of breath
- Duoneb® (albuterol-ipratropium); 1 vial via nebulizer inhaled Q.I.D. for shortness of breath
- Sodium chloride 0.9%; 1 vial via nebulizer inh every 4 hours for respiratory congestion

DP has increased chest congestion with cough. She has been using over the counter Robitussin® (guaifenesin) syrup around the clock for the past 2 days with sodium chloride via the nebulizer without relief. DP's physician is considering replacing sodium chloride with acetylcysteine via the nebulizer. How can you ensure that DP is effectively administering her respiratory therapies?

### **COPD MANAGEMENT CHALLENGES<sup>1,2</sup>**

COPD is primarily treated by the use of inhaled medications. A patient's age and stage of disease affects the extent to which inhaled medications reach the small airways most commonly affected by COPD. Advanced age changes the compliance of the chest wall, along with reduced respiratory muscle strength. In addition, age-related physical and cognitive impairment greatly affects treatment outcomes.

There are currently more than 200 inhaler products on the market making it difficult to know which product to choose. Assessment of inhaler administration technique should be performed at baseline and regular intervals to ensure that the device continues to meet patient needs.

The three most important factors affecting drug deposition in the airways are: (1) patient inhalation flow, (2) aerosol velocity and (3) inhaled particle drug size. The ability of the patient to achieve the correct inhalation flow is very important to get the desired benefit from the inhalation device. COPD is characterized by chronic inflammation of the airways that reduces airflow and impedes medication distribution. For inhaled medication to be effective, it must be deposited beyond the oropharyngeal region and distributed in the bronchial tissue. Factors that determine medication effectiveness include

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the size of the medication particles, breathing and airway conditions, and the ability of the cilia to clear mucus.

### **SELECTING THE BEST DEVICE FOR INHALED MEDICATIONS<sup>3</sup>**

Treatment of pulmonary disease should be customized to the patient. Although handheld inhaler devices are the most rapid and convenient way of delivering medication, many hospice patients lack the physical skill or cognitive ability to use them correctly. For those with advanced pulmonary conditions, successful medication administration from metered-dose inhalers (MDIs), dry-powder inhalers (DPIs) or soft-mist inhalers (i.e., Respimat) are impacted by inspiratory effort and breath control. When patients cannot use inhalers properly, the therapy does not reach the lungs, leading to poorly managed symptoms.

Once set up, nebulizers are easier for patients to use and allow for the inhalation of the medication using normal breathing, thereby ensuring proper delivery to the lungs. Unlike handheld inhalers, nebulizers do not require the patient to coordinate activation of the device with inspiration, nor does the patient need to hold their breath to deposit the medication in their lungs.

Nebulized treatments with albuterol, or albuterol with ipratropium, are good alternatives to handheld inhalers. Furthermore, for those with advanced pulmonary disease, oral corticosteroids such as prednisone are more effective than inhaled corticosteroids and may also help appetite and fatigue.

#### **Handheld Inhaler Devices<sup>4-6</sup>**

**Metered dose inhalers (MDI)**, such as Ventolin HFA<sup>®</sup>, Proventil HFA<sup>®</sup>, Symbicort<sup>®</sup>, Xopenex HFA<sup>®</sup> and QVAR<sup>®</sup>, use a pressurized aerosol canister containing medication dissolved or suspended in a liquefied gas propellant. The advantage of these devices is their small size (portable).

**Dry-powder inhalers (DPIs)**, such as Spiriva Handihaler<sup>®</sup>, Advair<sup>®</sup> Diskus, Foradil<sup>®</sup>, Serevent<sup>®</sup> Diskus are propellant-free, breath-activated devices for inhaling dry powder. They are small and portable but are complex to use. For example, opening the moisture resistant capsule packets of Spiriva handihaler<sup>®</sup> are difficult for patients with dexterity issues and it requires an eight step process to prep the inhaler properly.

**Soft Mist inhalers**, such as Combivent Respimat<sup>®</sup> and Spiriva Respimat<sup>®</sup>, are propellant-free, liquid multi-dosed inhalers. The inhaler forms an aerosol cloud with a higher fraction of fine medication particles than the MDIs and DPIs and inhalation using the Respimat depends less on inspiratory flow. There is less coordination needed than the MDIs, but they still require some degree of hand-breath coordination.

#### **Nebulization Devices<sup>7-9</sup>**

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Nebulizers deliver atomized particles of drug to the airways. Most require a power source but some are battery-operated or have a car plug-in adapter. All types can be used with a mouth piece and mask - both are considered equally effective. Face masks are useful in children and situations where the patient is unable to hold the mouth piece. Mouth pieces are recommended with steroids and anticholinergics to lessen exposure to the face and eyes.

**Jet nebulizers** work by compressing gas thru a narrow orifice and creating a low pressure that passes over a narrow tube. This forms small droplets of medication that will become aerosolized. The air compressor is loud and they tend to be heavy and hard to transport. They are low cost and easy to use.

**The ultrasonic nebulizer** uses a power source to rapidly vibrate an electrically polarized crystal within the reservoir of drug solution or suspension. Small droplets break free from the standing waves on the surface of the liquid and become aerosolized. These nebulizers are silent, smaller, quicker and perfect for transport, however tend to be more expensive.

**The mesh nebulizer** forces liquid medications through multiples openings in mesh in order to form an aerosol. They are battery or electric-powered, small, portable, quiet and provide quicker administration however there is a lack of efficacy data published supporting use.

### INDICATIONS FOR NEBULIZED THERAPY VS. HANDHELD INHALERS

Assess the person's ability to use their handheld inhalers and consider the following questions:

- Is the person frail and debilitated with poor inspiratory effort and/or unable to hold their breath for up to 10 seconds?
- Is the person unable to coordinate their breath during inhalation?
- Does the person have inadequate symptom relief with their inhaler?
- Do they have cognitive impairment and/or unable to follow instructions?
- Do they have decreased strength, or presence of arthritis or joint pain in their hands?

If the answer is YES to one or more of the above, switching the patient from their MDI, DPI or soft-mist inhaler to nebulized therapy is recommended to optimize treatment and reduce symptoms.

**Remember:** The addition of an oral corticosteroid, morphine and/or an anxiolytic such as lorazepam should also be considered to further manage dyspnea.

### SAMPLE SCRIPT FOR COMMUNICATING WITH PATIENTS/CAREGIVERS

- "We often find that people with severe lung disease can't benefit as well from their inhalers like they once did. I'd like to make some suggestions about changing your medications..."
- "Let's begin to address your shortness of breath by adding some low dose morphine to help your breathing before we make any changes to your pulmonary meds."

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- “Now that your breathing is easier with the morphine, I’d like you to consider using nebulized medication instead of your Symbicort®, since I think it will work better for you.”
- “How do you feel about my recommendation to stop your Symbicort® and use your nebs more often instead?”

### COMPATIBILITY AND EFFECTIVENESS OF MIXING NEBULIZER SOLUTIONS<sup>10,11</sup>

Certain medications can be mixed and given together via the nebulizer. This saves time and enables the patient to inhale several drugs at once without the need to clean, reassemble and refill the machine for each individual medication. However, the compatibility and stability of some medications mixed with others is a concern. Mixing medications can also alter the usual particle size, which can change where in the airway the medication is absorbed. Particles that are too large may be deposited in the upper airway and swallowed and not absorbed the lungs. Conversely, particles that are too small may be exhaled and minimally deposited in the airway.

There is limited information on the compatibility of mixing nebulized medications. It is important to watch for clinical response when administering mixed medications. The following list provides known compatibility information for some common nebulized medications. In the absence of information on a medication, avoid combining the medication with others to ensure effectiveness.

#### **Acetylcysteine (Mucomyst®)**

- Compatible with: Arformoterol, budesonide, cromolyn, ipratropium
- Incompatible with: Dornase alfa

#### **Albuterol (Proventil®)**

- Compatible with: Budesonide, cromolyn, ipratropium, tobramycin
- Incompatible with: Dornase alfa

#### **Arformoterol (Brovana®)**

- Compatible with: Budesonide, ipratropium, acetylcysteine
- Incompatible with: Dornase alfa

#### **Budesonide (Pulmicort®)**

- Compatible with: Albuterol, arformoterol, formoterol, levalbuterol, cromolyn, ipratropium, acetylcysteine
- Incompatible with: Tobramycin, dornase alfa

#### **Cromolyn (Intal®)**

- Compatible with: Albuterol, epinephrine, levalbuterol, budesonide, ipratropium, acetylcysteine
- Incompatible with: Tobramycin, dornase alfa

#### **Dornase alfa (Pulmozyme®)**

- Incompatible with: All medications

#### **Epinephrine**

- Compatible with: Cromolyn
- Incompatible with: Dornase alfa

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## **Formoterol (Perforomist®)**

- Compatible with: Budesonide
- Incompatible with: Dornase alfa

## **Levalbuterol (Xopenex®)**

- Compatible with: Budesonide, cromolyn, ipratropium
- Incompatible with: Dornase alfa

## **Ipratropium (Atrovent®)**

- Compatible with: Albuterol, arformoterol, levalbuterol, budesonide, cromolyn, acetylcysteine, tobramycin
- Incompatible with: Dornase alfa

## **Sodium chloride 0.9% solution**

- Compatible with most medications

## **Sodium chloride 3%, 7% & 12% solutions**

- Insufficient evidence to evaluate compatibility with above medications and should be avoided
- Incompatible with: Dornase alfa

## **Tobramycin (Tobi®)**

- Compatible with: Albuterol, ipratropium
- Incompatible with: Budesonide, cromolyn, dornase alfa

## **GUIDELINES FOR ACETYL CYSTEINE ADMINISTRATION VIA NEBULIZER<sup>12-14</sup>**

Acetylcysteine inhalation is used to treat chest congestion and is recommended to be administered via jet nebulizers made of glass, aluminum or plastic. Substances reactive with acetylcysteine in a nebulizer include iron, copper and rubber, so these materials should be avoided. Ultrasonic and mesh type nebulizers should also be avoided due to clogging issues.

The 10% solution (100mg/ml) can be used undiluted but the 20% (200mg/ml) should be diluted with sodium chloride 0.9% solution for injection or nebulizer solution OR sterile water for injection or nebulizer solution. Typically recommended dosing is 3-5ml of the 20% solution or 6-10ml of the 10% solution inhaled via nebulizer 3 to 4 times daily. It can also be used through direct instillation of a tracheostomy tube with a dose of 1-2ml of the 10 or 20% solution administered as often as every hour.

Acetylcysteine may have an unpleasant odor that should dissipate quickly. Once opened, the solution can change to a light purple color but the mucolytic effect doesn't change as a result of this chemical reaction. If used with a face mask, there may be stickiness on the face after nebulization that can be easily removed by rinsing with water.

## **Pharmacist Assessment**

DP has been using the Combivent Respimat inhaler more often than Duoneb via nebulizer because she feels it takes too long to administer, especially considering the multiple nebulizer treatments with

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budesonide and sodium chloride that she uses each day. However, she does admit to getting better symptom relief when using the nebulizer. When reviewing the questions to assess DP's inhaler technique, a "yes" response was assigned to the following:

- Is the person frail and debilitated with poor inspiratory effort and/or unable to hold their breath for up to 10 seconds?
- Is the person unable to coordinate their breath during inhalation?
- Does the person have inadequate symptom relief with their inhaler?

Atropine is an anticholinergic medication that may lessen oral secretions, however, has no effect on new pulmonary secretions. In addition, atropine may be worsening the chest congestion by making pulmonary secretions thicker.

Upon review of DP's current nebulizer therapies, all medication (albuterol-ipratropium, budesonide, sodium chloride 0.9%) are compatible when mixed together, presenting an opportunity to combine treatments. Combining treatments will not decrease administration time in this patient's case but may make it more convenient to administer at once. There is insufficient evidence to evaluate compatibility of acetylcysteine with albuterol. Acetylcysteine is compatible with ipratropium by itself and budesonide.

### Recommendations

- Encourage the use of the Duoneb instead of Combivent Respimat since there is no hand breath coordination required and the amount inspiratory flow needed to inhale the dose is much less. Utilize one of the "sample scripts" to communicate the benefit to DP.
- Discontinue atropine. Considering the use of this medication limited the success of guaifenesin and the sodium chloride 0.9% nebulizer therapy, it is reasonable to continue these therapies, now without the atropine, and assess for symptom relief. If at the end of the trial period DP is still not relieved, Acetylcysteine could be initiated by mixing 3ml (600mg) of the 20% solution diluted with 3ml of sodium chloride 0.9% solution and administer 4 times a day.
- Mix budesonide and Duoneb solutions and nebulize together.

**For additional information on this topic, please review these references:**

Enclara Pharmacia's On Demand Educational Webinar, "Palliative Care of the Patient with COPD". Click [here](#) to log in.

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