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**Respiratory Care Department – Sample Protocol**

**Document Title:** “Nebulized Morphine for Palliative Care”  
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**Author/Contact:** Michael McPeck, BS RRT FAARC

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### **Background Information**

#### **Indications and Usage**

The use of nebulized morphine (and other opioids) has been found to be effective for palliative care to reduce debilitating dyspnea (the conscious perception of breathlessness), paroxysmal cough and severe pain in selected patients with end-stage COPD, terminal cancer or related conditions where curative management is not possible or appropriate. Specific outcomes reported with the use of nebulized morphine include reduced shortness-of-breath, increased exercise tolerance and a subjective improvement in well-being.

#### **Pharmacology and Pharmacokinetics**

- Opioid receptors have been found on sensory nerves arising from all areas of the respiratory tract.
- Locally applied opioids have been shown to inhibit both cough and bronchoconstrictive reflexes, and the antitussive activity of systemically administered opioids has also been inhibited by opioid antagonists that act only at peripheral sites.
- *Nebulized* morphine has a relatively low systemic bioavailability when compared to more direct routes of administration, such as intravenous.
- Rapid appearance of morphine in plasma after nebulization.
- Peak concentrations by nebulization achieved in 10 minutes.
- Plasma concentration at 4 hours essentially the same for all routes (5 mg IV, 10 mg oral, and 50 mg nebulized).

#### **Warnings**

Potentially adverse effects of nebulized morphine (and other opioids) include constipation, nausea and vomiting, sedation and respiratory depression. However, since systemic absorption of nebulized opioids is low, they are relatively safe, even at high doses. Respiratory depression is much less likely to occur when the delivered dose is titrated and bolus administration is avoided.

#### **Precautions**

**Addiction** -- Addiction is generally not a valid consideration in palliative care of terminally ill patients. “Palliative medicine, appropriately, does not recognize the artificially created boundaries of the Medicare hospice benefit. The challenge for health care providers lies in providing individualized, symptom-oriented care with the best resources available.” (Stein & Min. Nebulized morphine for paroxysmal cough and dyspnea in a nursing home resident with metastatic cancer. *Am J Hospice & Palliative Care* 1997; 14: 52-56).

“The obligation to alleviate suffering is an essential component of the clinician’s broader ethical duties to benefit and not harm; it dictates that health professionals maintain clinical expertise and knowledge in the management of pain, even where present educational programs do not provide this.” (Cain and Hammes. Management of Cancer Pain, Clinical Practice Guideline No. 9, 1994).

**Bronchospasm** – Bronchospasm, presumably due to histamine release, is possible with nebulized morphine, particularly in asthmatics and patients with hyperactive airways. Preservative-free (i.e., sulfite-free) morphine should therefore always be used. Patients may be pre-treated with albuterol if bronchospasm becomes a problem.

### **Dosage**

There has been significant dose variation in published studies. It is believed that all the studies have described the amount of drug placed in the nebulizer reservoir at the beginning of the treatment. Drug concentration or addition of diluents has not been uniformly described. Reported “dosages” have ranged from 1 mg to 50 mg. Because most of the studies exhibit poor understanding or description of the aerosol delivery system, the amount of drug actually delivered to the patient can not be estimated.

One factor that seems to be very consistent throughout all the studies is that the frequency of treatments has been Q4 hours.

As with many medications, dose escalation has been reported. Therefore it is recommended to start therapy with the lowest effective dose and then titrate the dosage upwards according to the individual patient's response. Some patients exhibit a “threshold” dosage level at which they begin to perceive relief of symptoms. If therapy is discontinued at lower dosages, the effective threshold may not be discovered. Some treatment failures may be due to failure to deliver a dose at or above the threshold level.

## Recommended Delivery System

Typical inexpensive hospital nebulizers designed to administer bronchodilators are not appropriate for nebulized opioid therapy because they are inefficient, target only upper and central airways, take too long to administer the entire dose and lack exhalation port filtration that protects healthcare workers from inhaling some of the exhausted aerosol. A high efficiency aerosol drug delivery system, specifically designed to deliver special-purpose drugs to targeted areas while protecting the healthcare worker is required for nebulized morphine: The “Medicator<sup>®</sup> Plus Aerosol Maximizer,” # AM-602, is available from:

Healthline Aerosol Medicine  
4610 Littlejohn Street  
Baldwin Park, CA 91706  
Tel: (877) 626-2626; Fax: (626) 960-8700

### Relevant Features:

- Latex-free 1 L. reservoir bag (insures nebulized drug is inhaled rather than vented and wasted; promotes consistency of delivery to reduce variability of response)
- Fine-particle nebulizer Allegiance AirLife Misty Max 10 (MMAD of  $\sim 1.25 \mu\text{M}$  insures appropriate particle size for deposition at both central and peripheral opioid receptor sites)
- Integral Exhalation Port Filter (protects caregivers against breathing exhaled morphine aerosol)



Use of the Medicator Aerosol Maximizer has been described in the peer-reviewed literature:

Laube BL, Benedict GW and Dobs AS. Time to Peak Insulin Level, Relative Bioavailability, and Effect of Site of Deposition of Nebulized Insulin in Patients with Noninsulin-Dependent Diabetes Mellitus. *J. Aerosol Med.* 1998; 11: 153-173.

Laube BL, Jashnani R, Dalby RN and Zeitlin PL. Targeting Aerosol Deposition in Patients with Cystic Fibrosis: Effects of Alterations in Particle Size and Inspiratory Flow Rate. *Chest.* 2000; 118: 1069-1076.

Corcoran TE, Shortall BP, Kim IK, Meza MP and Chigier N. Aerosol Drug Delivery Using Heliox and Nebulizer Reservoirs: Results from an MRI-Based Pediatric Model. *J. Aerosol Med.* 2003; 16: 263-271.

## Protocol

### Policies:

1. A physician's written order stating "Nebulized Morphine Protocol Starting with 4 mg MSO4" is necessary to initiate this therapy. The order must comply with applicable hospital policies and state regulations concerning controlled substances.
2. A medication nurse or pharmacist must draw up the prescribed dose of drug and place it in the nebulizer reservoir supplied by the respiratory therapist who will administer the treatment.
3. A licensed respiratory therapist may administer the medication to the patient via aerosol drug delivery system, but any unused medication must be returned for proper disposal and logging to the nurse or pharmacist who dispensed it.
4. Valid indications for nebulized morphine include patients with end-stage COPD or terminal lung cancer who have advanced directives that include "do not intubate," "do not resuscitate," or "do not ventilate" orders.
5. If the patient develops bronchospasm and wheezing during the nebulized morphine or fentanyl treatment, the treatment will be stopped and 2.5 mg of albuterol sulfate may be administered by SVN and the prescribing physician notified.
6. If it is established that the patient develops bronchospasm and wheezing during opioid nebulization, the respiratory therapist should contact the prescribing physician to have the order changed to allow 2.5 mg of albuterol sulfate to be administered by SVN prophylactically prior to the administration of nebulized opioids. DO NOT mix albuterol and morphine or fentanyl in the same nebulizer. It is better to pre-treat the patient with albuterol and confer protection against bronchial irritation in advance of inhaling the opioid. Also, the additional nebulizer volume of the albuterol will dilute the concentration of opioid in the nebulizer and prolong the nebulization time.
7. Treatments will be given at a frequency not to exceed Q4H (every 4 hours). Between the hours of 11:00 pm and 7:00 am, sleeping patients will not be awakened to receive scheduled therapy although they may request a *prn* treatment if at least 4 hours has elapsed since their last treatment.
8. Attention must be paid to the total volume of solution in the nebulizer reservoir at the start of each treatment. Normal saline solution, quantity sufficient to make a total nebulizer volume of 3 mL, should be added as a diluent to the morphine placed in the nebulizer. The total nebulizer volume should not exceed 3 mL so as to keep treatment time under 10 minutes in order to avoid patient fatigue.
9. The starting "dose" of morphine sulfate placed in the nebulizer ("nebulizer charge"), by protocol, will be 4 mg. Add normal saline diluent as required to bring total volume to 3 mL.
10. Upon subsequent treatments separated by an elapsed time of approximately 4 hours, the dose may be titrated upwards by 2 mg increments as necessary in order to achieve a positive patient response. A positive patient response is defined as the onset of a subjective improvement in shortness-of-breath or pain, within 10 – 15 minutes of the conclusion of the treatment. The subjective improvement should be maintained for at least 4 hours.

11. The maximum allowable “dose” (nebulizer charge) under the protocol is 30 mg. The prescribing physician must be notified when incremented dosage reaches 30 mg. Dosages higher than 30 mg must be specifically prescribed by physician.

12. Only the Healthline “Medicator Plus Aerosol Maximizer” aerosol drug delivery system should be used for administering nebulized morphine in order to achieve an inhaled mass of at least 25% of the nebulizer charge with the appropriate particle size distribution.

### **Equipment and Supplies:**

1. Healthline Medical #AM-602 Medicator Plus aerosol drug delivery system with mouthpiece.
2. Noseclip (optional but recommended)
3. Optional lightweight portless mask if patient can not use a mouthpiece.
4. Optional Medicator Convenience Kit and Pole Mount Bracket to extend mouthpiece or mask
5. Oxygen or Medical Air flowmeter as appropriate.
6. Prescribed drug.
7. Normal saline solution.

### **Procedure:**

1. Verify the exact order in the patient's medical record.
2. Obtain proper dosage of drug and place in nebulizer reservoir. Add diluent as required. Mix.
3. Introduce yourself and ask the patient what his or her name is and check the identification band on the patient's wrist for confirmation.
4. Conduct appropriate patient/family education and explain the specific details of the procedure you are about to have the patient do. Do not use the word “narcotic” with patients or their families; that word has too many negative connotations in our society. Instead, say “pain medication” or “medication to relieve shortness-of-breath.” Depending on the educational assessment of the patient, consider giving a “training treatment” with saline prior to actually giving the first morphine treatment. Check for asthmatic history and prepare to give bronchodilators prophylactically or if bronchospasm develops.
5. Assemble the Healthline Medicator Plus aerosol delivery system making sure that all connections are tight. Attach the nebulizer that has just been filled with the prescribed drug to the nebulizer port on the Medicator manifold and hook up the supply gas source.
6. Ascertain that the appropriate filter is connection to the exhalation port of the Medicator manifold.
7. When the patient is ready to begin inhaling the drug, adjust the air or O2 flowmeter to 7 L/min and allow the patient to begin breathing from the system.
8. Place noseclip on the patient’s nose to encourage mouth breathing only. Coach the patient to breathe slowly and deeply, if possible. Instruct the patient to signal you if he/she wishes to temporarily stop the treatment in order to rest. If possible, turn off the flowmeter just before the mouthpiece or mask is removed

9. Observe the patient for signs and symptoms of adverse reactions to the medication and/or the procedure:

a. If the pulse rate changes by more than 25% during the treatment, stop the therapy, notify the nurse to help monitor the patient, notify the physician to report the adverse reaction, and include the details of the adverse reaction (including who was notified) in your written treatment note.

b. If the patient shows signs of respiratory depression (markedly slow respiratory rate or apnea), stop the therapy, notify the nurse to help monitor the patient, notify the physician to report the adverse reaction, and include the details of the adverse reaction (including who was notified) in your written treatment note. (Note: The physician may order Narcan (Nalaxone) 0.2 mg IV push stat).

c. If bronchospasm or wheezing develops, stop the therapy, notify the nurse to help monitor the patient, notify the physician to report the adverse reaction, and include the details of the adverse reaction (including who was notified) in your written treatment note. If permitted by specific order, standing order, or as part of the hospital-approved nebulized morphine protocol, administer 2.5 mg of albuterol sulfate by small volume nebulizer.

10. At the conclusion of the treatment, assess the patient for achievement of therapeutic outcomes:

a. If applicable, assess the patient for dyspnea or breathlessness according to hospital-accepted dyspnea scale.

b. If applicable, assess the patient for pain according to hospital-accepted pain assessment scale.

c. Although not a therapeutic outcome, assess the patient for the presence or absence of wheezing and bronchospasm.

Include the results of all applicable patient assessments in your written treatment note.

11. At the conclusion of the treatment, any unused medication must be returned to the nurse or pharmacist who dispensed it for proper disposal and logging. Thereafter, rinse out the medication nebulizer reservoir with sterile water and shake as much of the residual water out of it as possible. Dry the nebulizer reservoir and jet with air or oxygen, reattach the nebulizer to the Medicator manifold, and store the entire assembly in a plastic bag labeled with the patient's name and room number.

12. Complete the necessary forms and records for recording patient therapy in the patient's medical record and/or hospital or departmental computerized information system.

## Additional Reading

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Free instructional PowerPoint entitled: "Nebulized Opioids – A Novel Approach to Intractable Dyspnea" by Michael McPeck RRT FAARC is available online at:

[http://www.healthlinemed.com/PPT/Morphine/Nebulized%20Opioids%20\(McPeck\).PDF](http://www.healthlinemed.com/PPT/Morphine/Nebulized%20Opioids%20(McPeck).PDF)

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