Clinical Resource Guide: Nebulized Opioids

OVERVIEW OF NEBULIZED OPIOIDS

Nebulized opioids have been used for breathlessness due to their effect of reducing respiratory drive. There are two proposed mechanisms, including inhibition of acetylcholine release leading to induced contraction of the airway smooth muscle and another mechanism involving activation of opioid receptors associated with pulmonary nerve fibers leading to central neuronal activation. Administration of nebulized opioids has been seen as an attractive option due to the low cost, ease of use, and ready availability. The proposed mechanism of action of inhaled nebulized opioids is binding to the intrapulmonary opioid receptors relieves breathlessness. Due to limited systemic absorption, patients experience fewer side effects than when ingesting opioids.

Pharmacist Corner Objectives

1.) Provide an understanding of utilizing nebulized opioids and its uses
2.) Implement which nebulized opioid is preferred and when
3.) Identify when pharmacologic therapy is indicated

PATIENT SELECTION

While nebulized opioids are a viable option for the management of respiratory symptoms in hospice, oral opioids remain first-line therapy for the management of dyspnea and shortness of breath. The role of nebulized opioids is reserved for patients for which oral opioid therapy is not considered to be safe, effective and/or tolerable for the patient in the setting of refractory symptoms. A comprehensive assessment for indication for nebulized opioids is essential for when determining appropriateness of inhaled steroids for use. Clinicians should conduct a thorough evaluation that includes a detailed medical history, review of medication therapy, assessment symptom assessment, and evaluation of the patient's environment. Clinicians can also assess severity of respiratory side effects on the patient's physical activity, rest and exertion.

Indications include:

- Pain relief
- Relief of breathlessness associated with COPD
- Symptomatic congestive heart failure

PHARMACOLOGIC MANAGEMENT WITH NEBULIZED OPIOIDS

After a clinical assessment, it may be determined that pharmacologic interventions may be necessary to manage symptoms to improve quality of life. These interventions should be carefully considered from patient to patient. While additional research on nebulized opioids is ongoing, three opioids have been found to be effective in relieving respiratory symptoms and pain. These agents are: fentanyl, morphine and hydromorphone.

Nebulized opioids have demonstrated efficacy while simultaneously resulting in reduced systemic absorption, and subsequently a reduced risk/severity of side effects. Despite a decreased prevalence, monitoring patients initiated on nebulized opioid therapy remains essential to assess for tolerability and efficacy of the treatment. The decision to initiate nebulized opoioids should be made collaboratively, considering both clinician clinical judgment and patient/caregiver dynamics to optimal patient care.

PHARMACOLOGIC TREATMENT STRATEGIES FOR DEPRESSION IN THE HOSPICE SETTING			
Medication	**Initial Dosing**	**Monitoring**	**Notes**
Fentanyl	25mcg nebulized Q3-4 hours	Daytime sedation, respiratory depression, withdrawal	Used in fewer studies Less chance of hypotension, edema, itching gastric secretion, and bronchospasms compared to other nebulized opioids
Morphine	1mg nebulized Q4-6 hours	Daytime sedation, respiratory depression, withdrawal	Highest potential for inducing bronchospasms
Hydromorphone	5mg nebulized Q4-hours	Daytime sedation, respiratory depression, withdrawal	Less potential for inducing bronchospasm compared to morphine

- Fentanyl doses have been noted as high as 50mcg q3-4 hours
- Morphine dosed have been documented up to 20mg nebulized q4-6 hours or equivalent to patient's 4-hour systemic morphine requirement

PREPARATION AND ADMINISTRATION

1. Wash hands for no less than 20 seconds with soap and water
2. Place opioid into nebulizer ensuring to measure out correct dose
    a. When using morphine use 2 mL (0.5mg/mL) for a starting dose mixed with normal saline to form a solution

   b. When considering fentanyl, use 0.5 mL (50mcg/mL) for a starting dose mixed with 0.9% Sodium chloride
   c. When using Hydromorphone use 0.5 mL (10mg/mL) for a starting dose mixed with 0.9% Sodium chloride
3. Attach the mouthpiece and secure it to the nebulizer cup
4. Connect tubing to the nebulizer cup
5. Turn on air compressor put on mask
6. Continue inhaling for 10 to 15 minutes for full dose of medication or until mist stops
7. Turn off nebulizer and clean medicine cup and mouthpiece with warm soapy water and rinse with water.
8. Let air dry completely
9. Once a week, disinfect all parts nebulizer mouthpiece (excluding tubing) except tubing using white distilled vinegar and three parts hot water for one hour

SUMMARY

In conclusion, nebulized opioids offer a novel route of administration while continuing to play an integral role in relieving and managing pain and respiratory symptoms, intending to improve quality of life. While additional research will serve beneficial to expanding knowledge and optimizing management of nebulized opioids, current understanding of mechanism of activity and theoretical reduction in side effect risk make the use of nebulized opioids an intriguing alternative to systemic opioid therapy for symptomatic patients.

REFERENCES

1. Lippincott. (2014). Relief of Breathlessness. Inhaled nebulized and intranasal opioids for the relief of b... : Current Opinion in Supportive and Palliative Care (lww.com)
2. ClinicalTrials.gov. (2021). U.S. National Library of Medicine. https://clinicaltrials.gov/
3. Titilol M, Milap C, Vinita P. Nebulized opioids for the palliation of dyspnea in terminally ill patients. American Society of Health-System Pharmacists. 2017; 74:1053-61.
4. Weingartner V, Bausewein C, Higginson IJ, et al. Characterizing episodic breathlessness in patients with advanced disease. J Palliat Med 2013; 16:1275–1279

