Nebulized medications in the emergency department: A narrative review of nontraditional agents

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Purpose: This article summarizes emerging nontraditional therapies administered via the nebulization route for use in the emergency department (ED).

Summary: Although traditional routes of medication administration (eg, intravenous) have been the mainstay of administration modalities for decades, these routes may not be appropriate for all patients. Nowhere is this more readily apparent than in the ED setting, where patients with a variety of presentations receive care. One unique route for medication administration that has increasingly gained popularity in the ED is that of aerosolized drug delivery. This route holds promise as direct delivery of medications to the site of action could yield a more rapid and effective therapeutic response while also minimizing systemic adverse effects by utilizing a fraction of the systemic dose. Medication administration via nebulization also provides an alternative that is conducive to rapid, less invasive access, which is advantageous in the emergent setting of the ED. This review is intended to analyze the existing literature regarding this route of administration, including the nuances that can impact drug efficacy, as well as the available literature regarding novel, noncommercial nebulized medication therapy given in the ED.

Conclusion: Multiple medications have been investigated for administration via this route, and when implementing any of these therapies several practical considerations must be taken into account, from medication preparation to administration, to ensure optimal efficacy while minimizing adverse effects. The pharmacist is an essential bedside team member in these scenarios to assist with navigating unique and complex nuances of this therapy as they develop.

Keywords: administration, emergency service, inhalation, pharmacists

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Although the oral and intravenous (IV) routes have been the mainstays of medication administration modalities for decades, these options may not be appropriate for all patients for a host of different reasons (eg, level of consciousness, intolerance, obstructions, and trauma). Nowhere is this more readily apparent than in the emergency department (ED) setting, where patients with a variety of presentations receive care. This has led to increased exploration of alternative routes of medication administration, such as intramuscular (IM) and intranasal (IN) therapies.[1] Both have been shown to be viable and, in some cases, advantageous routes of medication administration by reducing the risk of needle-stick injuries, decreasing drug administration time, reducing the impact of body habitus on pharmacokinetics, and potentially eliminating the need for IV access altogether.[1] More recently, aerosolized drug delivery, more commonly known as nebulization, has gained popularity as another alternative route of medication administration. This modality holds great potential not only for the treatment of respiratory diseases, but also for systemic ones.[2] Direct delivery of medications to the site of action has the potential to yield a more

rapid and effective therapeutic response while also minimizing systemic adverse effects through utilization of a fraction of the systemic dose.[2] In addition, for the treatment of systemic diseases, this provides yet another "needle-free" system by which a wide variety of substances can be administered and bypass first-pass metabolism.[2] The enormous surface area and high permeability of the pulmonary membrane also allow medications to circumvent unique interpatient characteristics (eg, metabolism and gastrointestinal absorption) that would impact more traditional routes of administration.[2]

Physiology of aerosolized drug administration

Several factors are at play that influence the delivery of medications via aerosolization.[3] For example, particle size is a critical aspect to consider to ensure appropriate medication disposition, as particles larger than 15 μm in diameter are generally deposited in the mouth and nose. Particles in the range of 10 to 15 μm tend to reach the upper airways, while those smaller than 10 μm and 5 μm reach the large bronchi and lower airways, respectively.[4,5] Thus, to achieve higher drug concentrations at the tonsillar region and minimize drug delivery to the lower airways, aerosol particles in the range of 10 to 15 μm would be desired. This contrasts with the approach applied for typical nebulized bronchodilator medications in which the goal is to generate aerosol particles smaller than 5 μm to reach the large bronchi and alveoli of the lower respiratory system. Specific settings vary between nebulizer brands and types, but larger aerosol particles are generally achieved by using a lower gas flow rate or lower pressure. Whenever possible, use of a mouthpiece is preferred to use of a face mask, as the former decreases the amount of aerosol deposited onto the nose, eyes, and face.[4,5]

Preparation and administration

Unlike other modalities of medication administration in the ED, aerosolized drug delivery requires additional equipment (eg, a nebulizer and compressor), time, and expertise.[3] Further, manipulations of the pharmacological agent itself may be necessary to help ensure optimal and predictable drug delivery.[3] Ideally, aerosols should be prepared in a sterile, isotonic, pH-balanced, and pyrogen-free manner.[3] Tonicity is an important consideration in drug preparation, as both hypotonic and hypertonic nebulizer solutions can cause bronchoconstriction in patients with asthma.[6-8] In addition, this can also reduce the efficacy of the drug being administered for systemic effects and may explain the variable efficacy noted in some studies.[9,10] Most often, 0.9% sodium chloride (normal saline) or sterile water has been the preferred carrier fluid.[11] Additional ingredients such as preservatives should be avoided if possible. For example, phenol, a common preservative, can cause airway hypersensitivity with repeated exposure.[3] The "dead space" of the nebulizer should also be taken into consideration, as liquid occupying it will not be nebulized. Available data suggest that increasing the nebulizer fill volume decreases the amount of drug remaining trapped in the delivery system.[4,5,12] Hence, some drugs should be diluted to at least the recommended fill volume (typically 4 to 5 mL) of the nebulizer chamber. This may be particularly important with smaller doses, which tend to be used in younger patients. Further, the delivery device itself can also greatly influence the success of delivering the desired medication to the pulmonary system.[3] As an example, the amount of medication expelled from the device (ie, the respiratory fraction) can be impacted by the size and efficiency of the compressor and the design of the nebulizer.

KEY POINTS

- Aerosolized drug delivery provides an alternative route of medication administration conducive to rapid, less invasive access that may be advantageous in the unique setting of the emergency department.
- Practical considerations should be taken into account, from medication preparation to administration, to ensure optimal efficacy while minimizing adverse effects.
- Adequate evidence supporting implementation in the emergency department setting exists for calcium gluconate, fentanyl, hydromorphone, ketamine, naloxone, and sodium bicarbonate, while further evidence is necessary for other medications such as furosemide, magnesium, nitroglycerin, and tranexamic acid.

Nebulizer considerations

The type of nebulizer (ie, jet, mesh, or ultrasonic) itself may influence the efficacy of medications, given that this impacts particle size, rate of nebulization, and the subsequent amount of drug deposited.[11,13] The characteristics of different nebulizer types are summarized in Table 1. In certain conditions, drugs may need to be delivered to a more distant region of the bronchial tree, in which case ultrasonic and mesh nebulizers are more efficient at depositing drugs in these deeper lung areas. High-efficiency nebulizers can also improve onset and mimic the pharmacokinetic profile of IV-administered doses. When comparing jet, mesh, and ultrasonic nebulizers, many studies have shown that greater drug delivery appears to come from mesh nebulizers.[14] Breathing patterns are yet another factor affecting drug delivery. One study explored the impact that the different breathing patterns of healthy adults, patients with asthma, and patients with chronic obstructive pulmonary disease (COPD) had on nebulizer efficiency.[14] The authors concluded that patients with restricted lung capacity receive reduced doses from nebulizers.

Table 1. Nebulizer Considerations[5,14-16]

Type of nebulizer[a]	Advantage(s)	Disadvantage(s)	Comments
Jet nebulizer	Large output rate	• Large residual volume • Harder to nebulize smaller volumes • Distribution variations • Longer nebulization times	Traditionally, the jet nebulizer has been the gold standard.
Mesh nebulizer	• Greater output efficiency • Low to negligible residual volume • Nebulize small volumes • Shorter nebulization times	Not to be used with vicious liquids	Two types of mesh nebulizers, static (passive) and vibrating (active), are available; vibrating mesh nebulizers have greater efficiency.
Ultrasonic nebulizer	More effective drug delivery than with jet nebulizer	• Should not be used with suspensions • Large residual volume • Heat medications (may denature proteins)	Large and small volume ultrasonic nebulizers are available.

[a]In clinical practice and in the majority of studies, nebulizers are used with face masks. For jet and mesh nebulizers, drug delivery was higher with a valved mask. Ensuring a tight seal of the mask is essential for optimal function.

Literature search

A literature search of novel, noncommercial nebulized medication therapy use in the ED was conducted in PubMed and Google Scholar to identify primary literature, review articles, and current guidelines. Published reports on double-blind clinical trials were included in this review. Open-label studies of a given medication were included if no published double-blind studies were identified. In addition, referenced citations from publications identified in the search were reviewed.

Calcium gluconate

Calcium gluconate has been shown to improve morbidity and mortality when used as antidotal therapy after inhalational exposures to hydrofluoric acid, an agent commonly used in glass etching, brick cleaners, and other industrial processes.[17,18] After exposure to tissues, it dissociates into H^+ and F^- ions that then bind to calcium and magnesium ions, leading to severe pain, vasospasm, tissue necrosis, and possibly death. Although most toxicities occur after dermal contact, inhalational exposures have also been reported with resulting bronchospasm, wheezing, fever, and chills.[19-22] In combination with IV calcium, nebulized calcium gluconate (nCG) has been used to help facilitate chelation of F^- ions within the pulmonary tree, hence limiting toxicity.[17] The available data supporting nCG are limited to observational studies; however, the rationale for use has a solid scientific foundation and no adverse effects have been reported in 381 patients. Hence, it is reasonable to use nCG in this setting. Further, this recommendation is supported by the material safety data sheet for hydrofluoric acid, in conjunction with IV or dermal calcium preparations to enhance rapid clearance from affected sites.[17,23] All reported cases of nebulized calcium therapy have utilized the calcium gluconate salt formulation. Although calcium chloride is also available as an IV formulation, given its known irritant and vesicant nature, it seems most appropriate to use nCG at this time because of its reported efficacy and tolerability. Most existing evidence documenting nebulized calcium therapy utilized 4 to 6 mL of a 2.5% solution, which can be prepared by mixing 1.5 mL of a 10% calcium gluconate preparation with 4.5 mL of normal saline.

Furosemide

Furosemide is a loop diuretic frequently used in the ED in an IV or oral formulation for the treatment of numerous indications, including volume overload and edema.[24] Additionally, nebulized furosemide has also been studied in the ED to treat pulmonary edema, COPD, and asthma exacerbation.[24-31] The mechanisms of action of nebulized furosemide are likely multifactorial and dependent on the indication.[25,26] In individuals with asthma, nebulized furosemide has been postulated to interfere with ion and water movement across the airway epithelium, inhibit inflammatory mediators, inhibit carbonic anhydrase, and increase production of prostaglandin.[26] In dyspnea relief in patients with COPD, nebulized furosemide modulates the activity of pulmonary stretch receptors, which increases the activity of the pulmonary vagal afferent, leading to improvement in airway function and alleviation of the sensation of breathlessness.[25] A randomized trial compared the efficacy of nebulized and IV furosemide in patients presenting to the ED with pulmonary edema.[24] At 60 minutes after intervention, the mean arterial blood oxygen level was statistically higher in the nebulized group, although at 120 minutes it was higher in the IV group. The clinical significance, however, of the difference between these values of less than 1% is likely

negligible. Importantly, symptoms of pulmonary edema (eg, dyspnea, sweating, and crackles) improved in both groups. These limited data suggest that nebulized furosemide may have efficacy similar to that of IV furosemide in the treatment of pulmonary edema, although variations in the doses used in the 2 groups may have affected the outcomes.[24] The concentration of the dose nebulized (1 mg) was not reported and may be impractical depending on the available concentration. Additional studies conducted in the ED have evaluated nebulized furosemide for the treatment of COPD and asthma and have generated conflicting results. A meta-analysis of 8 studies comparing nebulized furosemide to placebo in patients with COPD suggested that it can improve vital signs and other respiratory variables but was plagued with severe heterogeneity.[25] A more recent randomized trial compared nebulized furosemide to β-agonist therapy, followed by a combination of the 2 therapies.[29] Combination of the 2 therapies significantly improved all spirometric parameters. In asthma exacerbation, 2 randomized trials evaluated the use of β-agonists in combination with nebulized furosemide or placebo, with both finding significant improvements in peak expiratory flow rates (PEFR) in the combination groups.[27,28] However, another randomized trial found no such benefit with combination therapy.[26] Currently, the role of nebulized furosemide in the setting of pulmonary edema, COPD, and asthma remains unclear. Available data suggest that this therapy has a low incidence of adverse effects and may be considered when IV access is delayed or unavailable, as well as when oral bioavailability is low; however, it should not be a substitute for the standard of care (ie, IV furosemide).

Ketamine

Ketamine is an *N*-methyl-D-aspartate/glutamate receptor antagonist frequently utilized in the ED for a variety of indications (eg, procedural sedation and pain management) via various routes of administration (eg, IV and IM).[32,33] More recently, nebulized ketamine has been studied in the ED for use in pain management, asthma exacerbation, and procedural sedation. Nebulized ketamine for managing acute pain in the ED was initially described in 2 case series in 10 patients and resulted in improvements in pain control at 60 minutes.[34,35] Another case series of 4 patients focused on the utilization of inhaled ketamine for analgesia following orthopedic trauma.[36] All patients had a significant reduction in pain score at 60 minutes with minimal adverse effects. A prospective, randomized, double-blind trial compared 3 different dosing strategies (0.75 mg/kg, 1 mg/kg, and 1.5 mg/kg) of nebulized ketamine for the management of painful conditions.[37] There was no difference in the primary outcome, with all 3 groups experiencing a similar reduction in pain score and similar rates of adverse events, highlighting that 0.75 mg/kg nebulized ketamine is safe and effective for the management of acute pain in the ED. On the basis of studies exploring the use of IV ketamine for the treatment of asthma, a randomized, double-blind study compared the effects of nebulized ketamine to IV magnesium in severe steroid-resistant asthma.[38-40] Nebulized ketamine resulted in an improvement of approximately 30% in PEFR at 60 minutes, although the difference was not significant. Unlike the previously discussed studies for acute pain management, the device used for nebulization of ketamine was unclear, as well as the total dose patients received. Further studies will be needed before introducing routine utilization of nebulized ketamine for management of asthma. Ketamine has commonly been used for procedural sedation in the ED, with one randomized study comparing nebulized ketamine to nebulized dexmedetomidine during shoulder joint reduction. A significant reduction in pain score was seen at 60 minutes with both medications; however, ketamine had a slower onset.[41] The average doses administered were not reported and adverse events were not described in this study, limiting its reproducibility. On the basis of the current data, there is insufficient information to recommend nebulized ketamine for asthma or procedural sedation; however, it can be considered for administration in acute pain management.

Magnesium

Although IV magnesium has been used extensively in the ED for the management of asthma exacerbation, some have also utilized nebulized magnesium for the same indication in adult and pediatric patients.[42,43] Its efficacy in this disease state relates to its involvement in smooth muscle relaxation, calcium blockade, and anti-inflammatory actions.[42] A review of 24 trials concluded that treatment with nebulized magnesium sulfate may result in modest benefits when added to traditional therapies.[42] However, the authors note that the available data are of limited quality, making it difficult to make strong recommendations. A systematic review of 6 trials and approximately 300 patients found a significant difference in the standardized mean difference (SMD) in pulmonary function between patients whose treatment included nebulized magnesium and those whose treatment did not.[44] There was also a trend toward a reduced number of hospitalizations. Another systematic review and meta-analysis in both adults and children concluded that nebulized magnesium was associated with significant effects on SMD in pulmonary function and hospital admission, but these effects were limited to adults.[45] The absence of effect in children was echoed by 2 similar meta-analyses finding no significant effect on respiratory function or hospital admission in the pediatric population.[46,47] Yet, in a randomized controlled trial and a separate meta-analysis of randomized controlled trials, respiratory function was not found to improve with nebulized magnesium.[48,49] In all studies, nebulized magnesium sulfate did not appear to be associated with an increase in serious adverse events in any population. Hence, its role as an add-on therapy following the failure of

more traditional agents may be most appropriate. On the basis of the available data, it appears that nebulized magnesium sulfate may have a role in the management of adult asthma exacerbation following the use of traditional agents; however, the current data do not appear to support use of this agent in the pediatric population.

Naloxone

Naloxone is a synthetic morphinan alkaloid and has a high affinity for the μ-, κ-, and δ-opioid receptors.[50,51] As an antagonist of the μ receptor, it allows for the reversal of opioid effects, most notably respiratory depression.[50] Several routes of administration have been studied, including IM, IV, subcutaneous, IN, and nebulization.[51] A single case report has published serum levels after a positive response to a nebulized naloxone dose, noting that serum levels and absorption of nebulized naloxone were similar to those with IN drug delivery.[52]

A retrospective prehospital analysis evaluated a standard protocol for patients with suspected opioid overdose in which naloxone was administered via nebulizer face mask if spontaneous respiration was present.[53] Approximately 80% of patients had some response to therapy, although definitions were not given for complete and partial response. Nineteen percent of patients were reported to have had no response; 11 cases (10%) received rescue IV naloxone. No cases required escalation in respiratory support, including intubation or assisted ventilation, and no adverse events occurred. A second prehospital retrospective analysis looked at the effectiveness of nebulized naloxone in treating heroin-induced bronchospasm in 21 patients.[54] The authors reported that 95% of patients had a clinical response to treatment and 2 patients worsened but did not require intubation. No adverse events were noted by the authors. The definition and evaluation criteria for heroin-induced bronchospasm were not provided in the brief report, limiting its generalizability. The first observational study done in the ED evaluated the use of nebulized naloxone in 26 patients who required naloxone for suspected opioid exposure and had a respiratory rate of greater than or equal to 6 breaths per minute.[55] Changes in sedation score were found to be statistically significant from before to after administration of the nebulized naloxone dose. Three patients had reported agitation and 2 experienced diaphoresis and vomiting, but none required intubation. Nebulized naloxone has the notable benefit of allowing patients to self-titrate the opioid reversal effect by self-removing their mask as they become more responsive.[55,56] This also potentially limits the precipitation of opioid withdrawal, agitation, and elopement.[55] Nebulization use is not without concerns, however, particularly in patients with poor respiratory drive, as is often the case with individuals experiencing an opioid overdose, who could potentially be underdosed.[53,57] These retrospective analyses appear to have largely included patients who did not exhibit severe symptoms, and so this route would not be appropriate in patients with profoundly suppressed respiratory drive. Nebulized naloxone can be considered in suspected opioid overdoses where respiratory drive is somewhat intact (a respiratory rate of 6 breaths per minute or greater). There is a perceived benefit allowing for self-titration and limiting opioid withdrawal.

Nitroglycerin (NTG)

NTG is commonly used in the ED for anginal chest pain secondary to coronary artery disease, hypertensive emergency, pulmonary edema, and congestive heart failure.[58,59] NTG forms free radical nitric oxide, producing vasodilatory effects on vascular smooth muscle, and dilates peripheral veins and arteries with more prominent venodilatory effects.[60,61] When administered by nebulization, NTG is an effective pulmonary vasodilator decreasing both mean pulmonary arterial pressure (MPAP) and pulmonary vascular resistance without causing systematic vasodilation.[62-64] Nebulized NTG has been evaluated for the treatment of acute respiratory distress syndrome (ARDS), right ventricular dysfunction, pulmonary hypertension, pulmonary embolism, refractory hypoxemia, and asthma exacerbation.[60-68] Although current evidence for the use of nebulized NTG is limited to case reports and small studies, with less robust evidence in the ED, NTG remains an attractive therapeutic option due to its wide availability and ease of administration compared to other IV and inhaled vasodilators.[60-68] In a case report, NTG sublingual tablets (three 0.3-mg tablets) dissolved in saline (3 mL) and later IV NTG were nebulized for the treatment of ARDS and hypercarbia related to coronavirus disease 2019 (COVID-19).[62] Additionally, nebulized NTG was used with systemic thrombolytic therapy to treat a hemodynamically unstable patient's acute right ventricle dysfunction that was caused by COVID-19–induced ARDS complicated by a pulmonary embolism.[65] When inhaled milrinone was compared to inhaled NTG to assess the effect on pulmonary and systemic hemodynamics in children with pulmonary hypertension, the authors found significant reductions in systolic and diastolic blood pressure as well as in MPAP.[68] A similar focal effect was seen in adults who inhaled NTG.[63] The authors found that inhaled NTG reduced MPAP, the pulmonary vascular resistance index, and the pulmonary vascular resistance/systemic vascular resistance ratio without affecting systemic pressures. The combination of inhaled NTG and dobutamine generated similar results without affecting systemic pressures. However, IV NTG alone and its combination with IV dobutamine resulted in a significant systemic vasodilatory effect. The potential impact of inhaled NTG on the treatment of patients with asthma was assessed in a double-blind crossover trial of 10 patients with asthma.[6] The addition of inhaled NTG to β_2-agonist therapy resulted in additive bronchodilatation as measured by a higher forced expiratory volume in 1 second (FEV_1) value. Another

study looked at the bronchodilating effect of nebulized NTG in 12 patients pretreated with nebulized norepinephrine and found improved bronchodilation with the coadministration of a vasoconstrictive agent.[67] Currently, there is insufficient evidence to support the routine use of nebulized NTG in the ED, and future prospective clinical studies are warranted to assess its role in the acute setting.

Opioids

Nebulized opioids have been evaluated in the ED for the treatment of acute pain secondary to abdominal pain, limb pain, and renal colic and for the treatment of dyspnea with end-stage lung diseases and terminal malignancies. Among the wide variety of opioids available, lipophilic opioids are naturally more ideal options as they are best absorbed across mucosa, including in the nasal passages, lungs, or oral mucosa.[69] Morphine, for example, is poorly absorbed via the IN route as it is more hydrophilic.[70] Fentanyl and hydromorphone, as more lipophilic opioids, can be administered via both the IN and inhalational route of administration, whereas morphine is best administered via the inhalation route.[69-74] The rapid onset and short duration of action of fentanyl make it an ideal agent for treatment as this allows for early reevaluation and limits less desirable hemodynamic adverse effects. The bioavailability of opioids given via the inhalational route has been shown to be approximately 20% that of a typical IV dose, but there is variability depending on the efficiency of the nebulizer and underlying lung pathology.[70,71,74] Nebulized fentanyl has been evaluated for the treatment of multiple acute pain conditions in the ED, including abdominal pain, acute limb pain, and renal colic.[71,73,75-80] For acute abdominal pain, nebulized fentanyl has been compared to IV fentanyl in multiple studies.[75,76,78,80] Nebulized fentanyl was found to be comparable to IV fentanyl with no difference noted in the need for rescue medications.[75] Nebulized fentanyl has also been compared to IV morphine, achieving similar results for treatment of acute abdominal pain.[76] Alternatively, nebulized fentanyl was not found to be superior to IV ketorolac in pediatric patients with renal colic, suggesting that ketorolac represents a better treatment option for this population.[80] Nebulized fentanyl has also been evaluated for acute pain secondary to orthopedic or limb injuries, albeit at higher doses (3 to 4 μg/kg vs 1 to 2 μg/kg), and has been compared to both IV morphine and IV fentanyl.[71,77,81] Studies have demonstrated that both adult and pediatric patients can achieve adequate pain relief using nebulized fentanyl as an alternative therapy, with equivalent patient satisfaction and no adverse effects.[77,81]

Opioids have also been utilized to suppress the sensation of dyspnea in patients with COPD and other end-stage lung diseases, as well as terminal malignancies.[82,83] It is hypothesized that nebulization of opioid analgesics causes depression of opioid receptors locally in the lung as well as in the spinal cord and produces depression of central respiratory centers.[82,84] Hydromorphone was the most commonly evaluated opioid in these studies, and nebulized hydromorphone at doses of 5 mg has been shown to be comparable to IV hydromorphone for relief of dyspnea or work of breathing.[85] When treating these end-stage lung conditions, the aim of using nebulized opioids may not necessarily be to improve ventilation, but rather to improve patient perception of shortness of breath. Subjective improvement in dyspnea may be more common in patients with malignancies than in those with other chronic respiratory diseases, which may be more difficult to manage due to excessive production of secretions, narrowing of the airways, or irreversible physiological destruction of lung tissue.[11,13,82] There is also a tendency for opioid-tolerant patients to see more subjective improvements compared to opioid-naive patients.

Evidence suggests that inhaled opioids are at least as efficacious as IV opioids for treatment of these conditions, but ketorolac may be a better option for treatment of pain due to renal colic. Following the initial dose (fentanyl 1 to 3 μg/kg or hydromorphone 1 mg), it is important to evaluate for the duration of effect and patient and provider perceptions of comfort. Doses can be increased by 25% to 50% if an adequate response is not achieved with the initial dose, and the interval can be decreased for more frequent dosing if an adequate duration of action is not seen.

Sodium bicarbonate

Sodium bicarbonate is commonly used in the ED for various indications, and the reasons for its use can generally be grouped into a few different physiological mechanisms: correction of metabolic acidosis, ionization of toxins, altering interactions between sodium channels and toxins, and direct neutralization of acid species.[86] It has been suggested that nebulization of the basic solution could be carried out to neutralize acid present within the pulmonary system.[87] Although bases should not generally be used to neutralize acids in any organ system due to the exothermic nature of the reaction, the large surface area of the lungs combined with the rapid exchange of air occurring during breathing helps mitigate this risk.[88] Multiple case series have reported efficacy for nebulized sodium bicarbonate, particularly in managing exposures to chlorine and chloramine gas.[89-91] Exposure to these gases most commonly occurs after inadvertent generation via mixture of household chemicals.[92] The toxic effects of these gases are primarily mediated by the generation of hypochlorous acid and hydrochloric acid upon chlorine's interaction with water on the lung mucosal surface, subsequently promoting cell injury and lysis. This process presents clinically through respiratory symptoms such as sore throat, wheezing, cough, and chest pain, with severe cases producing pulmonary embolism and progressing to ARDS.[51] In one randomized study of patients

Table 2. Nebulized Medications

Source	Study design	Study population	Intervention	Endpoints of interest	Results
Calcium gluconate					
Choe et al[19]	Observational cohort (N = 368)	HF exposures with symptoms of chemical tracheobronchitis and given nebulized calcium	Nebulized 2.5% calcium gluconate: 6 mL (N = 368)	• Adverse effects • ED return rate	• No adverse effects • 5.4% 1-month ED return rate for HF-related symptoms
Lee et al[21]	Case series (N = 13)	HF mist exposures presenting with minor upper respiratory tract irritation	Nebulized 2.5% calcium gluconate: 4 mL (N = 13)	Adverse effects	No adverse effects
Furosemide					
Barzegari et al[24]	Randomized controlled trial (N = 80)	Pulmonary edema	• IV furosemide 1 mg/kg (n = 40) • Nebulized furosemide 1 mg (n = 40)	• Hemodynamic parameters • Clinical severity of pulmonary edema	• At 60 minutes after intervention, difference in mean arterial blood oxygen between nebulization and IV (95.05% vs 94.1%, $P = 0.005$) • At 120 minutes after intervention, higher in IV group (96.4% vs 95.8%, $P = 0.012$) • Clinical symptoms of pulmonary edema in both groups improved
Ghaysouri et al[25]	Meta-analysis (8 studies; N = 465)	COPD	Nebulized furosemide	• $PaCO_2$ • FEV_1 • Heterogeneity	• Mean $PaCO_2$ of 48.3 vs 46.6 mm Hg in the case vs control group • Mean FEV_1 of 49.0% vs 46.7% of predicted in the case vs control group • Severe heterogeneity (72.2%)
Saba et al[29]	Randomized controlled trial (N = 69)	COPD	• Nebulized furosemide 40 mg alone (n = 35) • Nebulized furosemide 40 mg + salbutamol 5 mg (n = 34)	• FEV_1 • FVC • FEV_1/FVC • mMRC • Borg Dyspnea Score	• No significant difference between the 2 therapies in the spirometeric indices ($P > 0.1$) • Significant improvement in all spirometeric indices in combination therapy compared with monotherapy ($P < 0.0001$)
Masoumi et al[27]	Randomized controlled trial (N = 90)	Acute asthma	• Nebulized furosemide 40 mg + salbutamol 5 mg (n = 45) • Salbutamol 5 mg (n = 45)	PEFR	• Significant Improvements in PEFR in the combination group at times points at 15, 30, and 45 minutes ($P < 0.05$)
Pendino et al[28]	Randomized controlled trial (N = 42)	Acute asthma	• Nebulized furosemide 40 mg + salbutamol 2.5 mg (n = 21) • Salbutamol 2.5 mg (n = 21)	PEFR	Improvements in PEFR in combination group at time points at 12 and 30 minutes ($P < 0.05$)

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Table 2. Nebulized Medications

Source	Study design	Study population	Intervention	Endpoints of interest	Results
Karpel et al[26]	Randomized controlled trial (N = 24)	Acute asthma	• Nebulized metaproterenol 15 mg (n = 7) • Nebulized furosemide 40 mg (n = 8) • Combination of inhaled furosemide 40 mg and metaproterenol 15 mg (n = 9)	FEV_1	• Nebulized furosemide yielded a nonsignificant improvement in FEV_1 from baseline • Metaproterenol and nebulized furosemide plus metaproterenol did not result iin a significant improvement from baseline
Ketamine					
Drapkin et al[34]	Case series (N = 5)	Acute painful conditions	Nebulized ketamine: • 0.75 mg/kg (n = 1) • 1 mg/kg (n = 1) • 1.5 mg/kg (n = 3)	Pain score at 15, 30, 60, 90, and 120 minutes	• All patients experienced improvements in pain score at all time points • 2 patients experienced adverse effects, including dizziness, fatigue, and mood changes
Rhodes et al[35]	Case series (N = 5)	Traumatic joint pain	Nebulized ketamine: • 0.75 mg/kg (n = 2) • 1 mg/kg (n = 1) • 1.5 mg/kg (n = 2)	Pain score at 15, 30, and 60 minutes	• All patients experienced decreased pain scores • One pediatric case experienced light sedation that had resolved at 60 minutes
Fassassi et al[36]	Case series (N = 4)	Orthopedic trauma	Nebulized ketamine: • 1.5 mg/kg (n = 3) • 0.75 mg/kg (n = 1)	Pain score at 60 minutes	• All patients had a significant reduction in pain score at 60 minutes with 75% reporting a pain score of 0 • 50% of patients experienced adverse effects, including dizziness, nausea, and feeling of unreality
Dove et al[37]	Randomized controlled trial (N = 120)	Acute and chronic painful conditions	Nebulized ketamine: • 0.75 mg/kg (n = 40) • 1 mg/kg (n = 40) • 1.5 mg/kg (n = 40)	Pain score ≥5 on numeric rating scale at 30 minutes	• No difference in primary outcome among groups • Similar rate of adverse events, including dizziness and fatigue
Farshadfar et al[40]	Randomized controlled trial (N = 70)	Severe steroid-resistant asthma	• Nebulized ketamine 0.1-0.3 mL/kg (n = 35) • IV magnesium 2 g (n = 35)	PEFR at 30 and 60 minutes	Improvement in PEFR at 30 minutes (23.4% vs 12.7%; $P = 0.1$) and 60 minutes (29.4% vs 15.3%; $P = 0.1$)
Motamed et al[41]	Randomized controlled trial (N = 46)	Procedural sedation	• Nebulized ketamine 1 mg/kg (n = 23) • Nebulized dexmedetomidine 1 mg/kg (n = 23)	Visual analog scale pain score at 10, 20, 30, and 60 minutes	• Ketamine: significant reduction in pain score at 20, 30, and 60 minutes • Dexmedetomidine: significant reduction in pain score at 10, 20, 30, and 60 minutes

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Table 2. Nebulized Medications

Source	Study design	Study population	Intervention	Endpoints of interest	Results
Magnesium					
Blitz et al[44]	Systematic review (6 studies; N = 296)	Asthma	Nebulized magnesium 95-384 mg (N = 296)	SMD for pulmonary functions and relative risk for hospital admission	• SMD of 0.30 (95% CI, 0.05-0.55) • Reduced number of hospitalizations (RR, 0.67; 95% CI, 0.41-1.09)
Shan et al[45]	Systematic review (25 studies; N = 1,754)	Asthma	Nebulized magnesium 125-333 mg (N = 569)	SMD for pulmonary functions and relative risk for hospital admission	• Adult SMD (SMD, 0.23; 95% CI, 0.06-0.41; *P* = 0.009) • Adult hospital admission (RR, 0.63; 95% CI, 0.43-0.92; *P* = 0.02) • Pediatric SMD (SMD, 0.36; 95% CI, –0.14 to 0.86; *P* = 0.16) • Pediatric hospital admission (RR, 2.0; 95% CI, 0.19-20.93; *P* = 0.56)
Naloxone					
Weber et al[53]	Retrospective analysis (N = 105)	Suspected opioid overdose	Nebulized naloxone 2 mg (N = 105)	Patient response	• 81% had some response • 10% received rescue IV naloxone • No cases of intubation
Tataris et al[54]	Retrospective analysis (N = 21)	Heroin-induced bronchospasm	Nebulized naloxone 2 mg (N = 21)	Clinical improvement	• 95% of patients had a clinical response and 2 patients worsened • None required intubation • No adverse effects noted
Baumann et al[55]	Observational study (N = 26)	Suspected opioid exposure and respiratory rate of ≥6 breaths per minute	Nebulized naloxone 2 mg (N = 26)	Changes in GCS or RASS, incidence of withdrawal	• Significant improvement in GCS (11 vs 13; *P* = 0.001) and RASS (–3 vs –2; *P* = 0.0001) • 3 patients developed agitation • 2 patients developed diaphoresis and vomiting • None required intubation
Nitroglycerin					
Daxon et al[62]	Case report	COVID-19–associated ARDS and hypercarbia	Nebulized NTG	$PaCO_2$, arterial pH, PaO_2	$PaCO_2$ decreased; concurrently, arterial pH increased and PaO_2 increased
Karfunkle et al[65]	Case report	COVID-19–associated ARDS and pulmonary embolism	Nebulized NTG 4 mg (200 µg/mL) followed by systemic alteplase 100 mg over 2 hours	Right ventricle function	Improvement of right ventricle function with NTG, with decompensation of right ventricle when discontinued; right ventricle function improved once NTG was reinitiated

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Table 2. Nebulized Medications

Source	Study design	Study population	Intervention	Endpoints of interest	Results
Singh et al[68]	Randomized controlled trial (N = 35)	Acyanotic congenital heart disease and PAH	• Nebulized milrinone (n = 18) • Nebulized NTG (n = 17)	Systemic and pulmonary cardiac output	Systolic, diastolic, and mean pulmonary arterial pressure decreased significantly in both groups after drug nebulization, with no significant changes in systemic pressures
Mandal et al[63]	Randomized controlled trial (N = 40)	Secondary PAH	• Nebulized NTG 2.5 µg/kg/min (n = 40) • IV NTG 2.5 µg/kg/min (n = 40) • Nebulized NTG 2.5 µg/kg/min + IV dobutamine 10 µg/kg/min (n = 40) • IV NTG 2.5 µg/kg/min + IV dobutamine 10 µg/kg/min (n = 40)	Acute hemodynamic effects	• All drugs were of similar efficacy in reducing the pulmonary vascular resistance index • Nebulized NTG produced selective pulmonary vasodilatation, while IV NTG and its combination with IV dobutamine had a significant concomitant systemic vasodilatory effect
Rolla et al[67]	Randomized, double-blind crossover (N = 12)	Reversible airway obstruction induced in patients with asthma using nebulized norepinephrine 0.04 mg or placebo	Nebulized NTG 0.2 mg (N = 12)	FEV_1	Nebulized NTG resulted in significantly higher FEV_1 (73.8% vs 70% predicted; $P < 0.01$) in the norepinephrine group
Rolla et al[60]	Randomized, double-blind crossover (N = 10)	Patients with asthma	Pretreated with nebulized NTG 0.2 mg or placebo followed by salbutamol MDI 200 µg	FEV_1	FEV_1 was significantly higher in patients pretreated with nebulized NTG (2,694 vs 2,440 mL; $P < 0.001$)
Opioids					
Bartfield et al[75]	Randomized, double-blind, double-placebo–controlled trial (N = 50)	Acute abdominal pain	• Nebulized fentanyl 1.5 µg/kg (n = 25) • IV fentanyl 1.5-3 µg/kg (n = 19)	Pain score at 15 and 30 minutes	• Nebulized fentanyl was comparable to IV fentanyl in pain scores • No difference with respect to need for rescue medication
Deaton et al[76]	Randomized, double-blind, placebo-controlled trial (N = 40)	Acute abdominal pain	• Nebulized fentanyl 2 µg/kg (n = 20) • IV morphine 0.1 mg/kg (n = 20)	Patient and physician satisfaction scores at 10, 20, 30, and 40 minutes	• Significantly higher satisfaction noted in the nebulized fentanyl group in both patient and physician scores • Significantly fewer rescue medications administered in the nebulization group
Imamoglu et al[78]	Retrospective study (N = 115)	Renal colic	• Nebulized fentanyl 3 µg/kg (n = 53) • IV fentanyl 1.5 µg/kg (n = 62)	VPS and visual analog scale at 15 and 30 minutes	IV fentanyl provides a faster onset of pain relief and a greater degree of analgesic relief compared to nebulized fentanyl

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Table 2. Nebulized Medications

Source	Study design	Study population	Intervention	Endpoints of interest	Results
Rezaei et al[80]	Randomized, double-blind trial (N = 186)	Renal colic	• Nebulized fentanyl 3 µg/kg (n = 98) • IV ketorolac 0.9 mg/kg (n = 93)	• Numeric pain scale score at 15, 30, 45, 60, 75, 90, 105, and 120 minutes • Pain intensity scale score	At all time points, the severity of pain in the ketorolac group was lower than in the nebulization group
Farahmand et al[77]	Randomized, double-blind, placebo-controlled trial (N = 90)	Orthopedic or limb injuries	• Nebulized fentanyl 4 µg/kg (n = 47) • IV morphine 0.1 mg/kg (n = 43)	• Pain relief at 5, 10, 15, 30, 45, and 60 minutes • Patient satisfaction	No significant difference in pain relief between the 2 groups at any time point
Furyk et al[71]	Randomized, open-label trial (N = 77)	Orthopedic or limb injuries	• Nebulized fentanyl 4 µg/kg (n = 36) • IV morphine 0.1 mg/kg (n = 37)	Wong-Baker faces pain scale at 15 and 30 minutes	No significant difference in pain score between the 2 groups
Miner et al[81]	Randomized, double-blind trial (N = 41)	Orthopedic or limb injuries	• Nebulized fentanyl 3 µg/kg (n = 27) • IV fentanyl 1.5 µg/kg (n = 14)	Pain score every 10 minutes for 30 minutes	No significant difference in pain score between the 2 groups
Charles et al[85]	Double-blind, controlled crossover study (N = 20)	Dyspnea secondary to cancer-related illness	Nebulized hydromorphone 5 mg or 3 mL of saline	Perceived intensity of breathlessness using a 100-mmute visual analog scale	All treatments resulted in a significant improvement in visual analog scale score and respiratory rate at 10 minutes after treatment
Sodium bicarbonate					
Aslan et al[93]	Randomized controlled trial (N = 44)	Chlorine gas exposure (dyspnea, 82%; chest tightness, 82%)	Nebulized 4.2% sodium bicarbonate 4 mL (N = 22)	• FEV_1 at 120 and 240 minutes • Quality-of-life score	• Nebulized sodium bicarbonate resulted in significantly higher FEV_1 values at all time points • Nebulized sodium bicarbonate resulted in significantly greater improvement in quality-of-life score
Bosse[89]	Retrospective observational study (N = 86)	Chlorine gas exposure (cough, 52.3%; SOB, 51.2%; chest pain, 33.7%)	Nebulized 5% sodium bicarbonate 5 mL	Subjective symptom improvement	No patients deteriorated clinically after nebulized sodium bicarbonate administration

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Table 2. Nebulized Medications

Source	Study design	Study population	Intervention	Endpoints of interest	Results
Tranexamic acid					
Dermendjieva et al[4]	Case series (N = 8)	Post-tonsillectomy hemorrhage	• Nebulized TXA 500 mg (n = 6) • Nebulized TXA 1,000 mg (n = 2)	Complete bleeding cessation	• Hemostatic benefit noted in 6 patients • Complete bleeding cessation in 5 patients • 7 patients taken to operating room for definitive management
Wand et al[105]	Randomized, placebo-controlled trial (N = 47)	Hemoptysis	Nebulized TXA 500 mg three times a day (n = 25)	• Mortality • Hemoptysis recurrence rate at 30 and 365 days	• Greater resolution of hemoptysis within 5 days (96% vs 50%; $P < 0.0005$) • Shorter hospital length of stay (5.7 vs 7.8 days; $P = 0.046$) • Fewer required invasive procedures (0% vs 18.2%; $P = 0.041$) • Reduced recurrence rate at 365 days (4% vs 22.7%; $P = 0.009$) • No significant difference in mortality • No adverse effects noted
O'Neil et al[104]	Retrospective, observational study (N = 19)	Pulmonary hemorrhage	Nebulized or endotracheally instilled TXA: 250 mg once (n = 1), 250 mg every 6 hours (n = 1), 250 mg every 8 hours (n = 7), 250 mg every 24 hours (n = 1), 500 mg every 6 hours (n = 4), 500 mg every 8 hours (n = 4), 500 mg every 12 hours (n = 1)	Cessation of hemorrhage within 48 hours	• Cessation of pulmonary hemorrhage achieved in 95% of patients • No major adverse effects noted
Tsai et al[106]	Systematic review (4 trials; N = 183)	Hemoptysis: • IV TXA (n = 2 studies) • Oral TXA (n = 1 study) • Nebulized TXA (n = 1 study)	Nebulized TXA 500 mg (N = 47)	• Further intervention risk • Hemoptysis volume • Hemoptysis resolution • Bleeding duration	Significant reduction in • Bleeding volume (MD = –56.2 mL; 95% CI, –94.7 to –17.7 mL) • Further intervention risk (OR = 0.24; 95% CI, 0.08-0.67) • Length of hospital stay (MD = –1.62 days; 95% CI, –2.93 to –0.31 days)

Abbreviations: ARDS, acute respiratory distress syndrome; CI, confidence interval; COPD, chronic obstructive pulmonary disease; COVID-19, coronavirus diease 2019; ED, emergency department; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; GCS, Glasgow Coma Scale; HF, hydrofluoric acid; IV, intravenous; MD, mean difference; mMRC, modified Medical Research Council dyspnea score; NTG, nitroglycerin; OR, odds ratio; $Paco_2$, partial carbon dioxide pressure; PAH, pulmonary arterial hypertension; Po_2, partial oxygen pressure; PEFR, peak expiratory flow rate; RASS, Richmond Agitation-Sedation Scale; RR, relative risk, SMD, standardized mean differences; SOB, shortness of breath; TXA, tranexamic acid; VPS, verbal pain score.

Table 3. Practical Implementation Considerations

Drug	Indication	Nebulized dose	Concentration used	Dilution for administration	Diluent	Onset of action	Duration of action	Adverse effects
Calcium gluconate	Inhalational HF exposure	100-150 mg	10%	Dilute to a final concentration of 2.5%	NS	0-5 min	Unknown; repeat as necessary until resolution of symptoms	None noted
Fentanyl	Acute abdominal pain	1.5-3 µg/kg; approximate 20% bioavailability	50 µg/mL	+2 mL	NS or SWFI	10-15 min	60-120 min	Bitter or metallic taste; lower incidence of hypotension or itching than IV or SC
	Acute limb or orthopedic pain	3-4 µg/kg						
	Dyspnea	1-3 µg/kg (max 200 µg)						
Furosemide	Pulmonary edema	1 mg	Not reported	+2 mL	NS	15-60 min	120 min	Conflicting reports of no adverse effects: increased diuresis, transient nausea, sleeplessness, pharyngeal and substernal irritation, and intermittent cough
	COPD/asthma	20-40 mg	10 mg/mL	Undiluted or diluted to final volume of 5 mL		15 min	45 min	None
Hydromorphone	Acute pain and dyspnea	1 mg	1 mg/mL	2 mL	NS or SWFI	10-15 min	240 min	Bitter or metallic taste, Itching, bronchospasm, hypotension; lower incidence of hypotension or itching than IV or SC
Ketamine	Pain	0.75 mg/kg	50 mg/mL	Dilute to final volume of 5mL	NS	15-30 min	120 min	Dizziness, fatigue
Magnesium	Acute asthma	100-500 mg	100-500 mg/mL	2.5-15 mL/min; diluted to an osmolarity of 260-290 mOsm/L	SWFI	10-20 min	90-120 min	Dry and bitter mouth; no serious adverse effects
Naloxone	Opioid overdose	2 mg	2 mg/2 mL	+3 mL	NS	4-5 min	Unknown; repeat as necessary	Minimal adverse effects have been noted; most consistent with opioid withdrawal (agitation, diaphoresis, nausea/vomiting)

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Table 3. Practical Implementation Considerations

Drug	Indication	Nebulized dose	Concentration used	Dilution for administration	Diluent	Onset of action	Duration of action	Adverse effects
Nitroglycerin	ARDS, RVD, pulmonary hypertension, asthma exacerbation, pulmonary embolism, refractory hypoxemia	20 µg/kg to 5 mg	200 µg/mL (1 mg/mL if available)	Undiluted (200 µg/mL) or dilute (1 mg/mL) to final volume of 5 mL	NS	3-5 min	20-60 min	Minimal to no change in systemic vascular resistance
Sodium bicarbonate	Chlorine and chloramine gas exposure	4 mL of 3.75%, 4.2%, or 5% solution	3.75% to 5%	• 5%: 3 mL 8.4% + 2 mL diluent • 4.2%: undiluted or 2 mL 8.4% + 2 mL diluent • 3.75%: 3 mL 8.4% + 3 mL diluent	NS	0-5 min	Unknown; some have documented its use for 4 hours until symptom resolution	Minimal adverse effects have been noted; however, maintenance of inspiratory and expiratory effort is needed to help facilitate not only gas exchange but also heat exchange due to the exothermic reaction that occurs after administration
Tranexamic acid	Hemoptysis	250-500 mg	100 mg/mL	Undiluted	NS	48 h		None
	Post-tonsillectomy hemorrhage	500-1,000 mg	100 mg/mL	+5-15 mL		20-30 min	2 hours	

Abbreviations: ARDS, acute respiratory distress syndrome; COPD, chronic obstructive pulmonary disease; HF, hydrofluoric acid; IV, intravenous; NS, normal saline; RVD, right ventricular systolic dysfunction; SC, subcutaneous; SWFI, sterile water for injection.

presenting with reactive airway dysfunction syndrome due to chlorine exposure, patients were given nebulized sodium bicarbonate or placebo in addition to standard of care.[93] Patients presented with symptoms consistent with chemical airway injury, and those receiving nebulized sodium bicarbonate were found to have statistically significant improvements in FEV_1 values and quality-of-life scores after treatment. Similarly, an retrospective observational study conducted by the Kentucky Regional Poison Center reviewed 86 cases of chlorine gas inhalation treated with nebulized sodium bicarbonate at their recommendation.[89] Of the 86 cases of chlorine gas inhalation, 69 (80%) were treated with nebulized sodium bicarbonate. Only 17 (20%) required hospital admission. No patients developed pulmonary edema or required mechanical ventilation, and no adverse effects were noted. Additional case series have generally corroborated the findings of these larger studies.[87,91,94,95] Various formulations have been proposed for nebulization, ranging from an undiluted 4.2% nebulized solution to compounded 5% and 3.75% solutions. The highest level of evidence exists for the 4.2% solution, which may be compounded by adding equal parts of the 8.4% sodium bicarbonate solution and normal saline or by using the commercial preparation. An approximate 3.75% solution may be compounded by adding 3 mL of the 8.4% sodium bicarbonate solution to 3 mL of normal saline.[96] Sodium bicarbonate is officially recognized as a nonspecific antidote for chlorine and chloramine gas exposure by the Tactical Programs Division of the Administration for Strategic Preparedness and Response under the Department of Health and Human Services, and nebulization should be considered in gas exposures along with traditional therapies.[97]

Tranexamic acid (TXA)

The antifibrinolytic TXA has been demonstrated to reduce blood loss and transfusion rates in the operative theater when administered both

IV and topically.[98] In some scenarios, topical oral application of TXA yielded even higher salivary concentrations than IV administration.[99,100] Hence, the topical application of TXA has been suggested as a potential means to mitigate bleeding in the lungs, airways, and oral territories.[4,98] The most extensive documented experience regarding use of nebulized TXA in post-tonsillectomy hemorrhage comes from a retrospective cohort study in children conducted from 2016 through 2019.[101] The study found that use of nebulized TXA had no adverse effects and resulted in greater resolution of bleeding upon exam. These findings led the authors to conclude that nebulized TXA may be a safe first-line option for post-tonsillectomy hemorrhage. Another retrospective investigation looked at 27 adult and pediatric patients who received topical, nebulized, or IV TXA and found that TXA resulted in hemorrhage resolution in 77.8% of patients.[102] The utility of TXA in the setting of hemoptysis was explored in a pilot randomized controlled trial of 105 patients.[103] Patients presenting to the ED with active hemoptysis were examined and separated into one of 2 arms receiving nebulized or IV TXA. Hemoptysis cessation at 30 minutes after TXA administration was higher and the amount of hemoptysis was reduced in the 55 patients in the nebulized TXA arm. Another observational study of 19 pediatric patients looked at the efficacy of nebulized TXA in the cessation of pulmonary hemorrhage and found a success rate of 95% at 48 hours.[104] On the basis of the available data, it appears that TXA may be a viable option with a rapid onset of action in the setting of post-tonsillectomy hemorrhage refractory to traditional therapies, although more data are most certainly needed. Its role in the ED setting of hemoptysis management appears to be more in doubt, with a delayed onset of action and variations in reported efficacy.

A summary of the use of neubilized medications is provided in Table 2, while Table 3 details practical implementation criteria.

Conclusion

Although traditional routes of medication administration have a far larger evidentiary basis for use than the nebulization route, the evidence in this area continues to expand. This administration modality provides an alternative route conducive to rapid, less invasive access that is advantageous in the unique setting of the ED. The pharmacist is an essential bedside team member in these scenarios to assist with navigating the unique and complex nuances associated with this administration route as they develop.

Disclosures

These authors have declared no potential conflicts of interest

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