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Evaluation of The Efficacy of Preoperative Ketamine Nebulization on Postoperative Sore Throat due to Tracheal Intubation

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ABSTRACT

Background: Post-intubation sore throat (PIST) is a common postoperative disorder that is characterized with dysphagia, hoarseness and odynophagia. It is associated with multiple risk factors including mechanical trauma, high endotracheal cuff pressure and difficult intubation process. PIST is associated with patient's discomfort, which necessitate proper preventive measurement to reduce its incidence.

Objective: In this review we aimed to provide a comprehensive assessment of PIST, regarding its pathology, associated risk factors and treatment. Special focus is given to the role of nebulized ketamine in the treatment of PIST, due to its anti-inflammatory and analgesic effects.

Methods: We used Google Scholar, Science Direct, PubMed, and other internet databases for PIST, Ketamine, Difficult intubation, NMDA receptor antagonist and Airway management. Additionally, the writers combed through relevant literature for references, however they only included researches covering the years from 1999 to 2024. Due of lack of translation-related sources, documents in languages other than English were excluded. Also, works in progress, unpublished publications, abstracts from conferences, and dissertations that did not form part of broader scientific investigations were excluded.

Conclusions: We reported that difficult intubation is a major factor in the occurrence of PIST, emphasizing the need for accurate tools to predict difficult intubation and proper management. Additionally, our review demonstrated the ability of nebulized ketamine in reducing the incidence and severity of PIST due to its analgesic and anti-inflammatory actions based on its N-methyl-D-aspartate (NMDA) receptor antagonism. Ultimately, our review supports the recommendation for further high-quality studies to help establishing standardized protocol for the treatment of PIST.

Keywords: Post-intubation sore throat, Ketamine, Difficult intubation, NMDA receptor antagonist, Airway management.

INTRODUCTION

Sore throat following airway management is characterized by specific symptoms such as dysphagia, dysphonia, hoarseness, persistent throat pain, and pharyngeal dryness [(1)].

Among postoperative complications, PIST is ranked as the eighth most undesirable outcome, with incidence rates reaching up to 62% following general anesthesia (GA) [(2)]. Several factors have been identified as contributing to an increased risk of PIST, including female sex, prolonged intubation duration, multiple intubation attempts, younger age, elevated tracheal tube cuff pressure, use of a larger-sized tube, and airway trauma during intubation [(1,2)].

Typically, PIST is most severe within the first six hours after extubation, with symptoms gradually diminishing over time [(3)]. Although considered a minor postoperative complication, PIST can significantly impact patient satisfaction and recovery experience [(3,4)]. To mitigate PIST, various pharmacological and non-pharmacological interventions have been explored, though no single approach has been definitively proven to be superior [(4)].

Among pharmacological options, beclomethasone gel, azulene sulphonate gargles, ketamine, and licorice have demonstrated potential in reducing the severity and incidence of PIST [(3)].

Ketamine, an NMDA receptor antagonist, has been employed as a gargle to alleviate PIST due to its anti-nociceptive and anti-inflammatory properties [(5)]. However, nebulized ketamine presents distinct advantages over gargling, as it eliminates the bitter taste, requires a smaller volume, and reduces the risk of aspiration, thereby improving patient compliance and comfort [(6)].

The efficacy and safety of nebulized ketamine for PIST management have been extensively evaluated through randomized controlled trials, systematic reviews, and meta-analyses. These studies consistently reported that ketamine effectively reduces both the incidence and severity of postoperative sore throat associated with intubation [(7)].

Thus, this literature review aimed to provide a comprehensive analysis of the pathophysiology, preventive strategies, and treatment modalities for PIST, with particular emphasis on its association with difficult intubation. Additionally, it seeks to consolidate current evidence on the therapeutic application of ketamine, supporting clinical decision-making to achieve optimal efficacy while minimizing potential adverse effects.

Definition and prevalence of PIST: The term postoperative sore throat (PIST) lacks a precise definition and is often used to describe a broad spectrum of airway-related symptoms that arise in the early postoperative period. These symptoms may include pharyngitis, laryngitis, tracheitis, cough, hoarseness, or

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dysphagia, all of which can result from airway irritation and inflammation following tracheal intubation [2]. PIST is recognized as one of the most frequent postoperative complaints, with reported incidence rates ranging from 21% to 65%. This considerable variation can be attributed to multiple factors, including:

The type of airway device used (e.g., endotracheal tube vs. supraglottic airway). The technique of insertion and intubation-associated trauma. The use and type of lubricants applied to the airway device. Cuff pressure regulation, which affects tracheal mucosal perfusion. The duration of the procedure, influencing airway exposure to mechanical and chemical irritation. The choice of anesthetic agents, which may impact airway sensitivity. The evaluation methods used to assess postoperative throat symptoms. Patient-specific factors, such as age, sex, comorbidities, and individual airway anatomy. Given its multifactorial etiology, strategies to minimize the incidence and severity of PIST should focus on optimizing airway management techniques, selecting appropriate devices and lubricants, ensuring proper cuff pressure monitoring, and employing preventive pharmacological interventions when necessary [8].

Pathophysiology of PIST:

The pathophysiology of PIST is complex and multifactorial. It results primarily from mechanical trauma, pressure exerted by the endotracheal tube (ETT), and chemical irritation from anaesthetic agents [8].

The most common precipitating causes of PIST can be summarized as follows:

a) Mechanical trauma

Tracheal intubation is a traumatic process that disrupts the mucosal integrity of the upper airway. The insertion and removal of the ETT, especially when performed forcefully or repeatedly, can lead to direct injury to the tracheal mucosa, vocal cords, and larynx. This damage causes inflammation, soreness, and discomfort [8].

b) Cuff pressure and ischemia

The endotracheal tube cuff, when inflated too much, can compress the blood vessels in the tracheal mucosa, leading to ischemia and localized tissue injury. High cuff pressures, particularly with low-volume cuffs, contribute significantly to PIST. Studies recommend maintaining cuff pressures below 20–30 cm H_2O to minimize this risk [8].

c) Chemical irritation

Anaesthetic agents, including inhaled gases and intravenous drugs, can dry and irritate the mucosa, contributing to PlST. Chemical irritation, in combination with mechanical factors, exacerbates the discomfort [9].

Risk factors of PIST

Several factors are known to increase the risk of PIST, which include patient characteristics, intubation-related factors, and surgical procedure.

These factors can be classified as follows:

a) Tube size

Larger endotracheal tubes are associated with increased mucosal trauma, which directly correlates with higher rates of PIST [10].

b) Cuff pressure

High cuff pressures are one of the primary causes of PIST due to ischemic injury to the tracheal mucosa. So, the ideal cuff pressures less than or equal 25 cm H_2O and it significantly reduces PIST [10].

c) Duration of intubation

Longer intubation times result in more prolonged contact between the tube and airway tissues, increasing the risk of PIST. Studies indicate that intubations lasting more than two hours significantly raise the incidence of PIST [11].

d) Gender and age

Women tend to experience PIST more frequently than men, likely due to anatomical differences such as a smaller airway diameter. Older adults may also experience higher rates of PIST due to age-related changes in airway structure and mucosal function [12].

e) Difficult intubation

Difficult intubation, characterized by multiple attempts or prolonged procedures, is a known risk factor for PIST. The additional manipulation of the airway leads to more mechanical trauma, resulting in an increased risk of PIST [11,12].

f) Type of surgery (e.g., thyroid surgery)

Certain types of surgery, especially thyroid surgery, significantly increase the risk of PIST. The manipulation and positioning of the patient's head and neck can complicate the intubation process, leading to prolonged or difficult intubation attempts. Furthermore, direct manipulation of the airway during surgery, such as retraction, can exacerbate trauma to the trachea and vocal cords. Other surgeries involving the upper airway or head and neck, such as oral, nasal, or maxillofacial surgery, also elevate PIST risk due to similar airway manipulations [11].

g) Nasogastric tube (NGT)

The insertion of a nasogastric tube (NGT) postoperatively is another contributing factor to PIST. NGTs, particularly when used for abdominal surgery, can cause irritation to the mucosal lining of the throat and larynx, exacerbating postoperative discomfort. This irritation can increase the severity of post-operative sore throat when combined with the effects of intubation [12].

h) Uncuffed endotracheal tubes

In some cases, uncuffed endotracheal tubes are used, especially in paediatric patients or specific airway conditions. However, the lack of a cuff in these tubes can increase the risk of air leakage, and the increased friction between the tube and airway mucosa may lead to greater irritation and an increased incidence of PIST. Cuffed tubes, by providing a better seal, are generally associated with lower rates of PIST [12].

Prevention of PIST

To reduce the incidence of PIST, several strategies have been recommended. The use of smaller endotracheal tube has been suggested to reduce mechanical trauma to the tracheal mucosa, thereby lowering the incidence of PIST. Another helpful method is to optimize the cuff pressure, as maintaining appropriate cuff pressures is essential in preventing PIST [(3)]. Regular monitoring and keeping cuff pressures below or equal 25 cm H_2O has been associated with reduced mucosal injury. Finally, preoperative use of local anesthetic agents such as lidocaine or ketamine can be effective in preventing PIST by reducing inflammation and analgesia in the airway. Multiple evidence from published literature supports the hypothesis that lidocaine and ketamine can reduce the incidence of sore throat post-intubation [(4)].

Table (1): Means of reducing the incidence of postoperative throat symptoms [(13)]

General principles	After tracheal intubation	After LMA insertion
Experience of anaesthetist	Smaller tracheal tube	Correct size of LMA
Adequate anaesthesia/ relaxation of patient	Minimal cuff–tracheal contact area	?Inflation of cuff before insertion/ use of insertion aid
Careful technique	Monitoring and adjustment of intracuff pressure	Use of KY jelly/saline lubricant
Soft suction catheters	Avoidance of local anaesthetic/steroid lubricants	Minimisation of intracuff pressure

Difficult intubation

Difficult intubation is a significant challenge in anesthesiology, defined as the inability to intubate the trachea within a reasonable time or requiring multiple attempts, even when using standard laryngoscopy techniques. The incidence of difficult intubation varies between 1% and 10% of general anesthesia cases, depending on patient characteristics, operator expertise, and airway anatomy [(14)]. Furthermore, emergency intubation can be difficult in up to 8% of cases due to limited preparation and patient variability [(15)]. This condition poses substantial risks, including hypoxia, airway trauma, and even death if not managed effectively. Consistently, difficult intubation has been reported to be associated with various immediate and long-term complications. Immediate sequences include hypoxia and trauma, as prolonged intubation attempts reduce oxygen saturation, increase the risk of cardiac arrest and can result in laryngeal edema, mucosal bleeding and vocal cord injuries. On the other hand, long-term complications include laryngeal and tracheal stenosis. Difficult intubation is also a notable risk factor for PIST as repeated airway manipulations often lead to mucosal injury [(15, 16)].

Risk factors for difficult intubation: Several patient-related, anatomical, and procedural factors predispose to difficult intubation:

a) Patient-related factors:

• Obesity: Excess adipose tissue in the neck reduces mobility and hinders visualization of airway structures.

• Pregnancy: Increased airway edema and reduced functional residual capacity make intubation more challenging.

• Co-morbidities: Conditions like rheumatoid arthritis, cervical spine injury, or tumors compressing the airway increase the difficulty of intubation [(16)].

b) Anatomical factors:

• Reduced thyromental distance (< 6 cm): It suggests limited mandibular space for optimal laryngoscope insertion.

• Large tongue or Mallampati grade III/IV: Higher grades are predictive of difficult intubation due to obstructed airway visibility.

• Limited neck mobility: Conditions such as ankylosing spondylitis restrict neck extension essential for laryngoscopy [(17)].

c) Procedural factors:

• Lack of operator experience or inadequate preoperative airway assessment can lead to difficult intubation [(17)].

Relationship between difficult Intubation and PIST: Difficult intubation is a significant risk factor for PIST due to multiple contributing factors. Repeated intubation attempts can cause increased mechanical trauma to the airway mucosa, leading to greater inflammation, irritation, and potential injury [(18)]. The repeated passage of the endotracheal tube can also disrupt the mucosal barrier, making it more susceptible to post-procedural complications. Additionally, prolonged intubation time exacerbates the risk by subjecting the airway to extended mechanical stress, leading to higher mucosal pressure, ischemic injury, and localized inflammation, all of which predispose patients to PIST [(19)]. Furthermore, the use of adjunct airway devices, such as bougies and stylets—commonly employed in difficult intubations—can contribute to additional mucosal trauma. These devices, while useful in facilitating endotracheal intubation, increase friction and pressure on the delicate airway structures, further elevating the risk of developing PIST [(18)]. Given these factors, careful airway management strategies, including minimizing intubation attempts, optimizing technique, and using lubrication or smaller-diameter tubes when appropriate, are essential to reducing post-intubation complications and improving patient outcomes [(19)].

Prediction tools for difficult intubation

Accurate prediction of difficult intubation reduces its incidence and associated complications, including PIST [(19)]. Thus, multiple prediction tools have been developed to predict the difficulty of intubation including:

a) Mallampati grading (MPG)

The Modified Mallampati Grading (MPG) system is a widely used assessment tool for evaluating oropharyngeal visibility, which helps predict the likelihood of difficult intubation. The assessment is conducted by having the patient sit upright, open their mouth as widely as possible, and protrude the tongue without phonation. The examiner then observes and records the visible anatomical structures upon maximal mouth opening [20].

The classification is divided into four grades: Grade I: The soft palate, fauces, uvula, and tonsillar pillars are fully visible, indicating an open airway with minimal intubation difficulty. Grade II: The soft palate, fauces, and uvula are visible, though the tonsillar pillars may be partially obscured. Grade III: Only the soft palate and the base of the uvula are visible, suggesting a narrower oropharyngeal space and an increased likelihood of airway challenges. Grade IV: The soft palate is not visible at all, signifying a highly restricted oropharyngeal view and a significant risk of difficult intubation. Studies have shown that Mallampati grades III and IV are strongly associated with a higher incidence of difficult airway management, as reduced visibility of key oropharyngeal structures correlates with a more challenging laryngoscopic view and increased intubation difficulty [20].

b) Thyromental distance (TDM)

A TMD of < 6 cm indicates a higher risk of difficult intubation, as it suggests inadequate space for laryngoscope manipulation [21].

c) Cormack-Lehane grading

Cormack and Lehane developed a widely used classification system to describe laryngeal structures as seen through direct laryngoscopy, categorizing them into four grades based on visibility. Grade I is assigned when there is a full view of the glottic opening, allowing for an unobstructed passage of the endotracheal tube. Grade II is noted when only the posterior commissure of the glottis is visible, indicating a slightly more challenging airway but still manageable. Grade III occurs when the epiglottis is visible but the glottis itself is obscured, significantly increasing the difficulty of intubation. Grade IV, the most challenging scenario, is characterized by the complete absence of both the glottis and the epiglottis from view, posing a substantial challenge to successful airway management. Grades III and IV are classified as difficult laryngoscopy, requiring alternative intubation strategies to secure the airway safely [22].

Management of difficult intubation

Effectively managing difficult intubation necessitates a structured, stepwise approach, integrating meticulous preoperative planning, the use of specialized airway management techniques, and advanced airway devices to optimize patient safety and procedural success. The process begins with a comprehensive airway assessment, utilizing predictive screening tools to identify potential risk factors for difficult intubation, such as limited neck mobility, reduced mouth opening, or anatomical abnormalities [23]. This proactive evaluation allows anesthesiologists to anticipate challenges and formulate a tailored airway management plan. Ensuring the availability and preparedness of advanced airway equipment is fundamental in mitigating risks and improving the success rate of intubation. Essential devices include video laryngoscopes, fiberoptic bronchoscopes, supraglottic airway devices, and bougies, all of which enhance airway visualization and facilitate intubation in challenging cases. Video laryngoscopy has proven particularly beneficial in difficult airway scenarios by providing an improved line of sight, reducing the number of failed attempts, and minimizing trauma to airway structures, thus lowering the risk of PIST and other complications. In cases where difficult intubation is anticipated, awake intubation under local anesthesia is often the preferred technique, as it preserves spontaneous ventilation, reducing the likelihood of hypoxia and airway collapse [16].

The ability to maintain oxygenation during the procedure is especially critical for patients with severe airway compromise or limited respiratory reserve. Additionally, bougie-assisted intubation serves as an invaluable adjunct, particularly in situations where direct glottic visualization is inadequate. The use of a bougie—a flexible introducer—helps guide the endotracheal tube into the trachea, significantly increasing the likelihood of successful placement [23].

For the most complex and high-risk airway cases, fiberoptic intubation remains the gold standard, offering unparalleled precision in navigating the airway anatomy. By utilizing a flexible fiberoptic bronchoscope, clinicians can achieve real-time visualization of airway structures, allowing for a controlled and atraumatic passage of the endotracheal tube [16]. This technique is particularly advantageous in patients with airway tumors, severe anatomical distortions, or cervical spine instability, where conventional intubation methods may be unsafe or impractical. By employing a multifaceted approach that incorporates meticulous planning, advanced airway tools, and evidence-based techniques, clinicians can significantly enhance patient safety, minimize complications, and improve overall outcomes in the management of difficult airways.

What is Ketamine

Ketamine, a derivative of phencyclidine, was first described in 1965 and introduced into clinical practice in the 1970s. As an FDA-approved drug, it remains unique among anesthetics due to its combined analgesic, hypnotic, and amnesic properties. Unlike conventional anesthetic agents, ketamine induces a state of dissociative anesthesia, characterized by an electrophysiological disconnection between the limbic system and the cerebral cortex, leading to profound analgesia and altered consciousness [5].

Mechanism of Action: Ketamine exerts its effects on the central nervous system (CNS) while also possessing local anesthetic properties. Its primary mechanism of action involves noncompetitive antagonism of the NMDA receptor, specifically by blocking the Ca^{2+} channel pore [6]. This NMDA channel inhibition is considered the fundamental basis of ketamine's anesthetic and analgesic properties, both at the level of the CNS and spinal cord receptors. Additionally, ketamine suppresses the presynaptic release of glutamate, further contributing to its analgesic effects. Notably, the S (+) enantiomer exhibits a three- to four-fold higher affinity for the NMDA receptor compared to the R (-) enantiomer, making it the more potent isomer in clinical applications. Ketamine exerts its effects through multiple mechanisms beyond NMDA receptor antagonism. It interacts with mu and kappa opioid receptors, though with much lower affinity than NMDA receptors, and its analgesic effects are not reversed by naloxone. Ketamine exerts its effects through antagonistic interactions with monoaminergic, muscarinic, and nicotinic receptors, resulting in anticholinergic manifestations such as tachycardia and bronchodilation. At elevated doses, it demonstrates local anesthetic properties by inhibiting neuronal sodium channels. Its NMDA receptor blockade plays a pivotal role in preventing central sensitization of dorsal horn neurons, which are integral to pain signal transmission. Under typical physiological conditions, magnesium acts as a natural gatekeeper of the NMDA channel. However, sustained excitation removes this blockade, permitting calcium influx. This cascade of events fosters neuronal hyperexcitability, opioid resistance, heightened pain perception (hyperalgesia), and pain triggered by normally non-painful stimuli (allodynia), a process believed to be mediated by nitric oxide synthesis [24-26].

Among clinically available NMDA-receptor-channel blockers, ketamine is the most potent, selectively binding to the phencyclidine site when the channel is in its open conformation. In clinical practice ketamine is used for multiple purposes, including anesthetic agent especially in hemodynamically unstable patients due to its ability to preserve the airway, analgesic in pain management especially in patients resistant to other types of pain killers and sedative agent utilized pre-procedure in pediatric and trauma patients [27]. Whereas contraindications for ketamine include disorders like porphyria, hyperthyroidism, severe cardiovascular disease and previous psychotic illness [28].

Table (2): Indications and contraindications of ketamine [27].

Indications	Contraindications
Ketamine plays a versatile role in anesthesia and pain management across a wide range of clinical scenarios, including: **Induction of anesthesia:** Particularly valuable in patients with cardiovascular instability, shock, severe dehydration, severe hypovolemia, or severe anemia. **Respiratory considerations:** Effective in managing patients with respiratory failure, bronchospasm, COPD with bronchospasm, or reactive airway disease, especially when airway management poses a challenge. **Surgical Applications:** Used in major thoraco-abdominal procedures and brief surgical interventions. **Obstetric use:** Provides transient analgesia during delivery. **Adjunctive anesthesia:** Acts as a supplement for inadequate regional or local anesthesia. **Sedation and analgesia:** Administered in low doses for procedural sedation and analgesia. **Outpatient surgery:** Suitable for ambulatory procedures due to its rapid onset and recovery profile. **Age-Specific Use:** Employed in both adult and pediatric anesthesia. **Postoperative pain management:** Effective for analgesia in the recovery room and intensive care units. **Intensive care procedures:** Utilized for procedural sedation in critically ill patients, including pediatric cannulation and central line placement. **Resource-limited settings:** A valuable anesthetic agent in developing countries and field hospitals. **Chronic pain management:** Used for patients with persistent pain conditions. **Disaster and emergency medicine:** An essential agent for pain relief and sedation in trapped casualties.	**A high predisposition to laryngospasm or apnea** (e.g., active pulmonary infection, patients younger than 3 months). **Severe cardiovascular disease**, such as angina, heart failure, or malignant hypertension (because of cardio stimulant effects of ketamine, although this is controversial). **CSF obstructive states** (e.g., severe head injury, central congenital or mass lesions). **Intraocular pressure pathology** (e.g., glaucoma, acute globe injury). **Previous psychotic illnes**s (potential activation of psychoses) **Hyperthyroidism** or thyroid medication use (possibility of severe tachycardia or hypertension). **Porphyria** (possibility of triggering a porphyria reaction).

How ketamine can reduce the incidence of PIST:

The anti-inflammatory effects of ketamine combined with its capacity to provide local anaesthetic, and analgesic properties have demonstrated potential to decrease PIST [4]. Through its action as an NMDA receptor antagonist ketamine controls central sensitization and blocks excitatory neurotransmitters from release, which decreases hyperalgesia and pain intensity after airway instrumentation procedures [24]. Through its anti-inflammatory mechanisms ketamine restricts pro-inflammatory cytokine release while minimizing oxidative stress thus helping to decrease mucosal irritation from intubation procedures [27]. The sodium channel inhibition mechanism enables this substance to function as a local anaesthetic that helps reduce airway sensitivity and discomfort. Clinical research demonstrates nebulized ketamine administration as the most effective method for sore throat treatment because it provides sustained mucosal contact through nebulization and intravenous infusion and gargling methods [29].

The use of ketamine as a gargling solution for PIST prevention has a history of application based on its pain-relieving and anti-inflammatory characteristics. Research indicates ketamine gargles applied before surgery produce a protective layer on pharyngeal and laryngeal membranes that minimize damage when patients undergo intubation **[30]**. The use of ketamine as a gargling solution faces several drawbacks because it causes unpleasant tastes and nausea and allows some drug absorption into the bloodstream which may result in dizziness and hallucinations in certain patients. Gargling procedures show inconsistent patient cooperation which reduces their effectiveness in particular medical environments. Direct mucosal contact through nebulized ketamine has proven better than gargling by eliminating the discomfort of the latter approach. Through, nebulization the drug reaches a wider area of the respiratory tract resulting in equal distribution of medication that provides pain relief and anti-inflammatory benefits while producing minimal systemic side effects. Nebulization has become a preferred strategy for PIST prevention because it improves patient comfort and enhances compliance while showing increased popularity in clinical practice **[30-31].**

Ketamine nebulization for PIST: Ketamine nebulization presents distinct advantages over traditional gargling methods. By circumventing the bitter taste of ketamine and requiring a significantly smaller volume, nebulization mitigates the risk of aspiration associated with accidental ingestion, thereby enhancing patient compliance [32]. The efficacy of ketamine in this context is attributed to its potent NMDA receptor antagonism and anti-inflammatory properties, as evidenced by findings from animal models. While, ketamine primarily exerts its effects on the central nervous system and components of the limbic system, its administration via nasal, gargling, and rectal routes suggests an additional peripheral mechanism of action [33]. The practice of ketamine gargling has demonstrated considerable efficacy in reducing both the incidence and severity of PIST, primarily due to its anti-inflammatory effects. However, its clinical utility is hindered by its inherently bitter taste and the necessity of a larger volume, which increases the potential for aspiration [30]. In pediatric populations, honey is often incorporated to counteract its unpleasant taste. Alternative pharmacological interventions that have been explored in the management of PIST include aspirin gargles, benzydamine hydrochloride (BH) gargles, transdermal ketoprofen, lignocaine 10% spray, IV dexamethasone, beclomethasone gel applied to the tracheal tube, and magnesium lozenges, all of which have demonstrated effectiveness in alleviating PIST symptoms for up to 24 hours postoperatively [7].

Emerging evidence suggests that the use of a Glide Scope® video laryngoscope for endotracheal intubation significantly reduces PIST incidence compared to the Macintosh blade in patients with normal airways, particularly at the 6- and 24-hour postoperative intervals. In oxygen-driven nebulization systems, compressed air transforms liquid ketamine into an aerosol, producing hyperdispersed particles that undergo filtration through nebulizer baffles to eliminate larger droplets **[34]**. During the use of wall-mounted oxygen driven nebulization the liquid is broken up into droplets by the compressed air. The aerosol produced is hyperdispersed in size and is filtered within the nebulizer by baffles to remove the largest droplets **[34]**. The pneumatic nebulization technique generates particle sizes ranging from 10–25 μm, which predominantly settle in the oropharyngeal region, whereas smaller particles (5–10 μm) transition deeper into the airway. This targeted deposition likely contributes to the attenuation of PIST severity through the combined mechanisms of topical analgesia, anti-inflammatory action, and NMDA receptor antagonism **[35]**.

CONCLUSION

PIST is a common post-operative disorder that is associated with multiple risk factors, most commonly difficult intubation due to repeated attempts. Current treatment regimens for PIST include preventive measurement like adjusting the endotracheal tube size, optimizing the pressure of the endotracheal cuff and the utilization of anesthetic drugs like lidocaine and ketamine. Ultimately, ketamine nebulization has been proved to be beneficial prophylactic treatment in preventing the occurrence of PIST in patients.

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REFERENCES

1. **Mazzotta E, Soghomonyan S, Hu L (2023):** Postoperative sore throat: prophylaxis and treatment.

Front Pharmacol., 14: 1284071. doi: 10.3389/fphar.2023.1284071.

2. **Bhatta P, Shakya B, Bista N *et al.* (2020):** Effect of Preoperative Nebulized Ketamine on Incidence and Severity of Postoperative Sore Throat in Patient Undergoing General Anaesthesia with Endotracheal Intubation. Journal of Institute of Medicine Nepal., 42 (1): 12–6.
3. **Shinohara M, Iwashita M, Abe T *et al.* (2020):** Risk factors associated with symptoms of post-extubation upper airway obstruction in the emergency setting. J Int Med Res., 48 (5): 300060520926367. doi: 10.1177/0300060520926367.
4. **Ahuja V, Mitra S, Sarna R (2015):** Nebulized ketamine decreases incidence and severity of post-operative sore throat. Indian J Anaesth., 59 (1): 37–42.
5. **Shekhar S, Gupta A, Gupta S *et al.* (2019):** Comparison of Nebulized Ketamine and Ketamine with Clonidine in Postoperative Sore Throat. Anesth Essays Res., 13 (2): 313–6.
6. **Kuriyama A, Nakanishi M, Kamei J *et al.* (2019):** Topical application of ketamine to prevent postoperative sore throat in adults: A systematic review and meta-analysis. Acta Anaesthesiol Scand., 64 (5): 579–91.
7. **Varma S, Vazhakalayil S (2024):** Effects of Nebulization with Ketamine and Budesonide on Postoperative Sore Throat in Patients Undergoing Elective Surgeries Under General Anesthesia: A Randomized Controlled Comparative Clinical Study. Cureus, 16 (10): e72195. doi: 10.7759/cureus.72195.
8. **Yu J, Ren L, Min S *et al.* (2020):** Nebulized pharmacological agents for preventing postoperative sore throat: A systematic review and network meta-analysis. PLoS One, 15 (8): e0237174. doi: 10.1371/journal.pone.0237174.
9. **Sony S, Krishnamurthy J, Reddy K *et al.* (2023):** Comparison of Normal Saline and Alkalinized 2% Lignocaine to Reduce Emergence Phenomenon and Post-Intubation Morbidities: A Prospective, Double-Blind, Randomized Study. Cureus, 15 (1): e33910. doi: 10.7759/cureus.33910.
10. **Modak A, Rasheed E, Bhalerao N *et al.* (2021):** Comparison of Ketamine Nebulisation with Ketamine Gargle in Attenuating Post Operative Sore Throat Following General Anaesthesia with Endotracheal Intubation. Journal of Pharmaceutical Research International, 21: 129–36.
11. **El-Boghdadly K, Bailey C, Wiles M (2016):** Postoperative sore throat: a systematic review. Anaesthesia, 71 (6): 706–17.
12. **Ben Sasi O, Attia Z, Hassn A *et al.* (2022):** Effect of Nebulized Dexamethasone versus Nebulized Ketamine on Postoperative Sore Throat after Thyroid Surgeries. The Egyptian Journal of Hospital Medicine, 87 (1): 1613–8.
13. **McHardy F, Chung F (1999):** Postoperative sore throat: cause, prevention and treatment. Anaesthesia, 54 (5): 444–53.
14. **Malvi A, Jain S (2022):** Laryngeal Trauma, Its Types, and Management. Cureus, 14 (10): e29877. doi: 10.7759/cureus.29877.
15. **Cook T, MacDougall-Davis S (2012):** Complications and failure of airway management. Br J Anaesth., 109 (1): 68–85.
16. **Bradley J, Urman R, Yao D (2019):** Challenging the Traditional Definition of a Difficult Intubation: What Is Difficult? Anesth Analg., 128 (3): 584–6.
17. **Higgs A, McGrath B, Goddard C *et al.* (2018):** Guidelines for the management of tracheal intubation in critically ill adults. Br J Anaesth., 120 (2): 323–52.
18. **Puchner W, Drabauer L, Kern K *et al.* (2011):** Indirect versus direct laryngoscopy for routine nasotracheal intubation. J Clin Anesth., 23 (4): 280–5.
19. **Brodsky M, Akst L, Jedlanek E *et al.* (2021):** Laryngeal Injury and Upper Airway Symptoms After Endotracheal Intubation During Surgery: A Systematic Review and Meta-analysis. Anesth Analg., 132 (4): 1023–32.
20. **Yemam D, Melese E, Ashebir Z (2021):** Comparison of modified mallampati classification with Cormack and Lehane grading in predicting difficult laryngoscopy among elective surgical patients who took general anesthesia in Werabie comprehensive specialized hospital - Cross sectional study. Ethiopia, 2021. Ann Med Surg (Lond)., 79: 103912. doi: 10.1016/j.amsu.2022.103912.
21. **Wang B, Peng H, Yao W *et al.* (2018):** Can thyromental distance be measured accurately? J Clin Monit Comput., 32 (5): 915–20.
22. **Varela M, Carmo M, Lares A (2018):** Cormack-Lehane grading evolution to assess trainee's progress in laryngoscopy. Postgrad Med J., 94 (1114): 479. doi: 10.1136/postgradmedj-2018-135926.
23. **Kornas R, Owyang C, Sakles J *et al.* (2021):** Evaluation and Management of the Physiologically Difficult Airway: Consensus Recommendations From Society for Airway Management. Anesth Analg., 132 (2): 395–405.
24. **Deng M, Chen S, Pan H (2019):** Presynaptic NMDA receptors control nociceptive transmission at the spinal cord level in neuropathic pain. Cell Mol Life Sci., 76 (10): 1889–99.
25. **Ye S, Han Y, Wei Z *et al.* (2023):** Binding Affinity and Mechanisms of Potential Antidepressants Targeting Human NMDA Receptors. Molecules, 28 (11): 4346. doi: 10.3390/molecules28114346.
26. **Matveychuk D, Thomas R, Swainson J *et al.* (2020):** Ketamine as an antidepressant: overview of its mechanisms of action and potential predictive biomarkers. Ther Adv Psychopharmacol., 10: 2045125320916657. doi: 10.1177/2045125320916657.
27. **Zanos P, Gould T (2018):** Mechanisms of ketamine action as an antidepressant. Mol Psychiatry, 23 (4): 801–11.
28. **Rosenbaum S, Gupta V, Patel P *et al.* (2024):** Ketamine. In: StatPearls. Treasure Island (FL): StatPearls Publishing. http://www.ncbi.nlm.nih.gov/books/NBK470357/
29. **Tadesse M, Alimawu A, Kebede F *et al.* (2024):** Effectiveness of preoperative ketamine gargle to reduce postoperative sore throat in adult patients undergoing surgery with endotracheal tube; systematic review and meta-analysis of randomized control trials. BMC Anesthesiol., 24 (1): 449. doi: 10.1186/s12871-024-02837-7.
30. **Puri A, Ghosh S, Singh G *et al.* (2022):** Gargling with ketamine preoperatively decreases postoperative sore throat after endotracheal intubation in middle ear surgeries: A prospective randomized control study. Indian J Otolaryngol Head Neck Surg., 74 (3): 5739–43.

31. **Shrestha S, Bhattarai B, Singh J (2010):** Ketamine gargling and postoperative sore throat. J Nepal Med Assoc., 50 (180): 282–85.
32. **Liu X, Lang B, Zeng L *et al.* (2023):** Comparison of the effects of ketamine via nebulization versus different pharmacological approaches in pediatric sedation: a systematic review and meta-analysis of randomized controlled trials. BMC Anesthesiol., 23 (1): 375. doi: 10.1186/s12871-023-02298-4.
33. **Nguyen T, Mai M, Choudhary A *et al.* (2024):** Comparison of Nebulized Ketamine to Intravenous Subdissociative Dose Ketamine for Treating Acute Painful Conditions in the Emergency Department: A Prospective, Randomized, Double-Blind, Double-Dummy Controlled Trial. Ann Emerg Med., 84 (4): 354–62.
34. **Abdellatif A, Ali M (2014):** GlideScope videolaryngoscope versus flexible fiberoptic bronchoscope for awake intubation of morbidly obese patient with predicted difficult intubation. Middle East J Anaesthesiol., 22 (4): 385–92.
35. **Thomas D, Bejoy R, Zabrin N *et al.* (2018):** Preoperative ketamine nebulization attenuates the incidence and severity of postoperative sore throat: A randomized controlled clinical trial. Saudi J Anaesth., 12 (3): 440–45.