

Tranexamic Acid (TA) Inhalation Efficacy and Safety in Geriatrics on Anticoagulation Therapy -A Systematic Review

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ABSTRACT

Tranexamic acid is a lysine amino acid derivative and a synthetic anti-fibrinolytic agent. It suppresses plasminogen production by binding to lysine receptor sites on plasminogen. The electronic databases NCBI and PubMed, as well as studies of Google Scholar and grey literature up to 2022 in research utilizing tailored keyword searches, were all searched. Out of selected 50 articles, 7 publications were utilized following assessment. Nebulized tranexamic acid may be used to treat both major and non-massive hemoptysis caused by a variety of underlying conditions, according to some data. TA's antifibrinolytic characteristics, minimal risk of adverse effects, and inexpensive price make it an appealing off-label option for the elderly, although research and data are still lacking to back up its frequent usage in anticoagulation.



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1. INTRODUCTION

Tranexamic acid is a lysine amino acid derivative and a synthetic anti-fibrinolytic agent. It suppresses plasminogen production by binding to lysine receptor sites on plasminogen. There is no risk of significant bleeding since this avoids the fast destruction of the clots [22], [8]. For hemoptysis treatment, tranexamic acid is most often used intravenously, orally, and topically; however, just a few of research has examined its usage as an inhalation medication [10].

Off-label usage of systemic TA in children for the management of bleeding related to congenital heart surgery as well as orthopedic, neurosurgery, and trauma treatments has been shown to be effective [3]. Hemoptysis, or bleeding from the lungs, is increasingly being treated successfully in adults with systemic TA, according to a growing body of research [1]. Systemic (oral or IV) TA for hemoptysis was shown to be related to a substantial decrease in the duration of bleeding in adult patients in a systematic study [17]. Thromboembolism, neurotoxicity, and seizures may all occur when TA is administered systemically [14], [12].

Adult studies and case reports, on the other hand, show that TA breathed (inhaled TA) quickly stops

hemoptysis in healthy individuals after a single dosage, with no significant side effects [5]. TA breathed for hemoptysis was shown to be effective in 96% of patients within 5 days in the only randomized control study employing inhaled TA for hemoptysis [21].

Nausea, diarrhea, headache, muscular soreness, and dizziness are all common side effects of systemic injection, yet they are all typically minor and short-lived [9]. Systemic administration has been associated with an increased risk of clotting (myocardial infarction, stroke, pulmonary embolism, and deep vein thrombosis) [9]. Use in different bleeding diseases through intravenous, oral and topical methods notwithstanding its FDA-approved indications and dose is on the rise [9]. Topical TXA seems to be well tolerated since there have been few to no reports of any side effects [9]. There is the potential for nebulized TXA to be an easily accessible treatment alternative for hemoptysis in the emergency department, functioning as a bridge until additional definitive therapies can be organized. Additionally, nebulized TXA may be a viable choice for individuals whose treatment objectives need minimal invasive procedures [9].

TA's antifibrinolytic characteristics, minimal risk of adverse effects, and inexpensive price make it an appealing off-label option for the elderly, although research and data are still lacking to back up its frequent usage in anticoagulation. In this review, the efficacy of inhaled Tranexamic acid for anticoagulation in older age people is discussed.

2. Methodology

The electronic databases NCBI and PubMed, as well as studies of Google Scholar and grey literature up to 2022 in research utilizing tailored keyword searches, were all searched in a methodical manner. The databases were chosen because they are thought to be reliable and trustworthy sources. Duplicate research was removed and all of the data from the different databases were combined. The titles and abstracts were scrutinized to weed out any articles that were not relevant. The whole texts of publications that could be relevant were retrieved and examined. Finally, it was determined if any additional articles were connected by the highlighted publications' reference lists. During the first examination, 50 studies in all were found (see figure 1 below). 20 unrelated publications were eliminated after repetitions were removed. After reviewing the abstracts of the remaining 30 papers, a total of 20 publications were dropped from consideration. 15 articles' whole texts were assessed. 8 other publications were eliminated because they were unrelated to the subject of the study. 7 publications were utilized following assessment.

3. Results

The most common cause of hemoptysis in four male patients (ages 82, 58, 84, and 71) who were hospitalized to the respiratory department was lung cancer. A jet nebulizer with a 5 L of oxygen per minute flow rate of was used to give the tranexamic acid, and dosages of 2.5 or 5 mL were recommended based on clinical judgement, using a 500 mg/5 mL concentration. The nebulization process took 15 minutes on average. With a mean hemoptysis volume of 100 mL per day across all patients, the bleeding was categorized as moderate and there were no signs of severe hypotension, tachycardia, or hypovolemic shock. The use of inhaled TA resulted in adequate hemorrhage control and no instances of systemic side effects. After receiving the third dosage of TA, one patient experienced bronchospasm that was effectively managed with short-term bronchodilators. The results were in line with previous studies that suggested that using inhaled TA as a substitute for hemoptysis therapy significantly improves bleeding [18].

A therapeutic challenge arises when hemoptysis and pulmonary embolism (PE), two life-threatening respiratory crises, coexist. The study used the case of a 65-year-old man who had a pulmonary infarction, spontaneous submissive PE, and mild hemoptysis. Systemic anticoagulation was not possible due to

hemoptysis. Nebulized tranexamic acid was used when a cautious management approach failed. Hemoptysis had stopped following four 500 mg nebulized tranexamic acid doses spaced six hours apart. A successful start to intravenous heparin-based systemic anticoagulation was made 12 hours following the final episode of hemoptysis. Over the following five days, the patient was weaned off of high-flow nasal oxygen treatment without experiencing a repeat of hemoptysis. Tranexamic acid may be an effective non-invasive therapy for these illnesses despite the lack of clinical trials [2].

An invasive airway malignancy patient with significant hemoptysis arrived at the emergency room. The bleeding was controlled non-invasively with a nebulized tranexamic acid solution. 15 minutes after the nebulized TA treatment began, the patient's hemoptysis stopped. There were no known negative outcomes. hemorrhage control in selected patients may be possible using nebulized tranexamic acid, which seems to be safe, efficacious, and noninvasive. As a palliative treatment for persistent hemoptysis and as a tool for stabilizing hemoptysis acutely, nebulized TXA may be beneficial [6].

According to a study, a 70-year-old female patient with microscopic polyangiitis, end-stage renal disease (ESRD) requiring dialysis, atrial fibrillation, and no history of anticoagulation presented with dyspnea. She was first hospitalized for multiple lobe pneumonia, but when her hypoxia worsened, she had a cardiac arrest. Her hemoptysis was successfully treated with an I-TA dosage. Inhalation of I-TXA is both effective and safe in the treatment of hemoptysis caused by vasculitis, since major adverse effects may be avoided. In addition, the use of I-TXA may either allow for the resolution of hemoptysis or allow for further time for stabilization as a bridge to other treatments [13]. Study participants were hospitalized to the hospital with hemoptysis due to different causes, and they were given either nebulized TA, 500 mg twice a day, or normal saline as a control. Patients experiencing hemodynamic or respiratory instability, as well as significant hemoptysis (expected blood > 200 mL/24 h), were excluded from the study. The mortality and recurrence rate of hemoptysis were evaluated at 30 days and one year. All 47 individuals were randomized to either get TA inhalations or normal saline inhalations. On day 2 of admission, TA was linked with a substantial decrease in expected blood volume. More TA-treated patients than placebo-treated patients showed resolution of hemoptysis after 5 days of admission, a fewer patient needed invasive procedures such as interventional bronchoscopy or angiographic embolization to control the bleeding. Over the course of the follow-up period, neither group had any negative effects. At the 1-year follow-up, a lower recurrence rate was observed. Patients with non-massive hemoptysis may control bleeding using TA inhalations in a secure and efficient manner [21].

In a case study published in [10], a 69-year-old woman with significant hemoptysis was treated with nebulized TA in the emergency department (ED), which stopped the bleeding and prevented the need for endotracheal intubation. She received a test dose of nebulized TA (1000 mg in 20 mL normal saline). Her hemoptysis subsided, her respiratory distress eased, and her vital signs stabilized within 10 minutes after receiving TA [10].

TABLE- 1

Author	Year	Tranexamic acid (TA)	Conclusion
[6]	2015	TA inhalation over 30 to 45 minutes of 1000 mg/100-ml normal saline inhalation	After 15 minutes of administration, the bleeding had ceased.

Patel et al	2016	500 mg of TA nebulized every 8 hours for at least 48 hours.	Bleeding ceased.
[19]	2016	A 5 L/min flow rate of oxygen was used to give TA doses ranging from 250 mg to 500 mg.	With TA, bleeding was controlled.
[2]	2020	Nebulized TA 500 mg	Hemoptysis precluded systemic anticoagulation
[13]	2019	Inhaled tranexamic acid in combination with pulse steroids	Bleeding stopped after first tranexamic acid
[10]	2018	1000 mg (TA) in 20 mL normal saline	hemoptysis resolved
[21]	2018	Tranexamic acid 500 mg nebulized 2x/d; nebulized normal saline as a placebo.	The intervention group had a higher rate of hemoptysis resolution after five days.

4. Discussion

A synthetic lysine analogue called tranexamic acid functions as an antifibrinolytic by reversibly binding plasminogen [22]. In various conditions, it has been used effectively as a hemostatic agent. Systemic tranexamic acid has been linked to thromboembolic side effects [16]. Using a jet nebulizer with a 5 L/min oxygen flow rate, 500 milligrams of tranexamic acid were nebulized in 5 mL of normal saline. Nebulization took place for 15 minutes. For four doses, the dosage was repeated every six hours. No bronchospasm, hypotension, or tachycardia—local or systemic adverse effects—were seen during or after the treatment. After administering a further two doses to avoid recurrence since the hemoptysis had subsided after two doses, the medication was stopped [2].

Nebulized tranexamic acid could be able to quickly manage hemoptysis without causing systemic adverse effects. Nebulized tranexamic acid was successfully used in a recent randomized controlled study to treat mild hemoptysis brought on by bronchiectasis, infection, or cancer [21]. Nebulized tranexamic acid has been used in other observational investigations in cancer patients [20]. Despite the positive results of these investigations, thrombosis-related systemic adverse effects have not been researched. Because intravenous tranexamic acid administration has been linked to thrombotic problems, using it in nebulized form should be done so with caution [4].

A common surgical technique is the administration of TA, an anti-fibrinolytic medication, to stop severe bleeding. It is often administered intravenously and binds to plasminogen reversibly; nonetheless, extensive thrombosis is one of its significant adverse effects [11]. The effectiveness of inhaled forms in the management of hemoptysis has been examined in recent research. Massive hemoptysis often necessitates extensive treatments, and frequently need an experienced practitioner, to stop the bleeding [7]. Nebulized TA for hemoptysis was studied in a recent randomized experiment by [21] with encouraging results. However, individuals with significant hemoptysis were not included in this study's cohort since it focused primarily on

patients with COPD (Chronic obstructive pulmonary disease), bronchiectasis, infection, and cancer. The use of I-TA in a patient with significant hemoptysis brought to light in this instance efficiently and safely reduced the bleeding without causing any systemic adverse effects, giving the patient additional time to stabilize. I-TA became a life-saving treatment in this situation when there was significant hemoptysis. The administration of I-TA may either enable hemoptysis to resolve or provide additional time for stabilization as a transitional measure to other therapies [13].

According to [6], nebulized TA seems to be a successful and noninvasive technique for managing hemoptysis in selected individuals. If you are suffering from persistent hemoptysis, nebulized TA may help alleviate symptoms and stabilizes hemoptysis in the short term [18]. There were no documented side effects for the patient. Patients having cardiac surgery, those who have had a cardiopulmonary bypass, and those who were administered TA intrathecally have all been documented to have suffered seizures as a result of TA usage [6]. If TA's mechanism of action is correct, it might theoretically raise the risk of blood clots (such as a myocardial infarction or stroke), although there is currently no data to back this up. There is a chance that the use of a nebulizer to administer TA might result in bronchospasm, however, this has not been proven. Additionally, stomach disturbances, allergic skin reactions, and vision disturbances are also minimal side effects [15].

[19] found that inhaled TA reduced bleeding time without affecting systemic effects, which is in line with earlier research suggesting it as an alternative therapy for hemoptysis [17], [20]. Hemorrhagic fibrosis, bronchiectasis, and lung metastases may all cause hemoptysis. TXA has been shown to lessen the length and amount of hemoptysis in these individuals [14].

5. Conclusion

Nebulized tranexamic acid may be used to treat both major and non-massive hemoptysis caused by a variety of underlying conditions, according to some data. Bronchoconstriction is the only negative effect that has been recorded, and it may be quickly treated by using a bronchodilator. As a result, tranexamic acid in the inhaled form must be taken into account. More investigation is required.

6. References

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