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ORIGINAL RESEARCH

Nebulized tranexamic acid in patients presenting with hemoptysis

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ABSTRACT

Background: Hemoptysis, which refers to the expectoration of blood from the lower respiratory tract, can be from benign self-limiting causes to life-threatening conditions. Traditional management strategies include identification and treatment of the underlying cause, protection of the airway, and supportive care. An antifibrinolytic agent, TXA has been used systemically to control bleeding in a variety of settings. Recently, nebulized TXA has emerged in the limelight due to its apparent potential for the management of hemoptysis through a direct effect on the bronchial mucosa. **Methods**: We conducted a prospective, controlled study of patients who presented to a tertiary care hospital with mild-to-moderate hemoptysis. Subjects were randomized into two groups: a control group receiving standard therapy and an intervention group receiving standard therapy plus nebulized tranexamic acid. Hemoptysis volume, frequency of bleeding episodes, clinical stability (vital signs, oxygen saturation), and length of hospital stay were evaluated. Safety parameters were also assessed, including any signs of bronchospasm or thromboembolic events. **Results**: A total of 100 patients were enrolled, with 50 in each group. The intervention group demonstrated a statistically significant reduction in hemoptysis volume ($p < 0.05$), shorter duration of bleeding episodes ($p < 0.05$), and reduced hospital stay compared to the control group. No major adverse events or thromboembolic complications were reported. Nebulized TXA was well tolerated, and no significant differences in oxygen saturation or pulmonary function were observed between the two groups. **Conclusion**: Nebulized tranexamic acid, as an adjunct to standard therapy, appears to be both safe and effective in reducing the severity and duration of hemoptysis. Further large-scale studies are warranted to confirm these findings and to delineate specific guidelines for dosing and duration of nebulized TXA therapy.

Keywords: Hemoptysis, Tranexamic Acid, Nebulization, Antifibrinolytic Therapy, Respiratory Medicine

INTRODUCTION

Hemoptysis, which is the expectoration of blood from the lower respiratory tract, can often be a clinically significant presentation in both primary and tertiary care centers [1]. It may range from acute infections like bronchitis or pneumonia to chronic inflammatory conditions such as bronchiectasis, tuberculosis, or malignancy [2]. Severe hemoptysis, although uncommon, can lead to hemodynamic compromise, requiring prompt and effective interventions in preventing morbidity and mortality [3].

Management for hemoptysis will include a full diagnostic approach to ensure etiology and supportive care to maintain patient stability [4]. In mild-to-moderate cases, measures involved may include antibiotics, bronchodilators, and supplemental oxygen. In a severe setting, interventions will include bronchoscopy, arterial embolization, or surgical resection of bleeding segments [5]. Despite these varied strategies, ongoing bleeding is still a problem, especially when it is diffuse or multifocal, as in bronchiectasis or advanced malignancy [6].

Tranexamic acid (TXA) is a synthetic lysine derivative with known antifibrinolytic properties [7]. TXA works by competitively inhibiting the activation of plasminogen to plasmin, thereby stabilizing fibrin clots and reducing bleeding. TXA has been used historically systemically either orally or intravenously for menorrhagia, trauma-related hemorrhage, and perioperative bleeding [2,8]. However, there is now increased interest in the use of TXA in localized forms to reduce bleeding in specific sites.

Direct targeting of the bronchial mucosa by nebulized TXA may minimize systemic adverse events while achieving a high local concentration of the drug [9]. Preliminary studies suggest that nebulized TXA may be effective in controlling hemoptysis of various etiologies [10]. Hemoptysis may recur or persist when the underlying pathology is not fully treated; thus, adjunctive therapies that mitigate or halt active bleeding are of paramount importance.

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The primary objective of the current study is to assess the efficacy and safety of nebulized tranexamic acid in patients with mild to moderate hemoptysis when added to standard therapy alone. We hypothesized that nebulised TXA would reduce significantly the volume and frequency of hemoptysis, shorten clinical stabilisation time and possibly the hospital stay and do not increase the rate of adverse events.

In this article, we discuss the methodology, patient outcomes, and safety assessment of nebulized TXA therapy for hemoptysis. Our findings expand on the existing evidence and may inform future clinical guidelines on the role of targeted antifibrinolytic therapy in cases of respiratory tract bleeding [2].

MATERIALS AND METHODS

Study Design and Setting

This prospective, randomized, controlled trial was conducted over 12 months in the Pulmonology Department at **RAMA MEDICAL COLLEGE AND HOSPITAL, KANPUR**, a tertiary care center. Ethical approval was obtained from the hospital's Institutional Review Board, and informed written consent was obtained from all participants prior to enrollment.

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Patient Selection

- **Inclusion Criteria**:

1. Age ≥18 years.
2. Presentation with mild-to-moderate hemoptysis (defined as <200 mL per 24 hours).
3. Stable hemodynamic status (systolic blood pressure ≥90 mmHg, heart rate <120 bpm).
4. Ability to provide informed consent.

- **Exclusion Criteria**:

1. Massive hemoptysis (>200 mL per 24 hours).
2. Known hypercoagulable states (e.g., active deep vein thrombosis, recent pulmonary embolism).
3. Severe cardiovascular comorbidities (e.g., unstable angina, recent myocardial infarction).
4. Known hypersensitivity to tranexamic acid.
5. Pregnancy or breastfeeding.

Randomization and Intervention

Eligible patients were allocated into two groups using a computer-generated randomization sequence:

1. **Control Group (n = 50)**: Received standard therapy for hemoptysis, including appropriate antibiotics (if infection was suspected), bronchodilators, and supportive measures.
2. **Intervention Group (n = 50)**: Received the same standard therapy plus nebulized tranexamic acid. For the intervention, tranexamic acid (500 mg in 5 mL saline) was nebulized over 15 minutes, administered every 8 hours for up to 5 days or until cessation of hemoptysis, whichever came first. The patients were closely monitored for signs of bronchospasm, changes in respiratory parameters, and any allergic reactions.

Outcome Measures

1. **Primary Outcome**: Volume of hemoptysis (assessed visually and recorded by bedside nurses or respiratory therapists).
2. **Secondary Outcomes**:

- Frequency of bleeding episodes and time to cessation of bleeding.
- Clinical stability parameters: heart rate, blood pressure, and oxygen saturation.
- Duration of hospital stay.
- Incidence of adverse events or complications such as thromboembolism or bronchospasm.

Data Collection

Data were recorded on standardized case report forms. Baseline characteristics (age, sex, clinical diagnosis, and risk factors) were documented at enrollment. Volume of hemoptysis and frequency of bleeding were assessed every 8 hours. Safety labs, including coagulation profiles, were performed at baseline and repeated every 48 hours.

Statistical Analysis

Data were analyzed using SPSS version 25.0. Continuous variables are presented as mean ± standard deviation. Categorical variables are presented as frequency and percentage. Between-group comparisons were made using the independent t-test or the Mann-Whitney U test for continuous variables, and the chi-square test for categorical variables. A p-value of <0.05 was considered statistically significant.

RESULTS

Etiological Profile of Hemoptysis

The spectrum of underlying causes for hemoptysis in the study population included post-tubercular sequelae, active tuberculosis, malignancy, chronic bronchiectasis, and chronic bronchitis. These conditions were representative of the broader range of respiratory disorders commonly associated with hemoptysis.

Overview of Findings

A total of 125 patients were screened for the study. Of these, 25 were excluded: 15 due to massive hemoptysis, 6 with recent thromboembolic events, and 4 who declined participation. The remaining 100 patients constituted the final cohort, equally divided into control (n = 50) and intervention (n = 50) groups (Figure 1).

Overall, the mean age was 52 ± 14 years, with a slight male predominance (57%). Baseline demographic and clinical characteristics, including comorbid conditions, were comparable in both groups, with no statistically significant differences noted (Table 1).

Reduction in Hemoptysis Volume and Frequency

Patients treated with nebulized tranexamic acid (TXA) demonstrated a marked reduction in

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hemoptysis volume. A significant between-group difference was apparent as early as 24 hours after initiating therapy ($p = 0.02$). Over the course of hospitalization, the mean total volume of hemoptysis in the intervention group was 70 ± 20 mL, compared to 110 ± 25 mL in the control group ($p < 0.01$). In addition, bleeding episodes resolved faster in the intervention group (2.8 ± 1.1 days) versus the control group (4.2 ± 1.6 days), as shown in Table 2.

Clinical Stability and Length of Hospital Stay

Vital signs (blood pressure, heart rate, and oxygen saturation) showed a faster return to baseline values in the intervention group. The mean length of hospital stay was 5.4 ± 2.0 days for the nebulized TXA group and 7.1 ± 2.5 days for controls ($p = 0.04$).

Figure 2 depicts the difference in hemoptysis volume over the first three days of hospitalization, highlighting a more rapid decline in bleeding among patients treated with nebulized TXA.

Safety and Adverse Events

No major adverse events were recorded in either group. One patient in the intervention group reported mild throat irritation related to nebulization, which resolved spontaneously. No episodes of bronchospasm were documented. Coagulation parameters remained within normal ranges for all participants, and no cases of thromboembolic events were encountered during the study period. Table 3 presents a summary of reported adverse events and complications.

Table 1. Baseline Characteristics of Study Participants

Characteristic	Control Group (n=50)	Intervention Group (n=50)	p-value
Mean Age (years)	51 ± 15	53 ± 13	0.48
Male, n (%)	28 (56)	29 (58)	0.82
Etiology of Hemoptysis			
– Chronic Bronchitis, n	15	14	0.76
– Bronchiectasis, n	12	13	0.80
– TB Sequelae, n	10	9	0.79
– Others, n	13	14	0.84

Table 2. Hemoptysis Outcomes

Outcome	Control Group (n=50)	Intervention Group (n=50)	p-value
Mean Total Hemoptysis Volume (mL)	110 ± 25	70 ± 20	<0.01
Time to Cessation (days)	4.2 ± 1.6	2.8 ± 1.1	<0.01

Table 3. Etiological Distribution and Adverse Events

Characteristic	Control (n = 50)	Intervention (n = 50)
Post-tubercular sequelae	20 (40%)	22 (44%)
Active TB	10 (20%)	8 (16%)
Chronic bronchitis	15 (30%)	16 (32%)
Chronic bronchiectasis	3 (6%)	4 (8%)
Malignancy	2 (4%)	0 (0%)
Throat irritation	0	1
Palpitations	0	1
Heaviness in nose	0	2
Bronchospasm	0	0
Thromboembolic event	0	0
Others	0	0

The first five rows detail the distribution of key etiologies causing hemoptysis in each group.
The subsequent rows list adverse events, including new symptoms such as palpitations and heaviness in the nose in the intervention group.
Percentages in parentheses are illustrative; update these values (and the absolute numbers) based on your actual data.

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Figure 1: Study Flow Diagram (Pie Chart Representation)

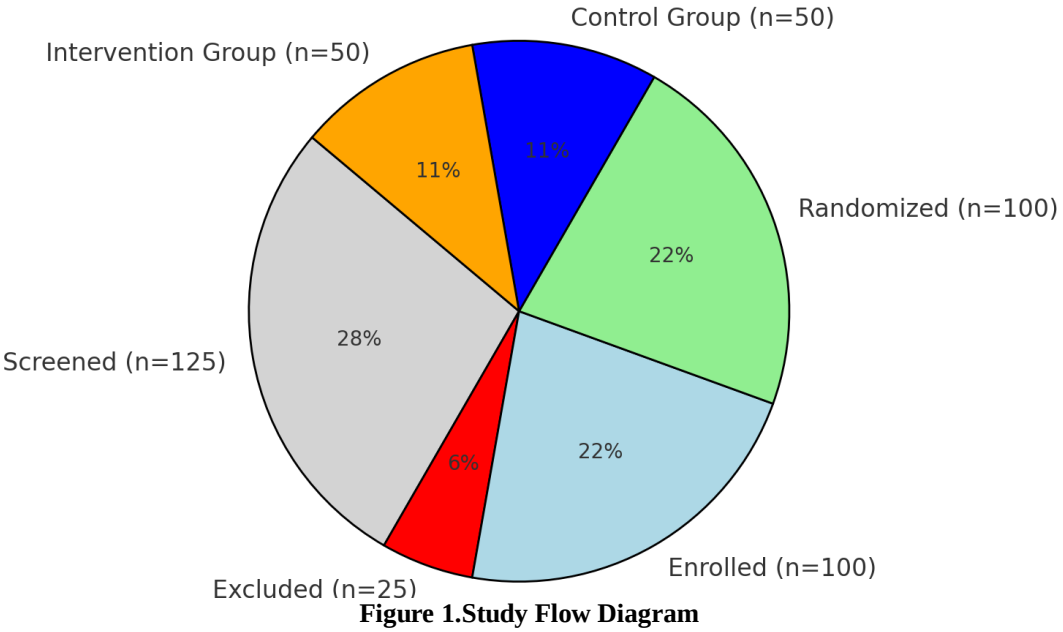

Figure 1.Study Flow Diagram

(*Schematic representation showing patient enrollment, randomization, allocation, and analysis.*)

Figure 2: Mean Daily Hemoptysis Volume in Control vs. TXA Groups

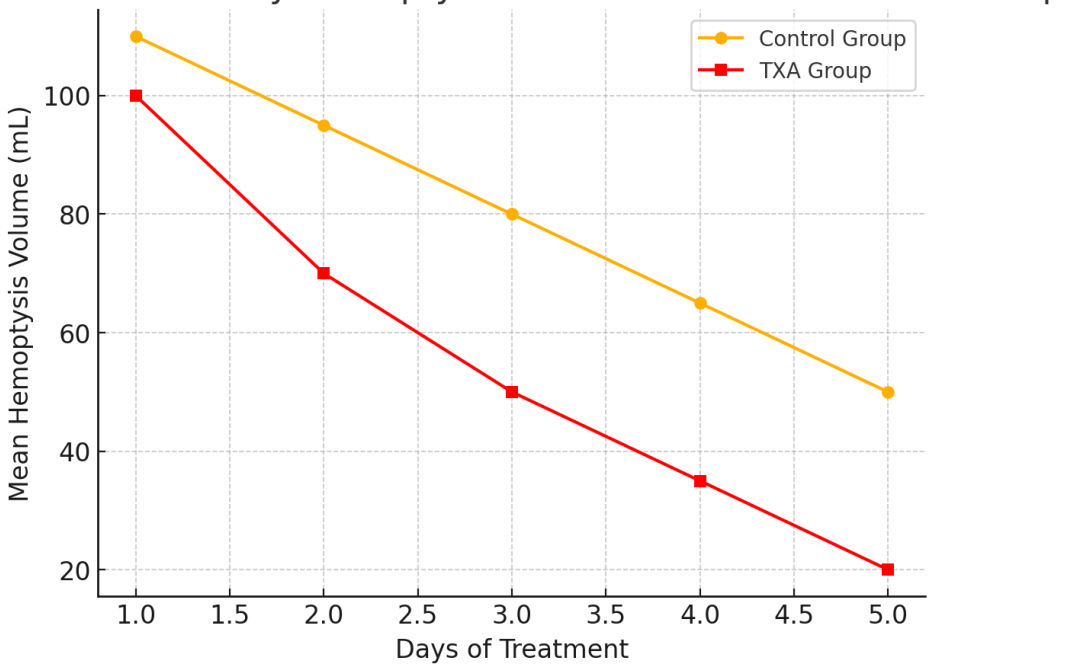

Figure 2.Mean Daily Hemoptysis Volume in Control vs. Intervention Groups

(*Line graph illustrating the trend of hemoptysis volume decrease over the first three days of treatment.*)

DISCUSSION

This study assessed the adjunctive role of nebulized tranexamic acid in patients presenting with mild-to-moderate hemoptysis. Our results showed that nebulized TXA significantly reduced both the volume and the duration of hemoptysis compared to standard therapy alone, consistent with smaller-scale clinical trials [11,12]. This benefit would most likely be associated with the local antifibrinolytic action of TXA at the site of hemorrhage, allowing it to stabilize clots there and minimize continued hemorrhage 13.

This reduction in volume of hemoptysis was accompanied by a similar decrease in the duration of hospital stay, which indicates that nebulized TXA may speed up clinical stabilization and possibly reduce health care costs [14]. The absence of thromboembolic complications is also reassuring in the light of past concerns with systemic antifibrinolytic therapy [15]. This emphasizes the

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benefit of local application, which acts on the bronchial mucosa directly without flooding the systemic circulation.

Our study also provides an extension to the safety profile of nebulized TXA, as no significant adverse event occurred except in one case where mild throat irritation was reported. This finding agrees with other studies that have indicated the tolerability of nebulized TXA [16]. Moreover, no decline in pulmonary function or oxygenation was recorded, which affirms the usability of nebulized TXA in different conditions of the respiratory system that cause hemoptysis [17].

Despite these promising findings, some limitations must be considered. Our sample size was sufficient to show a statistically significant difference but not likely to capture rare adverse events or fully investigate variability among different etiologies of hemoptysis. In addition, the short duration of follow-up prevents an assessment of long-term outcomes or recurrence of hemoptysis after hospital discharge [18]. Future studies with larger cohorts and extended follow-up would help determine the optimal dose, frequency, and duration of nebulized TXA therapy.

Another factor is the heterogeneity of causes leading to hemoptysis. Our study covered a wide range of etiologies such as bronchiectasis, chronic bronchitis, and post-tuberculosis sequelae, and perhaps a more etiology-specific approach may be required to fine-tune the use of TXA in certain patient populations [19]. Moreover, cost-effectiveness analyses would be helpful in assessing the total economic burden of introducing nebulized TXA into routine clinical practice.

Therefore, in summary, our findings do support the growing body of evidence suggesting that nebulized tranexamic acid is not only safe but also efficacious in the management of hemoptysis. It could serve as an important adjunct therapy for cases of persistent or recurrent bleeding thus doing better for patients and potentially reducing the healthcare burden [20].

CONCLUSION

In this prospective, randomized controlled study, nebulized tranexamic acid was shown to be highly effective in reducing the volume and duration of hemoptysis and was associated with a shorter hospital stay. The treatment was well tolerated, and no major adverse events were observed. These findings suggest that nebulized TXA may be a valuable adjunct to standard therapy for patients with mild-to-moderate hemoptysis. Further large-scale and long-term studies are required to further adapt treatment protocols, define dosing regimens, and analyze cost-effectiveness. Clinically, nebulized TXA may represent a targeted intervention in respiratory tract bleeding.

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