Efficacy of Nebulized Tranexamic Acid for Severe Hemoptysis at a Tertiary Academic Medical Center

Mary Kovacevic, PharmD, BCCCP; Afrah Alkazemi, MS, PharmD; Kevin Dube, PharmD, BCCCP; Julie C. Lauffenburger, PharmD, PhD; Adam Smith, BS RRT-ACCS; Stephen Malinowski, RRT; Gerald L. Weinhouse, MD

Brigham and Women's Hospital
Founding Member, Mass General Brigham

HARVARD MEDICAL SCHOOL TEACHING HOSPITAL

Background

- The management of severe hemoptysis mainly consists of invasive interventional procedures, such as angiographic bronchial artery embolization or various endobronchial interventions[1,2]
- There are limited non-invasive medical therapies available for the management of hemoptysis[2]
- Small studies show benefit with nebulized tranexamic acid (TXA), leading to a faster time to hemoptysis resolution and decreased need for invasive interventions[3,4]
- The objective of this analysis was to evaluate the efficacy and safety of nebulized TXA administration compared to conventional management in patients with hemoptysis

Methods

Design

- Single-center, retrospective, matched cohort study
- All patients with documented hemoptysis (ICD-10 R04.2) within the health record between January 1, 2018 - March 31, 2021
- Coarsened exact matching (CEM) was used to match up to 5 controls for all patients who received inhaled TXA based on the following severity criteria
  - Hemoptysis classification
    - scant < 5 ml, mild 5 - 30 mL, moderate 30 - 240 mL severe > 240 mL
  - Respiratory support
    - noninvasive ventilation, mechanical ventilation, none
  - SOFA score at the time of hemoptysis diagnosis

Major endpoint

- Need for invasive interventions for the management of hemoptysis
  - Interventional bronchoscopy
  - Angiographic embolization
  - Invasive surgical management

Minor endpoints

- Time to hemoptysis resolution
- Hemoptysis recurrence
- Duration of mechanical ventilation
- Intensive care unit (ICU) and hospital length of stay (LOS)
- Adverse effects
  - Thrombosis
  - Bronchospasm
  - Seizure

Statistics

- Data were analyzed using IBM SPSS Statistics (Version 27) software
- Continuous data were compared using Student's t-test (parametric) or Mann-Whitney U test (non-parametric)
- Chi-square test, with the Yates correction when appropriate were used for categorical data

Results

Baseline and Hemoptysis Characteristics

Baseline Demographics / Clinical Characteristics

Variable	Total (N = 80)	TXA (n = 15)	Control (n = 65)	*P*-value
Age (years)†	66 [51:72]	70 [65:72]	62 [43:72]	0.048
Gender, male	48 (80)	12 (80)	36 (55.4)	0.079
Weight (kg)†	71.1 [62.2:92.6]	88.5 [69.8:106.1]	70.3 [61.2:85.1]	0.036
Smoking history				
Never	37 (46.3)	4 (26.7)	33 (50.8)	0.091
Current	12 (15)	3 (20)	9 (13.8)	0.688
Former	30 (37.5)	7 (46.7)	23 (35.4)	0.416
Not assessed	1 (1.3)	1 (6.7)	0	0.187
Airway disease	34 (42.5)	10 (66.7)	24 (36.9)	0.036
Asthma	5 (6.2)	1 (6.7)	4 (6.2)	1
COPD	20 (25.0)	8 (53.3)	12 (18.5)	0.009
Bronchiectasis	6 (7.5)	1 (6.7)	5 (7.7)	1
Other*	2 (2.5)	0	2 (3.1)	1
COVID-19 positive at time of hemoptysis	2 (2.5)	2 (13.3)	0	0.033
Hypertension	42 (52.5)	8 (53.3)	34 (52.3)	0.943
Pulmonary hypertension	3 (3.8)	3 (20)	0 (0)	0.006
Malignancy	38 (47.5)	8 (53.3)	30 (46.2)	0.616
Vasculitis	18 (22.5)	3 (20)	15 (23.1)	1
On anticoagulant/antiplatelet	45 (56.3)	8 (53.3)	37 (56.9)	0.800

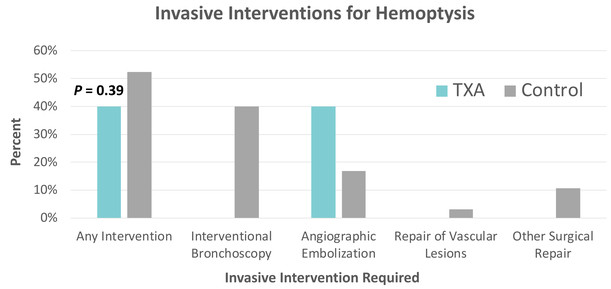
expressed as n (%) unless otherwise indicated
†median [IQR]
*Idiopathic pulmonary fibrosis, alpha-1-antitrypsin deficiency
COPD: chronic obstructive pulmonary disease
Comparison made between control group and TXA group

Baseline Hemoptysis Characteristics

Variable	TXA (n =15)	Control (n = 65)	*P*-value
Hemoptysis classification[β]			
Scant	0	0	-
Mild	1 (6.7)	7 (10.8)	1
Moderate	4 (26.7)	19 (29.2)	1
Massive	10 (66.7)	39 (60.0)	0.633
Required respiratory support[β]			
Mechanical Ventilation	6 (40)	33 (50.8)	0.452
ECMO	2 (13.3)	3 (3.7)	0.239
SOFA†[β]	6 [2:10]	5 [1:9]	0.436
Etiology			
Airway disease	4 (26.7)	24 (36.9)	0.336
Pulmonary vascular disease	3 (20.0)	1 (1.5)	0.020
Malignancy	1 (6.7)	13 (20.0)	0.450
Bleeding disorder	3 (20.0)	4 (6.2)	0.118
Acquired/Iatrogenic	3 (20.0)	13 (20.0)	1
Other	1	10 (15.4)	0.447
Undetermined	0	2 (3.1)	1.00
Bronchoscopy confirmed diffuse alveolar hemorrhage	3 (20.0)	8 (12.3)	0.423
Required ICU admission			
Yes	9 (60.0)	31 (47.7)	0.390
No	3 (20.0)	24 (36.9)	0.212
In ICU at time of hemoptysis	3 (20.0)	10 (15.4)	0.702

expressed as n (%) unless otherwise indicated
†median [IQR]
[β]Criteria used for CEM
ECMO: Extracorporeal membrane oxygenation, SOFA; Sequential organ failure assessment score

Major and Minor Endpoints



Nebulized TXA Use (n = 15)

Variable	Result
Nebulized TXA doses per patient†	9 [1:12]
Duration of TXA administration (hours)†	35.3 [12.3:151]
Location of administration	
ICU	9 (60)
Emergency Department	3 (20)
Floor	3 (20)
Dose	500 mg
Frequency	
Once	4 (26.7)
Every 6 hours	6 (40)
Every 8 hours	5 (33.3)

expressed as n (%) unless otherwise indicated
†median [IQR]

Results (Continued)

Minor Endpoints

	TXA	Control	*P*-value
Time to hemoptysis resolution (hours)	95.9 [21.5:227.3]	36 [16.5: 77.6]	0.061
Duration of MV (hours)	216 [175.5:385.1]	105.3 [44.1:328.8]	0.111
ICU LOS (days)	8.6 [1.8:19.5]	5.9 [2.4:18.7]	0.810
Hospital LOS (days)	23.1 [9.8:45.8]	10.7 [5.3:25.9]	0.071

All data presented as median [IQR]

Safety outcomes	TXA	Control	*P*-value
Pulmonary embolism	1 (6.7)	1 (1.5)	0.818
Deep vein thrombosis	0	8 (12.3)	0.341
Stroke	0	2 (3.1)	1.000
Bronchospasm	0	0	-
Seizure	0	1 (1.5)	1.000

All data presented as n (%)

Limitations

- Single-center, retrospective, observational study
- Unmeasured confounders may have impacted matching technique and patient selection
- Cessation of hemoptysis difficult to capture due to the retrospective nature and reliance on documentation

Conclusion

- Inhaled TXA did not have an impact on the requirement of invasive management for severe hemoptysis, however, no increase in adverse events was observed in the TXA group. Larger sample sizes may be warranted to determine the true impact of nebulized TXA for hemoptysis

References

1. Flume PA, Mogayzel PJ, Robinson KA, Rosenblatt RL, Quittell L, Marshall BC, et al. Cystic fibrosis pulmonary guidelines: Pulmonary complications: Hemoptysis and pneumothorax. Am J Respir Crit Care Med. 2010;182(3):298–306.
2. Earwood JS, Thompson TD. Hemoptysis: Evaluation and management. Am Fam Physician. 2015;91(4):243–9.
3. Wand O, Guber E, Guber A, Epstein Shochet G, Israeli-Shani L, Shitrit D. Inhaled Tranexamic Acid for Hemoptysis Treatment: A Randomized Controlled Trial. Chest. 2018;154(6):1379–84.
4. Solomonov A, Fruchter O, Zuckerman T, Brenner B, Yigla M. Pulmonary hemorrhage: A novel mode of therapy. Respir Med. 2009;103(8):1196–200.

The authors of this study have no conflict of interest to disclose