

Mini Review

Nebulized Tranexamic Acid for Hemoptysis

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ABSTRACT

The synthetic antifibrinolytic drug, tranexamic acid, is widely used intravenously, orally and topically to treat various bleeding complications. In recent years, there has been increasing evidence of its use as inhalation drug for hemoptysis. In this review, the available literature about aerosolized tranexamic acid is listed.

BACKGROUND

Hemoptysis is a common symptom in the emergency department.¹ It is defined as the expectoration of blood originating from the tracheobronchial tree or lung parenchyma.^{1,2} It is a symptom of diverse respiratory diseases such as lung cancer, infections and vasculitis.^{1,3,4} The severity can vary, ranging from immediate life-threatening hemorrhage to minimal blood-streaked sputum.³ Treatment options are diverse and mostly based on the underlying disease, for example radiotherapy for bronchial carcinoma, immunosuppressives for vasculitis or antibiotics for infections.^{3,4} For massive hemoptysis, interventional procedures such as angiographic bronchial artery embolization and various endobronchial interventions are used.^{1,3,5}

Tranexamic acid is a cheap, synthetic drug with anti-fibrinolytic activity based on inhibiting the activation of plasminogen.³ It is especially used intravenously, orally and topically to prevent and treat various bleeding complications, but only a few studies have investigated the effect of tranexamic acid as an inhalation drug for hemoptysis.² In this review, the available literature about aerosolized tranexamic acid for both massive and non-massive hemoptysis is listed.

MASSIVE HEMOPTYSIS

Massive hemoptysis is defined as hemoptysis that is more than 200 milliliters in 24-hours or hemoptysis that cause respiratory or hemodynamic instability.³ Review of the literature about the use of inhaled tranexamic acid for massive hemoptysis showed there are only case reports and case series available (Table 1). All cases except one demonstrated at least improvement and often

resolution of the bleeding after administration of nebulized tranexamic acid in patients of very different ages with varying underlying etiologies of the massive hemoptysis. There were no adverse events reported.^{2,4-10}

NON-MASSIVE HEMOPTYSIS

Non-massive hemoptysis is defined as hemoptysis less than 200 milliliters in 24-hours without respiratory or hemodynamic instability.³ Table 2 shows the available literature about nebulized tranexamic acid in non-massive hemoptysis. Calvo et al¹¹ showed in a case series of 4 males with moderate hemoptysis due to lung cancer or bronchiectasis that bleeding stopped after inhalation of tranexamic acid. One patient experienced bronchoconstriction as side effect which easily resolved after administration of a bronchodilator. In a randomized controlled trial of Wand et al³ 47 adults with non-massive hemoptysis of various underlying etiologies were randomized for getting nebulized tranexamic acid or nebulized normal saline. In the tranexamic acid group, the bleeding was stopped more frequently at day 5 and there was a shorter hospital stay than in the normal saline group. Moreover there was no need for invasive procedures in the tranexamic acid group while 18.2% of patients required angiography or bronchoscopy in the normal saline group.

DISCUSSION

There are some case reports and case series about the use of nebulized tranexamic acid in massive hemoptysis. Most showed improvement or even resolution of the bleeding after administration.^{2,4-10} Caution is needed since there is a high-risk of reporting bias as negative results are not often published. For non-

Table 1. Publications Regarding Inhaled Tranexamic for Massive Hemoptysis

Authors	Study Design	Study Population	Intervention	Results
Solomonov et al ⁵	Case series with 6 cases	Middle aged men and women with massive hemoptysis due to lung cancer (2), other types of cancer (3) or trombopenia (1)	500 mg tranexamic acid dissolved in water, sodium hydroxide or hydrochloric acid administered 3-4 x/day via inhalation (4) or via the bronchoscope (2). The duration of the therapy varied from one single dose up to 3-months	In all cases, the bleeding stopped with the first dose of tranexamic acid. No adverse events.
Hankerson et al ⁶	Case report	46-years-old man with massive hemoptysis via tracheostomy tube due to lung cancer	Inhalation of 1000 mg tranexamic acid dissolved in 100 ml normal saline over 30-45-minutes	Bleeding stopped 15-minutes after administration
Patel et al ⁷	Case series with 2 cases	One 75-years-old woman with massive hemoptysis due to bronchiectasis and one 79-years-old man with hemoptysis due to thrombocytopenia and chronic obstructive lung disease	500 mg nebulized tranexamic acid every 8-hours for a minimum of 48-hours	The bleeding stopped without other interventions.
Bernardo et al ⁸	Case series with 11 cases	Eleven children aged 0-18-year with pulmonary hemorrhage, mostly due to congenital heart disease, renal failure, malignancy and liver failure. All but one patient was intubated.	Inhalation of 250-500 mg tranexamic acid every 6-12-hours	Improvement of bleeding after 1 dose in all patients except 1. No adverse events.
Komura et al ²	Case report	69-years-old woman with massive hemoptysis post-chemotherapy for lung cancer on rivaroxaban. No effect of nebulized epinephrine.	Nebulization of 1000 mg tranexamic acid in 20 ml of normal saline	Bleeding stopped 10-minutes after tranexamic acid. No recurrence of bleeding.
Ng et al ⁹	Case report	30-years-old man with massive hemoptysis due to pulmonary tuberculosis. Bronchoscopy, angiography and intravenous tranexamic acid had failed.	48-hours of nebulized tranexamic acid (dose not mentioned in article)	Bleeding stopped after 48-hours
Modi et al ⁴	Case report	70-years-old woman with massive hemoptysis due to microscopic polyangiitis.	Inhaled tranexamic acid (dose not mentioned in article) in combination with pulse steroids	Bleeding stopped after first dose of tranexamic acid
Alabdrabalnabi et al ¹⁰	Case series with 3 cases	Three 14-66-years-old females with massive hemoptysis due to systemic lupus, vasculitis or anticoagulation. Two of them got intravenous tranexamic acid without resolution of bleeding.	Inhaled tranexamic acid 500 mg 3 x/day	Improvement in bleeding in all cases.

Table 2. Publications Regarding Inhaled Tranexamic for Non-Massive Hemoptysis

Authors	Study Design	Study Population	Intervention	Results
Calvo et al ¹¹	Case series	Four males, 58-84y old with moderate hemoptysis due to bronchiectasis (1) or lung cancer (3)	250-500 mg nebulized tranexamic acid 2-3x/day over 15 minutes	Bleeding stopped after 6-48 hours. One patient had bronchoconstriction as side effect, resolved after administration of a bronchodilator.
Wand et al ³	Randomized controlled trial	47 adult patients with non-massive hemoptysis of various etiologies	Intervention: 500 mg nebulized tranexamic acid 2x/d Placebo: nebulized normal saline	More frequent resolution of hemoptysis within 5 days in the intervention group. No need to interventional procedures in the intervention group. Shorter hospital stay in the intervention group.

massive hemoptysis there is 1 randomized controlled trail which showed beneficial effect of inhalation of tranexamic acid on bleeding time, need for invasive procedures and length of hospital stay.³ There is no ideal dosing known for aerosolized tranexamic acid. Moreover there are no comparative studies between intravenous, oral and nebulized tranexamic acid for hemoptysis. Further research with high quality randomized controlled trials is needed. In the meantime, nebulized tranexamic acid should be considered for patients with both massive and non-massive hemoptysis since there is some evidence, it is cheap and there are little side effects.

CONCLUSION

There is some evidence for the use of nebulized tranexamic acid in both massive and non-massive hemoptysis of various underlying causes. The only reported side effect is bronchoconstriction, easily resolved with administration of a bronchodilator. Therefore, aerosolized tranexamic acid must be considered. Further research

is needed.

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