

# Bronchoscopic, non-interventional management of hemoptysis in resource limited settings: insights from the literature

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**Abstract.** The non-invasive management of clinically significant hemoptysis by bronchoscopy remains a therapeutic challenge. Various agents have been used endobronchially in order to control hemoptysis, such as cold saline, tranexamic acid, and epinephrine. This review summarizes all available data in that view, especially in resource limited settings, where more advanced means of controlling hemoptysis are not available.

*Key Words:*

Hemoptysis, Cold Saline, Tranexamic Acid, Adrenaline, Bronchoscopy.

## Bronchoscopic Treatment Approach of Clinically Significant Hemoptysis

### *The "cold approach"*

The use of cold saline, as a mean to stop endobronchial bleeding, was first reported by Sahebji<sup>3</sup>, who described a case of hemoptysis that occurred during bronchoscopy, managed by endobronchial administration of 5 ml aliquots of iced normal saline, to a total dose of 35 ml, which completely stopped the bleeding<sup>3</sup> (level of evidence 5). Conlan and Hurwitz<sup>4</sup> reported a case series of 12 patients who presented with massive hemoptysis and who underwent rigid bronchoscopy with cold saline infusion (level of evidence 2b). Following blood and clot removal, the bleeding site was irrigated with aliquots of 50 ml normal saline at 4°C, which was subsequently sucked out after 30-60 seconds. The average volume required to stop the bleeding was 500 ml (range 300-750 ml) of cold saline. The procedure managed to stop the bleeding in all 12 patients and was successful in 2 cases where the bleeding relapsed<sup>4</sup>. In a larger series from Brazil<sup>5</sup>, 94 patients with massive hemoptysis underwent rigid bronchoscopy with cold saline infusion. The authors administered 30-50 ml aliquots of normal saline chilled at 4°C, with the average patient requiring 528 mL (range, 160 mL to 2500 mL) for the cessation of bleeding. The procedure was able to stop the bleeding in all 94 cases, as well as in 28 cases that relapsed<sup>5</sup> (level of evidence 2b).

In more recent series, it appears that cold saline continues to be utilized by bronchoscopists but in combination with other agents, such as epinephrine<sup>6,7</sup> (level of evidence 3a). Cold saline is also recommended by the British Thoracic Society (BTS) guidelines<sup>8</sup> as a measure to stop major bleeding that arises during bronchoscopy, using 5-10 ml aliquots of 4 °C saline<sup>8</sup>.

## Introduction

Hemoptysis constitutes a diverse clinical manifestation with varying severity and outcome that can be life threatening<sup>1</sup>, especially when the hemorrhage originates from the arterial circulation<sup>1</sup>. Computed Tomography (CT) of the chest with intravenous contrast is a crucial, mandatory, and usually initial step in the diagnostic and therapeutic approach to hemoptysis, followed usually by bronchoscopy. In many cases bronchoscopy is performed in an acute setting with limited resources<sup>2</sup>. This short literature review will present all relevant data for the acute bronchoscopic management of clinically significant hemoptysis in this setting.

## Materials and Methods

We searched the PubMed and Google Scholar databases for relevant articles, using the key words: "randomized controlled trial," "hemoptysis", "saline", "tranexamic acid", "adrenaline", "hemoptysis guidelines". Additional articles relevant to our theme were extrapolated from the references of the articles found at this search.

### ***The “vasoconstrictive approach”***

The use of epinephrine in bronchoscopy has also been recommended by the BTS guidelines<sup>8</sup> as a first measure to stop major bleeding that occurs during bronchoscopy, with a recommended dose of 5-10 ml 1:10000 epinephrine<sup>8</sup>. Endobronchial epinephrine should be used with caution, as it can lead to cardiac arrhythmias<sup>9</sup>.

A review<sup>10</sup> on the use of epinephrine as a hemostatic agent in bronchoscopy revealed that there are several recommended doses in the published literature, ranging from 0.5 ml of 1:20,000 to 20 ml of 1:20,000. The authors concluded that the use of epinephrine should be considered in cases where cold saline has already been tried and failed and mandates electrocardiographic monitoring. They recommended a dose of 2 ml aliquots of 1:100,000 epinephrine to a maximum dose of 0.6 mg<sup>10</sup> (level of evidence 3a).

Other local vasoconstrictive agents have also been used, mainly antidiuretic hormone derivatives, such as vasopressin, terlipressin, and ornipressin<sup>11,12</sup>. However, their use is limited in massive hemoptysis, as the massive bleeding dilutes the drug and washes it away<sup>6</sup>.

### ***The “thrombotic approach”***

Synthetic Tranexamic Acid (TA) is a cyclic aminocarboxylic acid that blocks the enzymatic breakdown of fibrin by plasmin reversibly, thereby inhibiting fibrinolysis<sup>13</sup>. Several studies have investigated the efficacy of TA in decreasing bronchial bleeding, either *via* oral or intravenous (IV) infusion. Nevertheless, their heterogeneous design has produced inconsistent results and low quality of clinical evidence<sup>7</sup>.

The infusion of TA through the bronchoscope has been reported as an effective mean to control bronchial bleeding, that occurred either spontaneously or following forceps biopsy<sup>14</sup> (level of evidence 2a). Furthermore, TA infusion through the bronchoscope in cases with visible lesions reduces the duration and volume of bleeding loss. Márquez-Martin et al<sup>15</sup> reported a prospective, non-randomized trial in which 48 consecutive patients with non-life-threatening hemoptysis were administered TA endoscopically, following ice-cold saline and adrenaline infusion. In the subgroup of patients that developed bleeding following an endobronchial biopsy (n=28), TA administration successfully stopped the bleed in all patients. However, in the subgroup of patients with spontaneous hemoptysis, endobronchial infusion of TA suc-

cessfully controlled the bleeding only in 11 out of 20 patients (level of evidence 2b)<sup>15</sup>.

Zamani<sup>16</sup> reported a case series of 20 patients undergoing bronchoscopic biopsy of tumoral lesions. In cases where persistent bleeding developed following bronchoscopic sampling of the lesions, the bronchoscopists administered an intratumoral injection of TA 250-500 mg using a 22-gauge Wang cytology needle. After a wait time of 2-3 minutes, multiple biopsy specimens were obtained by forceps from the tumoral lesions without producing active bleeding, in the entire group of patients. They did not report any procedure-related complications or side effects of TA injection (level of evidence 4)<sup>16</sup>.

A recent randomized controlled trial study<sup>17</sup> compared the efficacy of TA infusion (500 mg in 20 ml of saline) to that of adrenaline injections in controlling bronchial bleeding after endobronchial biopsies, in cases that the bleeding could not be controlled by cold saline infusion. The authors reported that the time to bleeding control did not differ among between the two groups (level of evidence 2b)<sup>17</sup>. Solomonov et al<sup>18</sup> in a case series study, demonstrated that, following endobronchial administration of TA, the addition of aerosolized TA 500 mg/5 ml 3-4 times daily, was able to reduce hemoptysis from an unidentifiable source of bleeding (level of evidence 4)<sup>18</sup>.

The abovementioned studies showed that endoscopic infusion of TA may be an effective alternative method in managing endobronchial bleeding, especially in centers without laser photocoagulation or other invasive techniques. Nevertheless, the studies that reported positive results are of moderate to low level of clinical evidence.

Beyond TA, thrombin has also been administered during bronchoscopy. The thrombin solution can be sprayed by syringe or applied directly either by soaking gauze or gelatin sponges instilled with the solution. Early studies<sup>19,20</sup> in cases of massive hemoptysis, revealed that the infusion of thrombin or prothrombin derivatives successfully stopped endobronchial bleeding (level of evidence 2b). Recently, Di Michiel et al<sup>21</sup> showed that the application of a topical fibrin sealant (TISSEEL) to the bleeding area, followed by deployment of an intrabronchial valve and a further application of TISSEEL over the valve, successfully controlled recurrent hemoptysis in two patients with malignancy (level of evidence 4).

## Conclusions

Multiple non-invasive modalities have been used in order to successfully control clinically significant hemoptysis, but the level of evidence remains questionable. Cold saline, TA, and adrenaline are the best studied treatment options, and are widely used in all bronchoscopy suits. Nevertheless, the level of evidence of studies supporting their administration reaches at best the 2b level. Notwithstanding, the administration of these modalities for the management of hemoptysis is recommended by all major guidelines. Thus, further randomized control trials are warranted in order to evaluate the best approach in this setting.

## Conflict of Interests

The authors declare that they have no conflict of interests.

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