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## RESEARCH ARTICLE

## THERAPEUTIC BRONCHOSCOPY IN HEMOPTYSIS - A STUDY OF 157 PATIENTS AND REVIEW OF LITERATURE

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### Abstract

**Objectives:** To study the role of fibreoptic bronchoscopy (FOB) in the management of hemoptysis. To study the efficacy of different bronchoscopic therapeutic maneuvers.

**Materials and methods:** 157 patients presenting with hemoptysis underwent FOB, out of which bleeding site was localized in 76 patients who were taken for different therapeutic maneuvers through bronchoscope. Control of bleeding was attempted by three methods: instillation of cold saline-epinephrine solution or a topical coagulant (botroclot) through the aspiration channel of the bronchoscope; and a tissue glue, n-butyl cyanoacrylate to the bleeding site through a polythene tube inserted via the bronchoscope.

**Results:** Instillation of cold saline-epinephrine solution via the bronchoscope as a therapeutic measure to control hemoptysis was very effective in 39.4% patients, somewhat effective in 42.4% patients and ineffective in 18.2% patients. Instillation of botroclot was very effective in 45.2% patients, somewhat effective in 35.5% patients and ineffective in 19.3% patients. Instillation of tissue glue n-butyl cyanoacrylate was very effective in 50% patients and somewhat effective in 50% patients.

**Conclusion:** Bronchoscopic therapeutic measures can be effectively used to control hemoptysis to buy time for more definitive therapies.

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## INTRODUCTION

Fibreoptic bronchoscopy (FOB) has been well established as a useful diagnostic procedure in evaluating hemoptysis. Hemoptysis is one of the most frequent indications for FOB, and it accounts for 10-30 % of bronchoscopic procedures in major medical centers<sup>1,2</sup>. Bronchoscopy is commonly performed, both for anatomic localization of bleeding site and to exclude neoplasm. Despite the potentially fatal outcome of hemoptysis, the underlying disease is usually otherwise benign and treatable<sup>3</sup>. The risk of death is particularly high when hemoptysis is massive<sup>4</sup>, and some investigators<sup>5</sup> estimate the risk of mortality with untreated massive hemoptysis to be in excess of 75%.

Bronchoscopy has been used for emergency management of endobronchial bleeding. The development of several endobronchial topical treatments has revolutionized the role of bronchoscopy in managing hemoptysis<sup>6</sup>. These measures are used mainly to control massive or life-threatening hemoptysis and can be combined with surgical treatment. Rigid bronchoscopy is generally preferred with massive bleeding, where need to remove large clots is anticipated, flexible bronchoscopy can also be used<sup>4</sup>. An iced saline solution can be instilled, along with vasoactive drugs such as epinephrine, to induce spasm of the bleeding vessels<sup>6</sup>. The bronchoscope itself can be used to stem the bleeding by tamponade of the bleeding site or to occlude the lumen of the bronchus from which the bleeding originates<sup>7</sup>. The same effect, perhaps with better local control, can be achieved with bronchoscopic balloon catheters<sup>8-13</sup>. Instillation of topical coagulants through the bronchoscope has reportedly been useful to control hemoptysis and several coagulants like bosmin<sup>14</sup>, reptilase<sup>15</sup>, thrombin<sup>16,17</sup>, fibrinogen-thrombin<sup>17-19</sup>, and fibrin

precursors<sup>17</sup> have been described. Sclerosing agents like cyanoacrylate have been used for local application at the site for control of hemoptysis<sup>20</sup>. Oxidized Regenerated Cellulose (ORC) mesh has also been used for the bronchoscopic hemostasis<sup>21</sup>.

## MATERIALS AND METHODS

The present study was conducted on 157 patients, who underwent bronchoscopy for hemoptysis, in the Department of Tuberculosis and Chest Diseases, Jawaharlal Nehru Medical College, Aligarh Muslim University, Aligarh. The study was approved by the local ethics committee. Patients with hemoptysis with normal or abnormal chest roentgenogram where bleeding was localized were included in the study for bronchoscopic therapeutic measures for control of hemoptysis. Patients who did not give consent for bronchoscopy were excluded from the study.

Detailed history and examination was done in all patients. The presenting quantity of hemoptysis was estimated as best as possible from the patient's history, and was classified arbitrarily according to the severity into mild(<30ml/day), moderate(30-200ml/day), or severe(>200ml/day) depending upon the amount of bleeding.

### Fibreoptic Bronchoscopy

All the patients underwent bronchoscopy using Olympus (BF Te2e) model in an endoscopy room or bedside. Medical records were analyzed for the quantity and duration of hemoptysis, prior diagnostic procedures, timing of FB (in relation to hemoptysis), endoscopic findings and results of any accessory procedures. A written and informed consent was taken. Fibreoptic bronchoscopy was done in the morning hours after an overnight fasting.

After mild sedation (intramuscular injection of promethazine, 25 mg, with atropine, 0.6 mg, 30 min before the procedure), the nose, pharynx, and upper airways were sprayed with lignocaine (4% solution), and fibreoptic bronchoscopy was performed. Transbronchial anaesthesia was obtained by nebulisation with lignocaine solution. Blood from the tracheobronchial wall was cleared by saline, and the bleeding segment/site was detected. This was further confirmed by asking the patient to cough, which resulted in fresh bleeding. Suspicious areas were routinely lavaged with sterile saline solution and reexamined to determine if they were the sites of bleeding. The duration of systematic inspection of the airways (to subsegmental levels) ranged from 30 to 40min or less, depending on the urgency of the situation and type of specimen collection, if any.

### Bronchoscopic Therapeutic Measures to Control Hemoptysis

As the FOB was already in place to confirm the diagnosis and, in view of the potentially serious consequences of continued hemoptysis, therapeutic measures were initiated immediately in patients in whom bleeding was localized. Great care was taken not to disturb any residual clot near the source of bleeding.

Control of bleeding was attempted by three methods: instillation of cold saline-epinephrine solution or a topical coagulant (botroclot) through the aspiration channel of the bronchoscope; and a tissue glue, n-butyl cyanoacrylate to the bleeding site through a polythene tube inserted via the bronchoscope.

#### 1. Cold Saline-Epinephrine solution Lavage through the Bronchoscope

A flexible bronchoscope with an aspiration channel of 2.8 mm was inserted to confirm the hemorrhaging site and clear the peripheral airways from blood. Once the exact bleeding location was determined, the bronchoscope was placed into a wedge position in the bleeding bronchus, blood was evacuated and irrigation with normal saline at 4°C in 20 ml aliquots was started, each 20 ml was sucked out after 30-60 seconds, and was followed by the instillation of a 1:20,000 epinephrine solution. The fibreoptic bronchoscope was retained in place for about 5 min following infusion and removed after confirming by aspiration, that hemostasis occurred.

#### 2. Use of Topical Coagulants (Betroclot, Jugat Pharma, India)

Bronchoscopy-guided topical hemostatic tamponade therapy (THT) THT was performed on patients with persistent endobronchial bleeding. The FOB was inserted in the usual manner and the hemorrhaging sites were confirmed by aspiration. After placing the bronchoscope in the hemorrhaging bronchus, blood from the tracheobronchial wall was cleared by saline, and the bleeding segment/site was detected. Five to ten mL of the hemostatic agent was infused directly through the channel used for aspiration to the bleeding site/segment. The hemostatic agent used was Betroclot topical solution (Sterile Haemocoagulase solution). On topical application the blood coagulation process starts immediately. It is indicated in localized capillary hemorrhages. The FOB, which was retained in place for about 5 min following the infusion, was removed after confirming, by aspiration, that hemostasis occurred. Betroclot is a haemocoagulant. The principal active ingredient is the purified haemocoagulase enzyme complex isolated from *Bothrops atrox* or *Bothrops jararaca*. Each mL of an aqueous solution of Betroclot contains 0.2 CU of haemocoagulase with 0.1% v/v chlorhexidine gluconate solution as a preservative.

#### 3. Bronchoscopic Endobronchial Sealing

FOB was inserted in the usual manner and confirmed hemorrhaging sites by aspiration. After placing the bronchoscope in the hemorrhaging bronchus, a polyethylene catheter with an outer diameter of 2 mm was passed through the bronchoscope channel to place it slowly into the bleeding segment. Thereafter, 0.5-1.5 mL of n-butyl cyanoacrylate glue was injected through the catheter with a water column behind, which was just adequate to flush the glue into the targeted area. N-butyl cyanoacrylate is a biocompatible adhesive that solidifies quickly on exposure to humidity with antibacterial effects. The catheter was withdrawn within a few seconds along with the bronchoscope. The scope was passed again after 2 to 3 min to confirm the absence of bleeding. The same procedure was repeated until the hemostasis was achieved.

Effectiveness of therapy and follow-up study:

The patients were followed up for a minimum period of 3 months to check for the recurrence of bleeding. In contrast to the criteria used by Tsukamoto & coworkers<sup>17</sup>, who classified therapy as very effective if hemoptysis did not recur within 14 days, somewhat effective when hemoptysis recurred after 24 hours but less than 14 days, and ineffective if hemoptysis continued post treatment, we classified therapy as very effective if hemoptysis did not recur within 3 months; somewhat effective if hemoptysis recurred after 2 weeks but less than 3 months and ineffective when hemoptysis continued post treatment or recurred within 2 weeks, and as was done by Kinoshita et al<sup>16</sup>. In cases where the treatment was ineffective, other treatment modalities were used to control the bleeding.

Statistical analysis:

Statistical analysis was done by Chi-square test. p value < 0.05 was taken as significant.

## RESULTS

The age of the patients ranged between 23 to 85 years. The mean age of the patients was 58.76 years. The total number of males in our study was 113(72%). Out of a total of 157 patients, mild hemoptysis (streaking or less than 30ml of blood/day) was present in 93 patients (59.2%), moderate (30-200ml/day) in 36 (22.9%) patients and severe (>200ml/day) in 28 (17.8%) patients. Tuberculosis (46.4%) and bronchiectasis (42.8%) were the most common etiologies in patients with severe hemoptysis.

Therapeutic bronchoscopy

Bleeding site was localized in 76 patients who were taken for therapeutic maneuvers through bronchoscope. Control of bleeding was attempted by three methods: instillation of cold saline-epinephrine solution (Group 1) or a topical coagulant (botroclot) through the aspiration channel of the bronchoscope (Group 2); or a tissue glue, n-butyl cyanoacrylate to the bleeding site through a polythene tube inserted via the bronchoscope (Group 3).

In all the patients undergoing therapeutic bronchoscopy, bleeding stopped immediately following the procedure. The patients were then followed up for a minimum of 3 months. The distribution of the patients undergoing therapeutic bronchoscopy in relation to severity of hemoptysis has been shown in table 1.

Table 1: Patients undergoing therapeutic bronchoscopy in relation to severity of hemoptysis

Cause	Mild Number	Moderate Number	Severe Number
Bronchitis (n=3)	3	-	-
Bronchogenic Carcinoma (n=29)	19	8	2
Tuberculosis (active) (n=15)	3	4	8
Tuberculosis (inactive) (n=6)	1	5	-
Bronchiectasis (n=18)	4	6	8
Pneumonia (n=1)	-	1	-
Lung abscess (n=1)	-	1	-
Aspergilloma (n=1)	-	1	-
Pseudo-hemoptysis	2	-	-
Bleeding from upper respiratory tract(n=2)			
TOTAL(n=76)	32	26	18

### Effectiveness of the Therapeutic Procedures

#### Group 1

The treatment was very effective (++, no recurrent hemoptysis within 3 months of treatment) in 13 patients, somewhat effective (+, hemoptysis within 3 months but after 2 weeks) in 14 patients and ineffective ( $\pm$ , hemoptysis continuing post treatment or recurring within 2 weeks) in 6 patients. In mild cases of hemoptysis the treatment was very effective in 12(70.6%) patients; in moderate cases of hemoptysis it was somewhat effective in 7(70%) patients while the treatment was ineffective in 4(66%) cases of severe hemoptysis (Table 2). No unusual complications followed the procedure, although a transient bradycardia was observed in 2 patients (Table 3). The effectiveness of the therapy decreased with the increase in the severity of hemoptysis.

#### Group 2

In group 2, the treatment was very effective in 14 patients, somewhat effective in 11 patients and ineffective in 6 patients. A similar pattern of response as seen in group 1 was seen in cases of group 2, i.e., the effectiveness of the therapy decreased with the increase in the severity of hemoptysis (Table 2 & 3). No unusual complications followed the procedure. Five patients complained of mild grade fever, which was probably due to the administration of the haemocoagulase, which subsided in a few days.

#### Group 3

Group 3 treatment was very effective in 6 patients and somewhat effective in 6 patients (Table 2). Six patients of malignancy were given group 3 therapy; the treatment was very effective in 2 patients and somewhat effective in 4 patients. In 3 patients each of tuberculosis (active & inactive disease) and bronchiectasis who were administered group 3 therapy, the treatment was very effective in 2 patients and somewhat effective in 1 patient each (Table 3). All the patients experienced post-procedure cough for which anti-tussives were prescribed. All the patients complained of expectoration of a granular material for a few days after the procedure.

**Table 2: Effectiveness of bronchoscopic therapeutic measures in control of hemoptysis in terms of severity of hemoptysis**

Hemoptysis grade	Group 1				Group 2				Group 3			
	No. of cases	++	+	$\pm$	No. of cases	++	+	$\pm$	No. of cases	++	+	$\pm$
Mild (32)	17	12	5	-	15	10	5	-	-	-	-	-
Moderate (26)	10	1	7	2	10	3	5	2	6	4	2	-
Severe (18)	6	-	2	4	6	1	1	4	6	2	4	-
Total(76)	33	13	14	6	31	14	11	6	12	6	6	-

++ very effective, no recurrent hemoptysis within 3 months of treatment  
 + somewhat effective, hemoptysis within 3 months but after 2 weeks  
 ± ineffective, hemoptysis continuing post treatment or recurring within 2 weeks

**Table 3: Effectiveness of bronchoscopic therapeutic measures in control of hemoptysis in terms of diagnosis**

Diagnosis	Group 1				Group 2				Group 3			
	No. of cases	++	+	±	No. of cases	++	+	±	No. of cases	++	+	±
Bronchitis (n=3)	3	2	1	-	-	-	-	-	-	-	-	-
Malignancy (n=29)	12	4	6	2	11	5	4	2	6	2	4	-
Tuberculosis (active) (n=15)	6	2	3	1	6	3	2	1	3	2	1	-
Tuberculosis (inactive) (n=6)	3	1	1	1	3	2	-	1	-	-	-	-
Bronchiectasis (n=18)	7	2	3	2	8	3	3	2	3	2	1	-
Pneumonia (n=1)	-	-	-	-	1	-	1	-	-	-	-	-
Lung abscess (n=1)	1	1	-	-	-	-	-	-	-	-	-	-
Aspergilloma (n=1)	-	-	-	-	1	-	1	-	-	-	-	-
Pseudo-hemoptysis Bleeding from upper respiratory tract (n=2)	1	1	-	-	1	1	-	-	-	-	-	-
<b>TOTAL (n=76)</b>	<b>33</b>	<b>13</b>	<b>14</b>	<b>6</b>	<b>31</b>	<b>14</b>	<b>11</b>	<b>6</b>	<b>12</b>	<b>6</b>	<b>6</b>	<b>-</b>
++ very effective, no recurrent hemoptysis within 3 months of treatment + somewhat effective, hemoptysis within 3 months but after 2 weeks ± ineffective, hemoptysis continuing post treatment or recurring within 2 weeks												

## DISCUSSION

Endoscopic therapy has been used extensively in every field of medicine. The bronchial tree is no exception. The rigid bronchoscope was mainly used for foreign body extraction and hemostasis from and in the bronchial tree. The invention of the flexible bronchoscope (FB) by Shigeto Ikeda in 1970 revolutionized the practice of diagnostic and therapeutic pulmonary medicine<sup>22</sup>. Management of haemoptysis not responding to conservative management is often difficult, requiring surgery or bronchial artery embolisation. Bronchial artery embolisation is costly and often not accessible, especially in the resource poor areas. Hence, surgery often remains the only therapeutic option despite its high morbidity and mortality. Therefore, an alternative easy but effective therapy is required for hemoptysis not responding to conservative management. Number of therapeutic bronchoscopic maneuvers have been investigated which may help to “buy time” to restore clinical stability and to perform essential diagnostic and definitive management. Treatments using the bronchoscope include lung isolation and airway control techniques,

endobronchial balloon or direct bronchoscopic tamponade, cold saline lavage, laser therapy, electrocautery, brachytherapy, and application of topical vasoconstrictors or coagulants<sup>23</sup>. But, none of these have qualified for widespread use. In the present study, control of bleeding was attempted by three methods: instillation of cold saline-epinephrine solution, a topical coagulant (botroclot) or a tissue glue (n-butyl cyanoacrylate). Instillation of cold saline-epinephrine solution via the bronchoscope as a therapeutic measure to control hemoptysis was very effective in 39.4% patients, somewhat effective in 42.4% patients and ineffective in 18.2% patients. Conlan and Hurwitz in a study on 12 patients successfully arrested bleeding in all patients with massive hemoptysis by bronchial irrigation with 50 mL aliquots of cold (4°C) normal saline administered through a rigid bronchoscope<sup>6</sup>. Repeated fiberoptic bronchoscopy with instillation of cold epinephrine-saline in intubated patients with life threatening hemoptysis was successful in 6 out of 7 patients.

Instillation of bistroclot was very effective in 45.2% patients, somewhat effective in 35.5% patients and ineffective in 19.3% patients. It is instantaneously effective in arresting capillary bleeding by accelerating the physiological process of hemostasis. Bistroclot (Haemocoagulase) has multifaceted haemocoagulant action. The thrombin like action of Bistroclot rapidly converts fibrinogen to fibrin monomer by releasing fibrinopeptide-A from the fibrinogen. These fibrin monomers polymerise end-to-end to form a cross-linked fibrin clot. Fibrinopeptide A free fibrin monomer, in the circulating blood, forms a complex with the native fibrinogen, which promotes the platelet aggregation and reduces the capillary permeability at the vascular damage site. The thromboplastin like enzymatic activity of Bistroclot at the site of bleeding activates the factor X. The activated factor Xa then helps in the formation of thrombin at the site of hemorrhage. Hence, Bistroclot can be used in patients with normal haemocoagulant factors or in patients showing anomalies in the coagulation biochemical process. Thrombin inhibitors like heparin do not affect the thrombin like activity of Bistroclot. Thus, Bistroclot shortens both the bleeding and coagulation time and saves every drop of blood. Tsukamoto and coworkers treated 19 patients with thrombin, and noted substantial efficacy in one patient, and failure to control bleeding in four patients (21%). In another 14 patients treated with fibrinogen-thrombin, substantial efficacy was noted in 11 (79%) and partial efficacy in three (21%)<sup>17</sup>. de Gracia et al did endoscopic instillation of fibrinogen/thrombin in 11 patients in whom BAE was not possible<sup>19</sup>. At first, instillation of cold saline-epinephrine solution and drying of the airway was achieved. Thereafter, fibrinogen-thrombin combination was instilled through a catheter within an FOB.

Instillation of tissue glue n-butyl cyanoacrylate was very effective in 50% patients and somewhat effective in 50% patients. Cyanoacrylate glues are already in use in different procedures in deep tissues with high degrees of success and safety. They have been used to prevent postoperative air leak from the bronchial stump after lung resectional surgery. The cyanoacrylate glues have prothrombotic properties such as increased platelet aggregation and possible enhancement of local thromboxane production. Although cyanoacrylates are significantly safe, they are volatile and chemically active materials reported to cause eczema, rhinitis, and asthma in occupational exposure. Occupational contact dermatitis has also been reported. There is also a chance of spillage of the glue more proximally on the bronchial tree or even at the tip of the endoscope<sup>20</sup>. Bhattacharyya and coworkers in 2002 used the same technique for 6 patients with hemoptysis. There was an immediate arrest of bleeding without any recurrence for a mean follow-up period of 127(±67.17) days<sup>20</sup>. Bhattacharyya and coworkers again in 2007 tried this method on 67 patients with a success rate of 80%<sup>23</sup>.

Valipour A and coworkers successfully performed bronchoscopy-guided Topical Hemostatic Tamponade (THT) therapy using Oxidized Regenerated Cellulose (ORC) mesh in the management of life-threatening hemoptysis<sup>21</sup>. Sakr L et al.<sup>24</sup> used endobronchial tamponade for massive hemoptysis. Bleeding airway was occluded with fogarty embolectomy catheter (4 Fr – segmental bronchi and 14 Fr for main stem bronchi). Catheter was passed through FOB and scope was removed over the catheter. Alternatively fogarty catheter was passed along the bronchoscope. Balloon at the distal tip of the catheter was inflated into the bleeding segmental bronchus as a hemostat. Argon Plasma Coagulation (APC) is noncontact electrocoagulation tool which is employed to conduct high-frequency electrical current through a flexible probe. APC allows effective dessication of a bleeding bronchus and stops hemoptysis. Morice et al<sup>25</sup> studied 31 patients with hemoptysis and 25 patients with both airway obstruction and hemoptysis treated by endobronchial APC therapy. Hemoptysis stopped in all patients.

The lack of a control group remains the major limitation in this study, and potential advantages of one technique over the other bronchoscopic or nonendoscopic techniques need to be assessed in future studies.

We conclude that endobronchial sealing by tissue glue n-butyl cyanoacrylate is more effective than instillation of cold saline epinephrine solution and haemocoagulant Bistroclot. Bronchoscopic therapeutic measures can be effectively used to control hemoptysis to 'buy time' for more definitive therapies.

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