

Type of Article: Original article**“ENDOBONCHIAL INSTILLATION OF TRANEXAMIC ACID TO CONTROL BLEEDING DURING BRONCHOSCOPIC PROCEDURE”****Dr. Anusha G N¹, Dr. Ajit Harsha², Dr. Srikanth Katare³, Dr. Alamelu Haran⁴**

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ABSTRACT

Background: Bronchoscopy is one of the most commonly performed safe procedures worldwide by pulmonologists for diagnostic and therapeutic purposes. It has a few complications such as bleeding, bronchospasm, laryngospasm, iatrogenic infections, atelectasis, and pneumothorax. The incidence of bleeding is low and rarely life-threatening, with a mortality rate of 0-0.04%. The greatest danger in a bleeding situation is aspiration and blood flooding of the alveoli (1,2). Cold saline is now regularly used to reduce bleeding during bronchoscopic operations, and other drugs such as adrenaline and terlipressin have also been employed. but either connected with difficulties or a scarcity of research (9,10). As a result, this study was conducted since there have been few studies on tranexamic acid, which requires greater assessment in terms of efficacy and safety. As a result, we conducted this study to evaluate the effectiveness and safety of tranexamic acid endobronchial instillation. **OBJECTIVES:** To assess the effectiveness and safety of tranexamic acid endobronchial instillation. **METHODS AND MATERIALS:** 50 Patients with endoscopically evident tumours and active bleeding were randomly separated into two groups of 25. The first group got 500mg of inj. tranexamic acid diluted in 20ml normal saline was administered through the bronchoscope for three efforts, whereas the second group received 20ml of cold saline for two attempts. After each try, 60-90 seconds were watched for bleeding cessation and hemostasis. **RESULT:** Endobronchial instillation of tranexamic acid stopped bleeding in all 25 cases (100%), whereas cold saline controlled bleeding in just 2 (8%) of the 25 patients. The cold saline group had 84%(21) of the patients hypoxemia and 36%(9) had severe cough, however, the tranexamic acid group had no side effects. **CONCLUSION:**When compared to cold saline, the current study suggests that the

instillation of tranexamic acid is safe and effective in the rapid management of bleeding following biopsy.

Keywords: Endobronchial instillation, cold saline, tranexamic acid, Bronchoscopy, Endobronchial Bleed

INTRODUCTION:

Bronchoscopy is an endoscopic technique of visualizing inside of the airways for diagnostic and therapeutic purposes. It is the most common procedure done by the pulmonologists. It examines the airways in a minimally invasive fashion, it is one of the most used procedure world wide⁽¹⁾.

Flexible fiber optic bronchoscopy is the most commonly performed method of bronchoscopy. During bronchoscopy the operator visualizes the vocal cords, trachea, large proximal airways. Bronchoscopy is performed in a designated procedure room, with the patient under conscious sedation, with or without an endotracheal tube in place. Bronchoscopy is used in evaluating a wide variety of clinical circumstances by different procedures, including evaluation of known or suspected respiratory infections-by BAL; suspected or known malignancy –by Endo bronchial biopsy, evaluation of lymphadenopathy by BLIND/EBUS guided TBNA, evaluation of interstitial lung diseases-by TBLB. Bronchoscopy is usually a safe procedure with less incidence of complications such as bleeding(0.26-5%), bronchospasm, laryngospasm, pulmonary atelectasis, pneumothorax, introduction or exacerbation of infection etc... Bleeding is one of the most frightening situations encountered in the daily practice. Mortality is rare with a reported death rate of 0-0.04%. However, in a case of excessive bleeding following biopsy, it may be life threatening with a risk of high mortality rate. The main threat in such situations is aspiration, due to flooding of airways and alveoli with blood. Maintenance of airway patency and control of bleeding will remain the main stay of management followed by identification of the site of bleeding. Bleeding also hinders the vision of the airways to the pulmonologist & results in forbidding the procedure²

Cold saline lavage is most commonly used to control bleeding during Bronchoscopy procedures⁽³⁾ which is not efficient always. Hence there is a need for other drugs for more efficient control of bleeding. Recent studies have proved the safety and effectiveness of Tranexamic acid in controlling bleeding.

This study was aimed to evaluate the efficacy & safety of endobronchial instillation of tranexamic acid in comparison with endobronchial instillation of cold saline.

METHODOLOGY:

Source of data:

After Institutional Ethics Committee Clearance Patients who presented to department of Respiratory Medicine at Vydehi Institute of Medical Sciences and Research Centre, Bangalore from January 2018 to June 2019.

Method of collection of data (including sampling procedure, if any):

Sample Size: 50 with simple random sampling

Type of study : Prospective interventional study

Inclusion criteria:

- Patients with endoscopically visible mass
- Patients who have given written informed consent for the study.

Exclusion criteria:

- Patients with H/O bleeding tendencies
- Patients with H/O chronic kidney disease, liver disease, bleeding disorders, on anticoagulants, haemophilias, von willibrand's disease, platelet disorders
- Patients below the age of 18 years.

Methods of Data Collection:

- Patients were recruited from department of Respiratory Medicine at Vydehi Institute of Medical Sciences and Research Centre.
- Detailed clinical history and examination were done and the following investigations were done.
- Chest X Ray PA view
- Sputum for AFB, gram stain Culture & Sensitivity
- HRCT/CECT THORAX if Sputum AFB is negative
- 2D ECHO, ECG
- PT/APTT/INR/ CBC/ RFT/ LFT
- Serology: HIV, HBsAg, HCV
- Parameters were analysed & the patients were taken up for bronchoscopy.
- Patients with endoscopically visible tumours with active bleeding following the first attempt of sampling were divided into 2 groups of 25 each randomly. First group received 500mg of inj.tranexamic acid diluted in 20ml normal saline was instilled through the bronchoscope for total 3 attempts. and 2nd group received 20ml of cold saline for total 2 attempts & after 60-90seconds of wait between each attempts multiple biopsies will be taken.

Statistical Analysis:

t test (independent)

Descriptive statistics

Graphical Representation

INVESTIGATION OR INTERVENTIONS:

- Chest X Ray PA view
- Sputum for AFB, gram stain Culture & Sensitivity
- HRCT/CECT THORAX if Sputum AFB is negative
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RESULTS:

	Tranexamic Acid	COLD SALINE
Female	16.0%	16.0%
Male	84.0%	84.0%
Farmer	56.0%	64.0%
Driver	12.0%	12.0%
Home maker	12.0%	8.0%
Ex BSF worker	4.0%	8.0%
Stone crusher	4.0%	4.0%
Software Engi.	4.0%	4.0%
Cloth Vendor	4.0%	0.0%
Student	4.0%	0.0%
No Significant Environmental Chemical Exposure	4.0%	12.0%
Smoker	76.0%	64.0%
Non smoker	16.0%	16.0%
Biomass Exposure	4.0%	8.0%

Table 1 : Demographic Data of Participants in the study and Grouped

- Endobronchial instillation of tranexamic acid controlled the bleeding in all the 25 cases (100%) with the dosage of 500mg in 20ml normal saline
- Cold saline controlled bleeding in only 2 (8%) out of 25 patients & remaining 23 (92%) cases received tranexamic acid(500mg diluted in 20ml normal saline).
- 11 subjects (44%) in cold saline group had no tachycardia , the normal physiological process during the procedure. 1 among them had bradycardia (58bpm) following cold saline instillation, 84%(21) of subjects had hypoxemia during the procedure & 36% (9) of subjects had severe cough following instillation of cold saline
- No adverse events to tranexamic acid were noted in tranexamic acid group

DISCUSSION:

This study was conducted with an aim to study the safety & efficacy of endobronchial tranexamic acid instillation in patients with bleeding after endobronchial biopsy

It was a prospective interventional randomized study consisting of 50 patients enrolled from Jan 2017- Jan 2019 in Vydehi Institute of Medical Sciences and Research centre , in the Department of Respiratory Medicine.

50 patients who were included in the study and their Demographic Data is shown in Table 1 and according to inclusion and exclusion criteria were randomized into two groups of 25 each . One was tranexamic acid group and another was cold saline group. In tranexamic acid group 25 patients received 500mg of tranexamic acid diluted in 20ml of normal saline . In cold saline group 25 subjects received 20ml of ice cold saline through the working channel of the bronchoscope. The mean age of participants in the tranexamic acid group was 52 +/- 14.22 years & that in the cold saline group was 53 +/- 13.65 years. Both the tranexamic acid & cold saline groups had predominant males, 21 (84%) in each group & females were 4 (16%) each in group.

Subjects in both the groups were smokers 19(76%) in tranexamic acid group & 16 (64%) in cold saline group , which was the risk factor for malignancy . 4 (16%) subjects in each group were non smokers, 1(4%) subject in tranexamic acid group & 2(8%) subjects in cold saline group had biomass fuel exposure. In both the groups all subjects had bleeding following 1st attempt of biopsy. In the tranexamic acid group bleeding was efficiently & immediately stopped in all subjects with endobronchial instillation of 500mg of tranexamic acid diluted in 20ml of normal saline. None of the patients received more than 20ml of 500mg tranexamic acid .On the other hand in cold saline group only 2 patients had efficient bleeding control with cold saline & remaining 23 patients required additional endobronchial tranexamic acid (500 mg diluted in 20ml of normal saline). In all the subjects bleeding control was confirmed by visualization of clot with no evidence of active bleeding. A similar study like mine was done by Sharma Chethan et al on 70 subjects. The patients were divided into 2 groups of 35 patients each. The 1st group of 35 patients received endobronchial instillation of tranexamic acid to control the biopsy induced bleeding and the 2nd group of 35 patients received cold saline.

In the 1st group all 35 responded to tranexamic acid & in the 2nd group 34 patients responded to cold saline. Author concluded that tranexamic acid was effective in controlling significant bleeding with less volume. Tranexamic acid revealed no clinical significant difference at 1% level of significance in comparison with cold saline ⁽⁷⁾. Whereas in this

study efficacy of tranexamic acid in controlling endobronchial bleeding had statistical significance with p value of 0.005 in comparison to cold saline.

Emad el din A KORraa et al study was a prospective, randomized, observational study carried out on 40 subjects scheduled to undergo bronchoscopy for management of haemoptysis or bronchoscopy induced bleeding. Patients were randomly subdivided into 2 groups of 20 patients each, the first group received endobronchial tranexamic acid where as the second group received endobronchial cold saline +/- adrenaline. In the first group out of 20 patients, 19 patients responded to tranexamic acid. 9 responded to 500mg of tranexamic acid, 8 responded to 1000mg of tranexamic acid & 2 patients responded to 1500mg. 1 patient responded to endobronchial adrenaline. In 2nd group 3 patients responded to cold saline, 11 responded to a single dose of 20ml of cold saline followed by 1mg adrenaline, 6 patients responded to 2 doses of 20ml cold saline followed 1 mg adrenaline. There was no significant statistical difference between both groups. Authors concluded that endobronchial instillation of tranexamic acid is an effective & safe modality of treatment for controlling bronchopulmonary bleeding⁽⁶⁾.

Similarly this study also showed tranexamic acid was effective in control of bleeding after biopsy and only 500mg of tranexamic acid very effectively controlled bleeding in all 25 patients (100%), whereas in Emad el din A KORraa et al study 10 patients (50%) required more than 500mg tranexamic acid for effective bleeding control.

Fekri MS et al in their study randomly selected 50 patients whose bleeding could not be controlled with cold saline lavage during bronchoscopy and therefore required another medicine. 20ml of Adrenaline (1mg of adrenaline diluted in 200ml of normal saline) in one group and tranexamic acid (500mg diluted in 20ml of cold saline) in another group were instilled through the bronchoscope. This was repeated thrice at 90 second intervals. If necessary in case of persistent bleeding, 90 second after the last dose, a second medicine was given for bleeding control. Authors concluded that tranexamic acid by endobronchial instillation was as efficient as adrenaline in controlling bleeding & required less frequent use of a second medicine. This study showed that cold saline was not efficient in controlling bleeding when compared to adrenaline & tranexamic acid⁽⁴⁾. This study also revealed a statistically significant difference favouring the efficacy of tranexamic acid in comparison to cold saline in controlling bleeding with a smaller dose.

Out of 25 patients in cold saline group in the present study, 44% (11) of subjects had no tachycardia during the procedure which was not proportionate to the physiological response usually seen during any procedure. Among them, 1 subject had bradycardia after cold saline instillation, this finding is probably attributed to increase in vagal tone following instillation of cold saline. 84% (21) of subjects had hypoxaemia during the procedure which was statistically insignificant with a p value of 0.062 and 36% (9) subjects had statistically significant severe cough following cold saline instillation through the bronchoscope. The above 2 findings are probably attributed to bronchospasm following endobronchial instillation of cold saline. Bronchospasm could be due to increased activity of nerve released nor epinephrine. No adverse events were recorded in tranexamic acid group.

In Sharma Chethan et al study, bradycardia was seen in subjects in cold saline group similar to this study⁽⁷⁾. One case report reported by Sagar et al noted a 3rd degree heart block following cold saline lavage (60cc)⁽⁵⁾ whereas in this study 1 patient developed bradycardia (58bpm) after endobronchial instillation of cold saline.

In Emad el din A KORraa et al study & Fekri MS et al found no adverse events were noted in the tranexamic acid group which was similar to this study^(4,6).

From the above studies it is concluded that Tranexamic acid had no adverse events & found to be safer & efficacious for controlling bleeding following endobronchial instillation.

LIMITATIONS:

- 1.Small sample size
2. Transbronchial lung biopsy patients were not included
3. Cough severity during the procedure was not scaled

RECOMMENDATIONS FOR FURTHER STUDY:

Large scale multicentric studies are required to assess further the efficacy & safety of tranexamic acid endobronchial instillation in controlling endobronchial bleeding following biopsy

SUMMARY:

The present study was done to compare endobronchial instillation of tranexamic acid with endobronchial instillation of cold saline in controlling bleeding following endobronchial biopsy in patients admitted in Vydehi institute of medical sciences & research centre, Bengaluru from jan 2018 to june 2019 with the following objectives

- To study the efficacy of endobronchial instillation of tranexamic acid
- To study the safety of endobronchial instillation of tranexamic acid

Highlighted findings were as follows

- Endobronchial instillation of tranexamic acid controlled the bleeding in all the 25 cases (100%) with the dosage of 500mg in 20ml normal saline
- Cold saline controlled bleeding in only 2 (8%) out of 25 patients & remaining 23 (92%) cases received tranexamic acid(500mg diluted in 20ml normal saline).
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- No adverse events to tranexamic acid were noted in tranexamic acid group

Conflicts of Interest:

No potential conflict of interest relevant to this article was reported.

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