

Original Article

# Bronchoscopic Voriconazole Instillation in Pulmonary Aspergilloma: A Single Center Experience

Prajowl Shrestha<sup>1</sup>, Ashesh Dhungana<sup>1</sup>

<sup>1</sup>Chest Unit, Department of Medicine, National Academy of Medical Sciences, Bir Hospital, Kathmandu Nepal

## ABSTRACT

**Introduction:** Saprophytic growth of *Aspergillus* species in preexisting lung cavities commonly presents with hemoptysis. Surgical resection is the preferred treatment for hemoptysis control in pulmonary aspergilloma. In patients who are not candidates for surgical resection bronchoscopic Voriconazole instillation may be an effective option.

**Materials and Methods:** In this retrospective study, data of patients presenting with active hemoptysis, radiological evidence of aspergilloma and those undergoing bronchoscopic Voriconazole instillation at National Academy of Medical Sciences from January 2018 to December 2018 were retrieved. Clinical details including the severity of hemoptysis, number, size and location of aspergilloma, number of Voriconazole instillation sessions and symptom control were assessed. Follow up CT scan after four to six sessions were also evaluated to compare the size of aspergilloma.

**Results:** A total of 11 patients presented with aspergilloma and hemoptysis. Of these, five (45.4%) patients underwent at least four sessions of bronchoscopic Voriconazole instillation. Two patients required six sessions whereas one required nine sessions for hemoptysis control. The procedure was successful in all patients; however, one had a recurrence after 3 months and required bronchial artery embolisation. In four patients there was a significant reduction in the size of aspergilloma on follow up CT scan. The procedure was well tolerated by all the patients except for mild increase in cough in the immediate post-procedure period.

**Conclusions:** Intrabronchial Voriconazole instillation is a safe and effective option for hemoptysis control in patients with pulmonary aspergilloma. However, the optimal dose, frequency and duration of Voriconazole instillation need to be further evaluated.

**Keywords:** Aspergilloma; Bronchoscopy; Hemoptysis; Voriconazole .

**Correspondence:**

Dr. Prajowl Shrestha, MD, DM  
Chest Unit, Department of Medicine,  
National Academy of Medical Sciences, Bir  
Hospital, Kathmandu, Nepal  
ORCID ID: 0000-0003-1956-1142  
Email: prajwolaiims@gmail.com

**Submitted:** 21<sup>st</sup> April 2019

**Accepted:** 15<sup>th</sup> May 2019

**Published:** 20<sup>th</sup> June 2019



**Source of Support:** None

**Conflict of Interest:** None

**Citation:** Shrestha P, Dhungana A. Bronchoscopic Voriconazole instillation in pulmonary aspergilloma: a single center experience. *Nep Med J* 2019;2(1):173-6. DOI 10.3126/nmj.v2i1.24495

## INTRODUCTION

Pulmonary aspergilloma is a condition characterized by saprophytic growth of *Aspergillus* species in preexisting lung cavities. In Tuberculosis endemic regions, healed tubercular cavities are the commonest predisposing factor for pulmonary Aspergilloma.<sup>1</sup> Recurrent hemoptysis is a common clinical presentation in patients with pulmonary aspergilloma. Depending upon the severity, hemoptysis in pulmonary aspergilloma is often

moderate to severe in up to 50% of cases.<sup>2,3</sup> Though surgical resection of affected lobe is the definitive treatment, in most of the cases it is not feasible due to bilateral lung involvement, complex aspergilloma and poor pulmonary reserve of the patients. Beside these factors, surgery is also associated with significant postoperative complications. Bronchial artery embolization (BAE) is an effective measure to control acute episode of

hemoptysis; however, BAE is not curative and recurrence rate is as high as 25% over the period of 1 year.<sup>4</sup> Other modalities such as percutaneous instillation of various antifungal agents like Amphotericin B, ketoconazole and Voriconazole has been tried with various success rate in the past.<sup>5-7</sup> Similarly, bronchoscopic instillation of antifungal agents into the affected lobe or segments for control of hemoptysis has been evaluated, though in smaller studies. Although the safety of the procedures has been established, the evidence of its effectiveness to control hemoptysis is just emerging. The aim of this study is to evaluate the efficacy and safety of intrabronchial Voriconazole instillation for control of hemoptysis caused by aspergilloma in post tubercular cavities.

## MATERIAL AND METHODS

This was a retrospective study conducted at National Academy of Medical Sciences, Kathmandu, Nepal from January 2018 to December 2018. Medical records of patients who presented to chest clinic with active hemoptysis with radiological evidence of aspergilloma and who underwent bronchoscopic Voriconazole instillation in affected lobe/segments were reviewed. Clinical details along with primary etiology, duration and severity of hemoptysis, extent of disease, size of aspergilloma, number of bronchoscopic sessions, dose of Voriconazole, control of hemoptysis and requirement of BAE were evaluated and analyzed. Diagnosis of aspergilloma was based on contrast-enhanced computed tomography (CECT) features of pulmonary cavity with a globular fungal ball with crescent of air above a fungal ball with no possible alternate etiology. All patients with radiological evidence of aspergilloma and active hemoptysis underwent bronchoscopy for localization of bleeding segment and a lavage was carried out at the same setting to rule out active tuberculosis. All patients were given standard treatment for hemoptysis which included, appropriate body positioning, tranexamic acid, antitussives and antibiotics as clinically indicated. Written informed consents were obtained from all patients before undergone bronchoscopic Voriconazole instillation. The

segment of Voriconazole instillation was decided based on the bronchoscopic findings and radiological location of aspergilloma. Flexible video bronchoscopy was performed under local anesthesia with 10% lignocaine spray in oro- and hypopharynx along with 2% xylocaine instillation as per spray-as-you-go technique. Supplemental oxygen and continuous hemodynamic monitoring was done during the bronchoscopy. During the procedure, bronchoscope was advanced and wedged into the segmental or subsegmental bronchus as per prior localization. Voriconazole 400mg (2 tablets of 200mg each) were crushed and dissolved in 20mL of 0.9% normal saline solution under aseptic conditions. Prepared solution was injected slowly into the desired segmental bronchus or into the cavity through the suction channel of bronchoscope. After the instillation, bronchoscope was kept wedged for 1 minute to prevent back leakage of the solution. Bronchoscope was then slowly withdrawn. Patient was kept in lateral decubitus with the affected lobe in dependant position for next 20 minutes to minimize coughing. Voriconazole instillation was performed weekly with concomitant clinical assessment of control of hemoptysis. A repeat CT scan was performed after 4 to 6 sessions for comparison of size of aspergilloma. Number of sessions of Voriconazole instillation, control of hemoptysis and subsequent recurrence, if any, were retrieved from the records. CT scans were compared for change in the size of aspergilloma or decrease/disappearance of the cavity. Assessment of hemoptysis control was done at the time of subsequent follow up at one and three months.

## RESULTS

A total of 11 patients were diagnosed to have pulmonary aspergilloma with significant hemoptysis requiring interventions based on the clinical and radiological features. Of these 11 patients 5 (45.45%) patients underwent intrabronchial Voriconazole instillation for hemoptysis control. The clinical and radiological details of the patients, the details of the procedure and the outcomes are presented in Table 1.

**Table 1: Clinical, radiological and bronchoscopic details along with the outcome of patients included in the study**

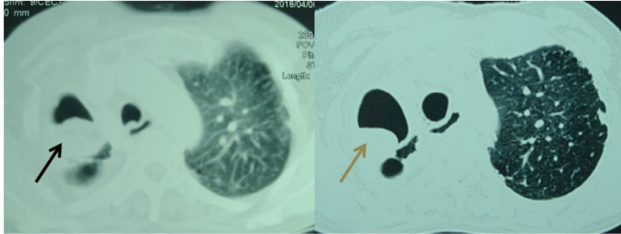
	Age/ Sex	Presentation	CT findings	Number of bronchoscopic session	Total dose of Voriconazole	Hemoptysis control	Recurrence of symptom	BAE required or not
Case 1	62/F	Exertional Dyspnea, Hemoptysis	RUL Aspergilloma Centriacinar emphysema of left lung	6	2400 mg	Yes	No	No
Case 2	61/F	Exertional Dyspnea, Hemoptysis	B/L fibrobronchiectasis with RUL aspergilloma	6	2400 mg	Yes	No	No
Case 3	42/M	Hemoptysis	Bilateral upper lobe fibrobronchiectasis with RUL aspergilloma	9	3600 mg	Yes	Yes	Yes
Case 4	58/M	Hemoptysis	RUL aspergilloma	4	1600 mg		No	No
Case 5	52/F	Hemoptysis Dyspnea	LUL Aspergilloma	4	1600 mg	Yes	No	No

RUL: Right upper lobe, LUL: Left upper lobe, B/L: Bilateral

Of the five patients, all were aged above 40 years and three were females. All patients had aspergilloma in post-tubercular cavities and significant hemoptysis that was not controlled with conservative treatment. Four out of five patients had aspergilloma in right upper lobe (RUL) whereas one had aspergilloma in left upper lobe (LUL). Two patients with localized disease (Case

4 and case 5) were given an option of surgical resection of involved lobe/segment but they refused surgery, hence underwent bronchoscopic Voriconazole instillation. All patients underwent minimum of 4 session of Voriconazole instillation, two patients underwent 6 sessions and one patient underwent 9 session of Voriconazole instillation. The procedure was well tolerated by all patients. There were no major complications associated with the bronchoscopic Voriconazole instillation. However, all

patients complained of mild increase in cough in the immediate post procedure period. In all five patients there was significant improvement in hemoptysis in follow up period up to 3 months post procedure. One patient had recurrence of hemoptysis after 3 months for which patient underwent bronchial artery embolization (BAE). A repeat CT scan of chest was performed in all patients after 1 month of Voriconazole instillation. In 4 patients there was significant reduction in size of Aspergilloma (Figure 1). One patient (case 3) did not show significant reduction in size of aspergilloma. This patient also had recurrence of symptoms and underwent BAE after the nine session of Voriconazole instillation.



**Figure 1: CT scan of chest (pre and post intrabronchial Voriconazole instillation) showing decrease in size of aspergilloma (arrow) in RUL cavity after four session of Voriconazole instillation**

## DISCUSSION

Ever since the first report of successful endobronchial treatment of 3 cases of aspergilloma with amphotericin B and sodium iodide by Ramirez<sup>8</sup> in 1964, various reports of local antifungal instillation for symptomatic aspergilloma have been reported showing variable results. In this study we assessed safety and efficacy of intrabronchial Voriconazole instillation in five patients. The procedure was successful in four patients. One patient required BAE following Voriconazole instillation.

In another case series by Yamada et al<sup>9</sup>, successful endobronchial administration of antifungal agents was reported in 3 of out of 5 patients with aspergilloma. Percutaneous intracavitary instillation of antifungal agents has also been described in literature. Adelson and Malcolm<sup>10</sup> first reported successful percutaneous intracavitary instillation of sodium iodide for aspergilloma in 2 patients. The efficacy of percutaneous administration using amphotericin has been demonstrated to be 85% for hemoptysis control in patient with aspergilloma.<sup>11</sup> The efficacy of intrabronchial instillation of azole has not been well studied. One of the earliest study about the intrabronchial use of azole has reported intracavitary ketoconazole instillation for successful hemoptysis control.<sup>12</sup>

Intracavitary Voriconazole has been used successfully in past to treat hemoptysis due to mycetoma.<sup>13</sup> Similarly, endobronchial intracavitary itraconazole instillation has been successfully used

to treat a case of chronic necrotizing pulmonary aspergillosis with fungal ball.<sup>14</sup> One of the largest case series of intracavitary Voriconazole instillation for hemoptysis control in patients with pulmonary aspergilloma has been reported recently by Mohan A et al in 2017.<sup>15</sup> In their retrospective case series of 82 patients with pulmonary aspergilloma, they used four sessions of intrabronchial Voriconazole (400 mg dissolved in 20 ml of 0.9% normal saline) at weekly intervals. The most common underlying etiology for pulmonary aspergilloma was post tubercular sequelae (95.1%) in their study. The procedure was successful in 68.3% of patients. Prior history of BAE and the baseline aspergilloma size were the potential risk factors for recurrence of hemoptysis after the procedure. In view of scant literature regarding optimum dose of Voriconazole, we used 400 mg of Voriconazole instillation weekly as described by Mohan et al.<sup>15</sup>

In this study 4 out of 5 patients achieved significant hemoptysis control without any recurrence. Various studies have reported rapid improvement in hemoptysis following antifungal instillation.<sup>9,12</sup> Very few studies have evaluated the effect of multiple instillations of antifungal agents for hemoptysis control in patient with aspergilloma.<sup>12,15</sup> One patient in our study had recurrence of hemoptysis requiring BAE for hemoptysis control. The recurrence rates of hemoptysis after various procedures have been reported from 24 to 30 % at 12 months.<sup>16</sup>

None of the patient in our study had any major complications related to the procedure. All patients had mild increase in cough immediately after the procedure which did not require any interventions or treatment. Transient post-procedure cough was reported by 46.3% of patients in case series reported by Mohan et al.<sup>15</sup> All case reports and case series reported till date have found endobronchial antifungal instillation as a safe procedure.<sup>9,15,17</sup>

This study has several limitations. The retrospective nature of the study, small numbers of patients and lack of long term follow up are the major limitations of this study. Similarly, the symptomatic assessment for hemoptysis control was subjective and patient reported. Use of protocolised symptomatic assessment tool would have better delineate the control of symptoms. However, this study has highlighted the safety and efficacy of bronchoscopic Voriconazole instillation in patient with aspergilloma and active hemoptysis. To our knowledge this is the first study of bronchoscopic Voriconazole instillation for control of hemoptysis in patients with aspergilloma to be reported from Nepal.

## CONCLUSIONS

Intrabronchial Voriconazole instillation is safe and effective option for hemoptysis control in patients with pulmonary aspergilloma. It provides hemoptysis control without major adverse effects. However the optimal dose, frequency and duration of Voriconazole instillation needs to be further evaluated and standardized.

## REFERENCES

1. Smith NL, Denning DW. Underlying conditions in chronic pulmonary aspergillosis including simple aspergilloma. *European Respiratory Journal* 2011;37:865-72. [Crossref](#)
2. Glimp RA, Bayer AS. Pulmonary aspergilloma. Diagnostic and therapeutic considerations. *Arch Intern Med.* 1983;143:303-8. [Crossref](#)
3. Rafferty P, Biggs BA, Crompton GK, Grant IW. What happens to patients with pulmonary aspergilloma? Analysis of 23 cases. *Thorax.* 1983;38:579-83. [Crossref](#)
4. Shin BS, Jeon GS, Lee SA, Park MH. Bronchial artery embolisation for the management of haemoptysis in patients with pulmonary tuberculosis. *Int J Tuberc Lung Dis.* 2011;15:1093-8. [Crossref](#)
5. Ortiz de Saracho J, Perez-Rodriguez E, Zapatero J, Navío P, Flores J. Therapeutic alternatives in complicated nonsurgical pulmonary aspergillomas. *Arch Bronconeumol.* 1995;31:83-5. [Crossref](#)
6. Klein JS, Fang K, Chang MC. Percutaneous transcatheter treatment of an intracavitary aspergilloma. *Cardiovasc Intervent Radiol.* 1993;16:321-4. [Crossref](#)
7. Krakowka P, Traczyk K, Walczak J, Halweg H, Elsner Z, Pawlicka L. Local treatment of aspergilloma of the lung with a paste containing nystatin or amphotericin B. *Tubercle.* 1970;51:184-91. [Crossref](#)
8. Ramirez J. Pulmonary aspergilloma: endobronchial treatment. *N Engl J Med.* 1964;271:1281-5. [Crossref](#)
9. Yamada H, Kohno S, Koga H, Maesaki S, Kaku M. Topical treatment of pulmonary aspergilloma by antifungals. Relationship between duration of the disease and efficacy of therapy. *Chest.* 1993;103:1421-5. [Crossref](#)
10. Adelson HT, Malcolm JA. Endocavitary treatment of pulmonary mycetomas. *Am Rev Respir Dis.* 1968;98: 87-92. [Crossref](#)
11. Kravitz JN, Berry MW, Schabel SI, Judson M. A modern series of percutaneous intracavitary instillation of amphotericin B for the treatment of severe hemoptysis from pulmonary aspergilloma. *Chest.* 2013;143:1414-21. [Crossref](#)
12. Guleria R, Gupta D, Jindal SK. Treatment of pulmonary aspergilloma by endoscopic intracavitary instillation of ketoconazole. *Chest.* 1993;103:1301-2. [Crossref](#)
13. Kravitz JN, Steed LL, Judson MA. Intracavitary Voriconazole for the treatment of hemoptysis complicating *Pseudallescheria angusta* pulmonary mycetomas in fibrocystic sarcoidosis. *Med Mycol.* 2011;49:198-201. [Crossref](#)
14. Tani S, Tomioka H, Tsuchimoto K, et al. A case of pulmonary aspergilloma successfully treated with transbronchial intracavitary itraconazole. *The Journal of the Japanese Respiratory Society.* 2008;46:997-1002.
15. Mohan A, Tiwari P, Madan K, Hadda V, Poulouse R, Bhalla A. Intrabronchial Voriconazole is a Safe and Effective Measure for Hemoptysis Control in Pulmonary Aspergilloma. *J Bronchol Intervent Pulmonol* 2017;24:29-34. [Crossref](#)
16. Shin BS, Jeon GS, Lee SA, Lee, Park MH. Bronchial artery embolisation for the management of haemoptysis in patients with pulmonary tuberculosis. *Int J Tuberc Lung Dis.* 2011;15:1093-8. [Crossref](#)
17. Rumbak M, Kohler G, Eastrige C, Winer-Muram H, Gavant M. Topical treatment of life threatening haemoptysis from aspergillomas. *Thorax.* 1996;51:253-5. [Crossref](#)