Original Article

Prevalence of Venous Thromboembolism in Acute Exacerbations of Chronic Obstructive Pulmonary Disease: An Indian Perspective

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ABSTRACT

Background. Chronic obstructive pulmonary disease (COPD) will be the third leading cause of death by 2020. Recent studies reveal that pulmonary embolism (PE) may be a trigger of acute deterioration in patients with COPD. Patients with COPD have approximately twice the risk of PE than those without COPD.

Objective. The primary objective was to assess the prevalence of venous thromboembolism (VTE) in patients with acute exacerbation of COPD (AE-COPD) in India.

Methods. We conducted this prospective study on patients admitted for AE-COPD in a tertiary care hospital in Mumbai, India. We considered the prevalence of deep venous thrombosis (DVT) to reflect the occurrence of VTE. The screening tool used was a colour Doppler of the bilateral lower limbs.

Results. One hundred patients enrolled, were in stage II to stage IV COPD; 9% had DVT. Eight of these nine patients had unilateral DVT. Two patients had developed PE and died.

Conclusions. Our results show a lower prevalence of unsuspected DVT in Indian patients admitted for AE-COPD. Future prospective, randomised studies are needed to confirm the findings of the present study and to determine whether a systematic evaluation for VTE is justified in these patients, and hence, be recommended. **[Indian J Chest Dis Allied Sci 2011;53:207-210]**

Key words: COPD exacerbation, Venous thromboembolism.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a major public health burden worldwide. It is the fourth leading cause of mortality and morbidity, accounting for more than three million deaths annually. By 2020, COPD will be the third leading cause of death, after ischaemic heart disease and stroke.[1] Most COPD related deaths occur during periods of exacerbation.[2,3] Earlier estimates[2] suggest that 50% to 70% of all exacerbations of COPD are precipitated by an infectious process, while 10% are due to environmental pollution; up to 30% of exacerbations are caused by an unknown aetiology. Thus, the cause of acute exacerbation of COPD (AE-COPD) is often difficult to determine.

Pulmonary embolism (PE) may be a trigger of acute dyspnoea in patients with COPD. A study[4] suggests that patients with COPD have approximately twice the risk of PE and other venous thromboembolic events than those without COPD. Since thromboembolic events can lead to cough and dyspnoea (similar presentation as infectious events), PE may be another common cause of AE-COPD.[5]

Unlike infectious aetiologies, which are effectively treated by antimicrobial agents, bronchodilators, inhaled corticosteroids and systemic corticosteroids, thromboembolic diseases require specific anti-coagulant therapy. Studies have revealed that significant delays in the treatment are associated with poor outcomes.[6,7]

There are no Indian data looking into the prevalence of PE in patients with of AE-COPD. The primary objective of our study was to assess the prevalence of venous thromboembolism (VTE) in patients with AE-COPD in Mumbai, India who required hospitalisation for their disease.

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MATERIAL AND METHODS

We conducted a prospective, observational, epidemiological study to determine the prevalence of VTE on patients admitted with AE-COPD, in the wards and intensive care units (ICUs) of a tertiary care referral hospital in Mumbai. Since deep venous thrombosis (DVT) and PE are part of the spectrum of the same disease, we looked into the prevalence of DVT in patients admitted with AE-COPD as a reflection of the occurrence of a VTE in this subgroup of patients.

A sample size calculation was not performed a priori.

This prospective observational epidemiological study included consecutive patients (n=100) who required hospital admission for AE-COPD between February 2005 and February 2007.

Clearance of the Ethics Committee of our hospital was taken and informed consent of all the patients enrolled in the study was obtained.

The AE-COPD was defined as an event in the natural course of the disease characterised by a change in the patient's baseline dyspnoea, cough, and/or sputum production that is beyond the normal day-to-day variations, acute in onset, and warranting a change in regular medication in a patient with underlying COPD. Spirometric classification of the severity and stages of COPD was done according to the Global Initiative for Chronic Obstructive Pulmonary Disease (GOLD) classification[8] as follows:

Stage I: mild COPD; ratio of forced expiratory volume in the first second (FEV_1) to forced vital capacity (FVC) less than 0.70, FEV_1 greater than or equal to 80% predicted;
Stage II: moderate COPD; FEV_1/FVC less than 0.70, FEV_1 less than 80%, more than 50% predicted;
Stage III: severe COPD; FEV_1/FVC less than 0.70, FEV_1 less than 50%, more than 30% predicted; and
Stage IV: very severe COPD; FEV_1/FVC less than 0.70, FEV_1 less than 30% or FEV_1 less than 50% with signs of respiratory failure or cor-pulmonale.

Patients with COPD who had an associated malignancy, cardiac failure, pneumothorax or a neurological disease were excluded from the study.

The primary outcome studied was the prevalence of DVT among patients who required hospitalisation for AE-COPD. Venous Doppler examination of both the lower limbs were done from the common femoral vein up to the calf vein. Lack of compressibility of the veins, presence of filling defects and ecogenic material within the veins were considered as evidence suggestive of DVT. This was done on two occasions; first on the day of admission and for the second time on the seventh day of hospital stay, or on the day of discharge, whichever was earlier. Venous Doppler examination of both the lower limbs was done on the first day of hospitalisation to determine the prevalence of DVT at initial presentation. The test was repeated on the seventh day of hospital stay or at the time of discharge from the hospital (whichever was earlier), in order to identify the occurrence of new onset DVT during hospital stay.

Other details recorded includes the age at presentation, duration of hospitalisation, the microbiological aetiology of AE-COPD, details of various therapentic options, such as, antibiotics, low molecular weight heparin (LMWH), corticosteroids, intubation and mechanical ventilation; and mortality.

RESULTS

One hundred patients were studied prospectively in our case series. All the patients had stage II to stage IV COPD. Their median age was 71 years (range between 36 to 84 years). The AE-COPD was found to be three times more common among males, than in females. The median stay in the hospital was nine days, (range 5 to 12 days). At initial presentation 28% patients were admitted directly to the ICU and 72% were admitted in the wards.

Overall 9% patients had DVT, out of which 7% had isolated calf veins thrombosis and 2% had an extension of the thrombus to the femoral veins. Unilateral DVT was observed in eight of the nine patients, while only one patient had bilateral disease. Two patients developed PE. Of these nine patients, seven had DVT at admission and two patients developed DVT during hospital stay.

Deep vein thrombosis prophylaxis with LMWH or a synthetic pentasaccharide (Fondaparinux) was administered to 26 patients who had severe functional disability and restricted physical activity due to the severity of COPD.

Thirty-six percent cases were smokers; 28% were ex-smokers and 36% were non-smokers. The co-morbidities present in these patients included diabetes mellitus (40%), ischaemic heart disease (28%), hypertension (21%) and other diseases like hypothyroidism and cerebrovascular accidents (6%). Repeated admissions (range 2 to 4 times per year) were required in 21% patients. Both the patients with PE (2%) died.

DISCUSSION

Chronic obstructive pulmonary disease represents a huge medical and economical burden for the healthcare system. Clinical presentation of AE-COPD includes worsening of dyspnoea, increased quantity of sputum production and increased purulence of sputum. Although this clinical criteria, i.e.

Anthonisen's classification have been used to determine which patient should be treated with antibiotics,[2] these criteria are neither sensitive nor specific enough to exclude other causes of dyspnoea in this population. Other frequent clinical conditions may mimic the symptoms of AE-COPD, including congestive heart failure (CHF), pneumonia, pneumothorax, pleural effusion and PE.

In patients with COPD, PE can have important pathophysiological implications, including decompensated right ventricular failure. Both acute PE and COPD can cause cor-pulmonale.

Chronic obstructive pulmonary disease is often cited among the risk factors for acute VTE and was recently identified as an independent predictor of PE.[9] Poulsen[10] showed that COPD is an independent risk factor for PE. In another study,[11] it was observed that PE was an absolute predictor of death and/or re-hospitalisation at three months in patients with CHF; in this study population, COPD was significantly more common in patients with CHF and PE than those with CHF and no PE.[10]

Our prospective study was aimed to determine the prevalence of VTE in patients getting admitted with AE-COPD, using a validated diagnostic strategy based on the venous Doppler of bilateral lower limbs. We found the prevalence of VTE was 9%. A thorough Medline search revealed a paucity of data from the Indian subcontinent on this subject. *To the best of our knowledge*, this was the only study from India, evaluating the prevalence of VTE in patients presenting with AE-COPD.

In the Prospective Investigation of Pulmonary Embolism Diagnosis (PIOPED) study,[7] the prevalence of PE in patients with COPD was 19%. The Advances in New Technologies Evaluating the Localisation of Pulmonary Embolism (ANTELOPE) study[12] showed a 29% prevalence of PE among patients with COPD. The PIOPED,[13] ANTELOPE,[12] studies were not designed to specifically look at all patients with COPD. Thus, their observations regarding the prevalence of PE does not resolve the dilemma that the primary care and the emergency doctors face when taking care of AE-COPD.

Autopsy studies have shown a 28% to 51% prevalence of PE in patients with COPD.[13,14]

More recently, Shone *et al* in their study (n=341) showed that the prevalence of PE in patients with COPD was 18%.[16] In another study,[17] the prevalence of PE in a cohort of patients with severe AE-COPD with unexplained dyspnoea was found to be 25%. This was the first prospective analysis of patients with severe AE-COPD. This result differed from the observations reported by Rutschmann *et al*[18] who found the prevalence of PE among 123 patients with AE-COPD evaluated in an emergency department to be only 3%.[17] There could be several explanations for these differences.

First, the imaging method used for diagnosing PE is a crucial factor. Ventilation-perfusion scintigraphy was used in previous studies.[12] Although scintigraphy is an acceptable tool for the diagnosis of PE in patients without underlying lung diseases, the interpretation of lung scintigraphy is difficult in patients with COPD, which might have led to an over-estimation of the true prevalence of PE in that population.[12] We used a validated algorithm based on the findings of the lower limb venous Doppler which should have minimised the risk of false-positive findings.

Secondly, most studies exploring the relationship between AE-COPD and DVT or PE were retrospective studies or were based on autopsy findings,[11-15] while the present study was a prospective, observational and epidemiological study.

Nevertheless, none of these explanations account for the difference between our findings (9%) and the 25% prevalence of PE recently reported in another study.[17] However, it is indeed important to identify PE in COPD patients because PE when present, increases the morbidity and mortality of patients with COPD. In another report,[18] a higher (53%) 1-year mortality rate was observed among patients with COPD and PE, as compared with the figure of a 29% observed among those with COPD alone.[19]

CONCLUSIONS

Our results show a lower prevalence of unsuspected DVT/PE in Indian patients admitted for an AE-COPD. Future prospective, randomised studies are needed to confirm our findings in similar group of patients and to determine whether a systematic evaluation for VTE is justified in these patients, and hence, be recommended.

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