Universal Prophylaxis for Prevention of Invasive Aspergillus in Lung Transplant Recipients

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Background
Invasive pulmonary aspergillosis is a significant complication status post lung transplantation with an incidence of 6% to 16%. Early diagnosis of invasive aspergillosis in lung transplant is hampered by the lack of specific clinical signs and by the low sensitivity of culture-based diagnostic methods. Thus, the efficacy of bronchoalveolar lavage galactomannan for early diagnosis is explored in this study.

Methods
A retrospective analysis was performed on 45 consecutive lung transplant recipients between January 2015-February 2016. All patients were placed on itraconazole post-transplant for Aspergillus prophylaxis. Surveillance bronchoscopies were performed at 2 weeks, 1 month, 3 months, 6 months, 9 months, and 12 months post-transplant. During each bronchoscopy, bacterial, fungal, and acid-fast bacterial cultures along with bronchoaveolar lavage Aspergillus galactomannan (an optical density index of ≥0.5 considered positive) were obtained. If bronchoalveolar lavage galactomannan was ≥1.0, the patient was switched to voriconazole for further treatment. Computed tomography of the chest was also evaluated. If bronchoalveolar lavage galactomannan remained ≤1.0 at the 6-month interval, then prophylaxis was complete. Invasive aspergillosis was defined using the EORTC/MSG criteria for invasive fungal disease (i.e., patient classified as either having proven, probable or possible invasive aspergillosis).

Results
There was a total of 225 observations obtained from the 45 patients. Two patients (4.4%) had proven invasive aspergillosis with a mean Aspergillus galactomannan of 4.153 (SE, 0.629). Seven patients (15%) had probable invasive aspergillosis with a mean of 2.169 (SE, 0.409).

There was no correlation between the following: cold ischemic time (p = 0.88), primary graft dysfunction (p = 0.38), presence of either Candida species (p =0.048) or non-tuberculous mycobacteria in bronchoalveolar lavage (p=0.044) or viral pneumonitis (p =0.047) with a positive bronchoalveolar lavage Aspergillus galactomannan.

All nine patients with Aspergillus galactomannan >1.0 were switched to voriconazole from itraconazole, which resulted in negative Aspergillus galactomannan levels on follow-up bronchoscopies.

Conclusions
Our data suggest that the implementation of universal antifungal prophylaxis with itraconazole may not be efficacious in preventing invasive aspergillosis in lung transplant recipients. Furthermore, surveillance with bronchoalveolar lavage Aspergillus galactomannan is a strategy that can lead to early detection of invasive aspergillosis in patients during the first year after lung transplantation.

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