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Primary or Secondary Antifungal Prophylaxis in Resource-limited Settings

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Primary or secondary antifungal prophylaxis in resource-limited settings

Patients with malignancy are vulnerable and inclined to invasive fungal infections (IFIs). The incidence of invasive fungal infection increases with the severity and duration of neutropenia. IFI is rarely seen in patients undergoing chemotherapy with a low myelotoxic risk, as in the treatment of solid tumors. Invasive aspergillosis (IA) is mortal and common in patients with hematological malignancies or hematopoietic stem cell transplantation due to severe neutropenia or immunosuppression [1]. IA is a mortal and relapsing infection in those patients group. Primary prophylaxis is implemented to prevent IA before occurring IA. Seconder prophylaxis is implemented to prevent relapsing of previous IA [2]. Fluconazole, itraconazole, amphotericin B, posaconazole, voriconazole, micafungin were reported to be used for prophylaxis in patients with hematological malignancies [3,4].

Posaconazole prophylaxis was reported to reduce the incidence rates of IFI and to improve overall survival (16 versus 22%) compared to itraconazole and fluconazole prophylaxis in patients with neutropenia secondary to chemotherapy for acute myelogenous leukemia or the myelodysplastic syndrome [5]. Posaconazole was reported to be as effective as fluconazole in preventing IFI and did not show superiority in preventing probable or proven aspergillosis. Overall mortality was no different between posaconazole and fluconazole groups, but death due to IFD was lower in the posaconazole group (1 versus 4%) [6]. Thus, posaconazole is recommended as antifungal prophylaxis in the hematopoietic stem cell transplantation recipients with graft versus host diseases and in neutropenic patients with acute myelogenous leukemia or myelodysplastic syndrome who are at high risk for IA [7]. Clinical failure was reported to be 25% at posaconazole plasma level and did not improve much at higher concentrations [8]. However, antifungal prophylaxis is not recommended in settings that have relatively high incidence of invasive mould infections and have not facilities for early diagnosis and treatment [9]. In addition, cost of antifungal prophylaxis is an important challenge for hospitals with limited sources. Posaconazole and liposomal amphotericin B were reported to cost the highest expenditures and those expenditures may be a challenge for resource-limited settings [10]. Fluconazole is still a cheaper choice for health care resource-limited settings. Azole resistance should be taken into account and be surveilled in settings implemeting azole-based antifungal prophylaxis. Antifungal drug should be chosen takine into account health care settings' financial situations and azole resistance rates.

Relapsing IA has higher mortality rates between 88-100% than primary IA [11]. Secondary antifungal prophylaxis may be alternative for resource-limited settings. Voriconazole tablet form was reported to reduce the cost related to secondary antifungal prophylaxis [10]. Voriconazole was reported to fail in 40% of patients received as targeted, empirical, pre-emptive, prophylactic regimens [12]. Physicians should be careful for relapsing IA in patients receiving voriconazole for secondary antifungal prophylaxis. Hallucination, visual disturbances and elevated liver enzymes and were reported side effects of voriconazole [13]. It was reported that caspofungin would be ineffective as primary antifungal prophylaxis in patient with hematological malignancies, but could be effective for secondary prophylaxis chronic invasive candidiasis (hepatosplenic candidiasis) [14,15]. Caspofungin may be an alternative antifungal drug for azole-resistant Candida infections as well. Central venous catheter, urinary catheter, comorbid conditions, total parenteral nutrition, surgery, transfusion, mechanic ventilation, broad-spectrum antibiotic use were reported to be risk factors for invasive Candida infections.

As a results, each health care setting should define their antifungal prophylaxis protocol depends on setting conditions and financial status.

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