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Investigation of Azol Resistance in Aspergillosis Caused by Gradient Test and Agar Plaque Methods

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Abstract : Objective: Invasive fungal infections are a serious threat in terms of morbidity and mortality, especially in immunocompromised patients. The most frequently isolated agents are Aspergillus genus fungi, and sensitivity to azoles, which are the first choice in treatment, decreases. In our study, we aimed to investigate the use of the agar plate screening method as a fast, easy, and practical method in determining azole resistance in Aspergillus spp. species. Methods: Our study was conducted with 125 Aspergillus spp. isolates produced from various clinical samples. Aspergillus spp. isolates were identified by conventional methods and azole resistance was determined by gradient test and agar plate screening method. Broth microdilution method was applied to resistant isolates, and CypA-L98H and CypA-M220 mutations in the cyp51A gene were investigated. Results: In our study, 55 A. fumigatus complex (44%), 42 A. flavus (33.6%), 6 A. terreus (5%), 4 A. niger (3%) and 18 Aspergillus spp. (14%) were identified. With the gradient test method, resistance to VOR and POS was detected in 1 (1.8%) of A.fumigatus isolates, and resistance to ITR was detected in 3 (5.45%). With the agar plate method, 1 of the A.fumigatus isolates (1.8%) had VOR, ITR, POS, 1 of the A.terreus isolates (16.7%) had VOR, 1 of the A.niger isolates (25%) had ITR. Resistance to VOR and POS was detected in 2 Aspergillus spp. isolates (11%), and resistance to ITR was detected in 1 (5.6%). Sensitivity and specificity were determined as 100% for VOR and POS in A. fumigatus species, 33.3% and 100% for ITR, respectively, 100% for ITR in A. flavus species, and 100% for ITR and POS in A. terreus species. By broth microdilution method in 7 isolates in which resistance was detected by gradient test and/or agar plate screening method; 1 A.fumigatus resistant to ITR, VOR, POS, 2 A.fumigatus resistant to ITR, 2 Aspergillus spp. ITR, VOR, POS MICs were determined as 2µg/ml and 8µg/ml, 8µg/ml and >32µg/ml, 0.5µg/ml and 4µg/ml, respectively. CypA-L98H mutations were detected in 5 of these isolates, CypA-M220 mutations were detected in 6, and no mutation was detected in 1. CypA-L98H and CypA-M220 mutations were detected in 1 isolate for which resistance was not detected. Conclusion: The need for rapid antifungal susceptibility screening tests is increasing in the treatment of aspergillosis. Although the sensitivity of the agar plate method was determined to be 33.3% for A.fumigatus ITR in our study, its sensitivity and specificity were determined to be 100% for ITR, VOR, and POS in other species. The low sensitivity value detected for A.fumigatus showed that agar plate drug concentrations should be updated in accordance with the latest regulations of EUCAST guidelines. The CypA-L98H and CypA-M220 mutations detected in our study suggested that the distribution of azole resistance-related mutations in different regions in our country should be investigated. In conclusion, it is thought that the agar plate method, which can be easily applied to detect azole resistance, is a fast and practical method in routine use and can contribute to both the determination of effective treatment strategies and the generation of epidemiological data.

Keywords : Aspergillus, agar plate, azole resistance, cyp51A, cypA-L98H, cypA-M220
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