Recognition of Azole-Resistant Aspergillosis by Physicians Specializing in Infectious Diseases, United States

Tiffany Walker, Emory University
Shawn R. Lockhart, Centers for Disease Control and Prevention
Susan E. Beekmann, University of Iowa
Philip M. Polgreen, University of Iowa
Scott Santibanez, Emory University
Rajal K. Mody, Centers for Disease Control and Prevention
Karlyn D. Beer, Centers for Disease Control and Prevention
Tom Chiller, Emory University
Brendan R. Jackson, Centers for Disease Control and Prevention

Journal Title: Emerging Infectious Disease
Volume: Volume 24, Number 1
Publisher: Centers for Disease Control and Prevention | 2018-01-01, Pages 111-113
Type of Work: Article | Final Publisher PDF
Publisher DOI: 10.3201/eid2401.170971
Permanent URL: https://pid.emory.edu/ark:/25593/th5g9

Final published version: http://dx.doi.org/10.3201/eid2401.170971

Copyright information:
© 2017, Centers for Disease Control and Prevention (CDC). All rights reserved.

Accessed July 19, 2019 3:19 AM EDT
Recognition of Azole-Resistant Aspergillosis by Physicians Specializing in Infectious Diseases, United States

Infections caused by pan–azole-resistant Aspergillus fumigatus strains have emerged in Europe and recently in the United States. Physicians specializing in infectious diseases reported observing pan–azole-resistant infections and low rates of susceptibility testing, suggesting the need for wider-scale testing.

Infections with strains of Aspergillus fumigatus that are resistant to all azole antifungal medications have become common in western Europe and have been documented in other regions since 1998 (1,2), but until recently, had...
testing occurred off-site rather than in their hospital. For those reporting off-site testing, 8 (4%) physicians typically received results within 1 week and 42 (19%) reported receiving results ≥3 weeks after request, excluding the minority (n = 6, 4%), who were unsure. Of the 224 physicians who had access to susceptibility testing, 127 (57%) reported that ≥1 of their patients had an isolate tested, and 56 (25%) reported that >50% of patients had isolates tested. Forty-one (19%) reported a patient isolate with resistance to ≥1 azole, and 16 (7%) reported a patient with a pan–azole-resistant isolate.

Sixteen (8%) physicians practicing in the southern and 14 (9%) practicing in the western US census regions reported seeing >8 patients who had aspergillosis during the previous year, compared with 5 (3%) in the Northeast and 9 (5%) in the Midwest (χ² = 6.3, p = 0.18). Other findings were generally similar across regions, including proportions reporting clinical failure, azole resistance in azole-naive patients, susceptibility testing availability, routine versus physician-prompted testing, and location of testing.

Of 224 physicians with access to susceptibility testing, 8 (16%) of 51 physicians in the South reported that >50% of their patients’ isolates were tested, compared with 17 (27%) of 63 in the Midwest, 8 (21%) of 37 in the Northeast, and 22 (31%) of 70 from the West (χ² = 4.3, p = 0.37). Of 51 physicians in the South, 13 (26%) reported observing isolates resistant to ≥1 azole, compared with 9 (14%) of 63 from the Midwest, 5 (14%) of 37 from the Northeast, and 13 (19%) of 70 from the West (χ² = 10.2, p = 0.04). Pan–azole-resistant isolates were reported by 4 (8%) of 51 physicians in the South, 7 (11%) of 63 in the Midwest, 2 (5%) of 37 in the Northeast and 3 (4%) of 70 in the West (χ² = 4.4, p = 0.36).

In summary, approximately 50% (348/709) of surveyed infectious disease physicians were familiar with azole-resistant A. fumigatus and 14% (100/709) were aware of a possible link to environmental fungicide use. Of physicians who had treated patients diagnosed with aspergillosis within the past year, 21% (75/364) lacked access to susceptibility testing and 57% (127/224) who had access tested an isolate in the previous year. A small proportion of 19% (41/224) reported observing any azole resistance and only 7% (16/224) reported pan-resistance. Of note, physicians in the southern states more commonly observed resistance to ≥1 azole, compared with physicians from other regions.

Because only a small fraction of patients with invasive aspergillosis have a positive culture (13), a survey of resistance in culture-positive aspergillosis is not necessarily representative of all cases; but this fact highlights the importance of monitoring available cultures to inform broader practice. Another gap in our understanding of azole-resistant A. fumigatus is that the Clinical and Laboratory Standards Institute has not established breakpoints for azole susceptibility for A. fumigatus because inadequate clinical data exist
to support breakpoints. The institute uses epidemiologic cut-off values, reflecting the minimal inhibitory concentration of 95% of wild-type isolates (13). However, there is some evidence that infection with resistant isolates by currently used thresholds is associated with worse outcomes in patients treated with azole monotherapy (13). Patients with hematologic or oncologic diseases are more likely to be infected with azole-resistant aspergillosis, and those with resistance have been shown to have higher case-fatality rates (2). However, it remains unclear to what degree these failures are attributable to underlying immunosuppression in these patients or to resistance-mediated treatment failure.

Conclusions

Our findings support that azole-resistant A. fumigatus infections, including those with pan-azole resistance, are occurring in the United States, and that broader susceptibility testing may be warranted to guide patient care. Systematic surveillance for aspergillosis, including collection of clinical data and isolates, could aid in detecting emergence of regional resistance patterns, assessing the role that resistance plays in treatment failure, and determining locally tailored treatment options. Awareness by physicians of azole-resistant aspergillosis and the possible link to environmental fungicide use are essential.

This work was funded by the Centers for Disease Control and Prevention (cooperative agreement no. 1 U50 CK000477-01).

Dr. Walker is an internal medicine physician who completed training in the Epidemic Intelligence Service in the Mycotic Diseases Branch, Division of Foodborne, Waterborne, and Environmental Diseases, National Center for Emerging and Zoonotic Infectious Diseases, CDC, Atlanta. She is currently investigating the incidence of influenza in adults with underlying conditions through the Southern Hemisphere Influenza and Vaccine Effectiveness Research & Surveillance project supported by the Institute of Environmental Science and Research Limited, Wellington, New Zealand, in conjunction with CDC.

References


Address for correspondence: Tiffany A. Walker, Centers for Disease Control and Prevention, 1600 Clifton Rd NE, Mailstop C09, Atlanta, GA 30329-4027, USA; email: twalker603@gmail.com