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Management and outcome of culture-positive invasive aspergillosis in an area with high prevalence of voriconazole resistance

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Background: Treatment of invasive aspergillosis (IA) is complicated due to increasing triazole resistance of *Aspergillus fumigatus*. We previously reported a resistance frequency of 26% in the ICU of our tertiary care medical center (Euro Surveill. 2016;21(30)). In 2014, we introduced a new treatment algorithm in our center incorporating disease severity, previously used antifungals, rapid diagnostics and early switch to treatment with liposomal amphotericin B (L-AmB) when voriconazol resistance was suspected or diagnosed.

Material/methods: To evaluate the effect of this algorithm, we performed a single center 5-year retrospective cohort study from the period between 2011 and 2015. The medical records of patients with an *A. fumigatus* in culture were evaluated for treatment of IA and outcome, using similar criteria as the Nijmegen study group. Cases of IA were included when classified probable, putative or proven

according to the EORTC/MSG criteria, and those proposed by Blot et al. We compared cohorts of cases with voriconazole-susceptible (VS) and voriconazole-resistant (VR) strains for overall mortality and attributable mortality at 90 days.

Results: During the study period, 63 cases were identified with IA classified as: putative IA (15), probable IA (40) and proven IA (8). Forty cases (63.5%) were admitted to the ICU during admission, and 35 (55.6%) had an underlying hematological malignancy. Twenty cases (31.7%) were associated with VR *A. fumigatus*, while 43 (68.3%) harbored a VS strain. All-cause mortality within the VR cohort was 52.6% (10/19) compared to 58.1% (25/43) in the VS cohort. The attributable mortality to IA was 42.1% (8/18) in VR versus 39.5% (17/43) in VS. Mortality in both VR and VS cohorts decreased throughout the years from: 66.7% (8/12) in 2011, 70.0% (7/10) in 2012, through 63.6% (7/11) in 2013, to 45.5% (5/11) in 2014 to 44.4% (8/18) in 2015. The mortality in the VR cohort decreased with 80.0% (8/10) in 2011-2013 to 20% (2/10) in 2014-2015.

Conclusions: The introduction of a new algorithm for the management of fungal infection in an area with high prevalence of azole resistance resulted in a decrease of overall mortality; a trend is evident though larger cohorts would be necessary to prove this. No significant difference was found between patients infected with azole resistant or azole susceptible *A. fumigatus* in our center.