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Commentary

Fungal superinfection in patients with COVID-19: Role of antifungal stewardship?



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An area of great interest to the antimicrobial stewardship community is the presence of fungal superinfection, specifically invasive pulmonary aspergillosis (IPA), in patients with COVID-19. Classically a disease of the immunocompromised, isolated reports indicate a potentially increased risk for IPA in patients with COVID-19 who are nonimmunocompromised at baseline.¹⁻⁴ During hospitalization, patients with COVID-19 have additional risk factors for IPA associated with interventions such as intubation and corticosteroid therapy.⁵ Isolated reports from France and Germany suggest patients who were admitted to the intensive care unit with COVID-19 show potential IPA rates as high as 33% and 26%, respectively.^{2,6}

Further complicating the true incidence of IPA in patients with COVID-19 is the difficulty diagnosing these infections, especially in the setting of the SARS-CoV-2 pandemic. Bronchoscopy with bronchoalveolar lavage is traditionally utilized in disease work-up but requires prolonged patient contact and increases the risk of aerosol transmission; many clinicians are minimizing bronchoscopy to preserve personal protective equipment and minimize additional transmission risk.^{1,2} The SARS-CoV-2 pandemic has also decreased the occurrence of autopsies which limits our understanding of the true incidence of these infections.^{1,2} Some authors have called for the empiric use of antifungals even if data for IPA are limited.^{2,3}

Voriconazole is the first-line treatment for IPA and must be closely monitored to prevent neurotoxicity and hepatotoxicity. Voriconazole also has significant drug-drug interactions.¹ Other IPA-focused therapies carry their own potential toxicities.¹ Antifungal stewardship presents an attractive target for antimicrobial stewardship programs (ASPs) given the complexities in diagnosing infections in these patients and the potential toxicity of the therapies involved.

To assess whether the COVID-19 pandemic affected empiric antifungal use, we examined antifungal usage trends at Virginia Commonwealth University (VCU) Health System, an 865 bed urban academic medical center.

Days of therapy per 1,000 patients days (DOT/1,000 PDs) were examined for 5 commonly used antifungals (voriconazole, posaconazole, isavuconazonium, liposomal amphotericin B, and micafungin) for our Medical Intensive Care Unit and a progressive medicine unit; COVID-19 patient care constituted approximately 30% and 65% of the total patient days for these units respectively. A 2 sample t test assuming equal variances was used to test the null hypothesis that antifungal usage in April 2020 was the same as the average use from April 2019 to March 2020. The same procedure was repeated for May 2020. Full results are in [Table 1](#).

We found that there was no significant increase in antifungal use for either April 2020 or May 2020 when compared to April 2019–March 2020. There was a significant decrease in use of micafungin ($P = .011$) in the Medical Intensive Care Unit for May 2020. This may be due to a shift in the traditional patient population for the unit (with more patients with COVID-19 being housed in the unit in May). A limitation of our analysis is that we did not look at the incidence of IPA or candidemia in patients with COVID-19.

These data are an indirect indicator that empiric antifungals were not used widely at our hospital despite the increase in hospitalized patients with COVID-19. The true incidence of IPA in patients with COVID-19 is not known and diagnosing these infections can be challenging. Additionally, the therapies for these infections carry significant potential toxicities. ASPs have the potential to play a significant role with antifungal stewardship during the pandemic. Programs can help clinicians optimize the work-up for IPA by identifying patients at high risk and creating local evaluation and empiric treatment protocols. Additionally, ASPs can utilize antifungal restriction to help limit suboptimal antifungal use. We advocate for close antifungal use monitoring and ASP involvement in antifungal stewardship in the setting of the current pandemic.

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Table 1.
Antifungal use Trends for April and May of 2020

Unit	April COVID-19 PD	May COVID-19 PD	Antifungal	Mean April'19- March'20 (DOT /1000 PD)	April'20 (DOT /1000 PD)	April'20 vs mean P value	May'20 (DOT /1000 PD)	May'20 vs mean P value
MICU	156 (28% of total PD)	212 (30% of total PD)	Voriconazole	21	19	.91	0	.10
			Posaconazole	6	3	.74	0	.52
			Isavuconazonium	17	0	.25	0	.25
			Lip. Amphotericin B	7	3	.55	1	.40
			Micafungin	46	51	.74	0	.01
PM	280 (64% of total PD)	304 (69% of total PD)	Voriconazole	1	2	.57	0	.61
			Posaconazole	0	2	.21	0	.79
			Isavuconazonium	2	0	.60	0	.60
			Lip. Amphotericin B	2	0	.66	0	.66
			Micafungin	8	2	.48	0	.38

DOT, days of therapy; MICU, medical intensive care unit; PD, patient days; PM, progressive medicine unit.

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