

Letter to the Editor

Impact of antimicrobial stewardship interventions on reducing antifungal use in hospitals in Jordan

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To the Editor—Antimicrobial resistance (AMR) poses a significant threat to health and human development worldwide. The overuse and misuse of antimicrobials has increased the risk of emergence and spread of AMR globally.² Recent developments in antifungal resistance have highlighted the importance of implementing effective antifungal stewardship in hospitals and the need to do so.³ Whereas significant work has been done to describe and evaluate antibiotic stewardship interventions in hospitals, experience with antifungal stewardship interventions is limited. In February 2018, King Abdullah University Hospital (KAUH), a 533-bed tertiary teaching hospital in Jordan, implemented an overarching antimicrobial stewardship program (ASP) that aimed toward optimizing antibiotic and antifungal use.⁴ The impact of the ASP on antibiotic consumption was evaluated separately.⁴ The objective of this study was to evaluate the impact of an ASP on reducing antifungal use in hospitalized patients.

This retrospective ecological evaluation took place at KAUH using data from January 2014–December 2019. The ASP in February 2018 was considered and evaluated as an intervention, and 2 study periods were defined: before the ASP intervention (January 2014–January 2018) and after the ASP intervention (February 2018–December 2019). The study population included all adult inpatients admitted to KAUH during the study period. Approval of the institutional review board (IRB) at Jordan University of Science and Technology and KAUH was obtained for this study. Monthly quantities of antifungals used (ie, conventional amphotericin B, caspofungin, anidulafungin, voriconazole, and fluconazole) were converted into a number of defined daily doses (DDD; 2019 WHO/ATC index) and normalized per 100 occupied bed days (OBD). The ASP involved several components including awareness and education, an antimicrobial restriction policy that included restricted antibacterial and antifungal drugs with prior approval, and tracking via audit of compliance to the restriction policy and feedback.⁴

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A key intervention was the strict antifungal approval policy, which required that a prescriber seek approval from an infectious diseases consultant before using conventional amphotericin B, caspofungin, anidulafungin, or voriconazole. The usual uses of antifungals in our hospital were mainly for prophylactic, empiric, or definitive therapies, with no or little role for pre-emptive therapy. We followed the Infectious Diseases Society of America (IDSA) guidelines for therapy.^{1,5} Education and awareness about appropriate use of antifungals comprised a major part of this ASP; these measures included grand rounds and regular lectures directed mainly toward healthcare providers in the hospital. They also included direct, easily accessible links integrated into the electronic medical system for information about different antifungals including dosing and dosing adjustment.

The impact of the ASP on the restricted antifungal consumption was evaluated using a segmented regression of interrupted time series.^{4,6} Caspofungin and anidulafungin use were grouped under the echinocandins category. In addition, the potential overall increase in awareness of the issue of antimicrobial use and resistance due to the introduced ASP interventions on the use of fluconazole was assessed. The final model was simplified by removing insignificant terms using a backward stepwise approach based on the Bayesian full information criteria (BIC). Any outliers discovered during residual diagnostics were adjusted for in the model as additive outliers.⁴ Analyses were performed using SCA Statistical System version 8.1 software (Scientific Computing Associates, River Forest, IL).

The average total restricted antifungal use was 0.78 DDDs per 100 OBD, and the total antifungal use (including fluconazole) was 1.81 DDDs per 100 OBD. The average conventional amphotericin B use was 0.09 DDDs per 100 OBD; echinocandin use was 0.45 DDDs per 100 OBD; voriconazole use was 0.25 DDDs per 100 OBD; and fluconazole use was 1.04 DDDs per 100 OBD. The results of our analysis of the impact of the ASP on antifungal use are presented in Table 1 (a and b). Statistically significant decreases in the level of fluconazole (regression coefficient, -0.3793 ; $P = 0.0091$) and total antifungal use (regression coefficient, -0.5735 ; $P = 0.0108$) were observed after the introduction of the ASP (Table 1b). A statistically significant

Table 1. Changes in Antifungal Use After the Intervention Using Segmented Regression Analysis, January 2014–December 2019

Terms ^a	Intercept	P Value	Trend	P Value	Level Change After Intervention	P Value	Trend Change After Intervention	P Value	ARMA Adjustment (coefficient; P Value)	R ³
(a) Full model										
Conventional amphotericin B	0.0931	.0033	−0.0021	.0503	0.0990	.0518	0.0050	.1085	N/A	0.5880
Echinocandins	−0.0623	.4470	0.0131	.0000	−0.1109	.4353	0.0128	.1462	N/A	0.5847
Fluconazole	0.2600	.0083	0.0193	.0000	−0.3793	.0091	−0.0241	.0131	AR1 (0.264; .00912)	0.6257
Voriconazole	0.0525	.3382	0.0037	.0553	−0.1482	.1030	−0.0041	.4689	AR1 (0.404; .00003)	0.5515
Restricted antifungals	0.2755	.0067	0.0139	.0002	−0.0867	.6127	0.0060	.5695	N/A	0.4400
All antifungals	0.5980	.0006	0.0276	.0001	−0.4489	.0694	−0.0177	.2507	AR1 (0.245; .03894)	0.5203
(b) Most parsimonious model										
Conventional amphotericin B	0.0396	.0092	N/A	N/A	0.0870	.0010	N/A	N/A	N/A	0.5570
Echinocandins	−0.0961	.1531	0.0145	.0000	N/A	N/A	N/A	N/A	N/A	0.5713
Fluconazole	0.2600	.0083	0.0193	.0000	−0.3793	.0091	−0.0241	.0131	AR1 (0.264; .00912)	0.6257
Voriconazole	0.1084	.0007	N/A	N/A	N/A	N/A	N/A	N/A	AR1 (0.459; .00000)	0.5084
Restricted antifungals	0.2714	.0010	0.0139	.0000	N/A	N/A	N/A	N/A	N/A	0.4368
All antifungals	0.6209	.0003	0.0244	.0001	−0.5735	.0108	N/A	N/A	AR1 (0.281; .01479)	0.5106

Note. ARMA, autoregressive moving average. N/A, not applicable; AR1, first-order autocorrelation coefficient; DDD, defined daily dose; OBD, occupied bed days.

^aAntibiotic use expressed as DDD/100 OBD.

decrease in the slope after intervention for fluconazole (regression coefficient, −0.0241; $P = .0131$) was observed (Table 1b). For echinocandins and total restricted antifungals, significantly increasing trends were observed before the intervention ($P \leq .001$ and $P = .0002$, respectively). This trend was halted in the post-intervention period ($P = .1462$ and $P = .5695$, respectively) (Table 1a). A significant increase in the level of conventional amphotericin B (regression coefficient, 0.0870; $P = .001$) was observed after the introduction of the ASP. We detected no change in voriconazole use (Table 1).

The assessment demonstrated the impact of the ASP in a hospital with low use of antifungal agents, on average 1.8 DDDs per 100 OBD, compared with other studies.^{7–9} Although fluconazole was not on the restricted antifungals list, our analysis of these data revealed a decrease in its use in the post-ASP period, possibly as the result of the overall impact of the ASP and the increased awareness among prescribers. Other studies have reported reduced use of nontargeted drugs, such as fluconazole, as a result of their educational and bedside intervention.¹⁰ Notably, we detected a significant increase in trend during the preintervention period for echinocandins (caspofungin and anidulafungin); however, this trend stopped after the intervention. The reduction in echinocandin use had a significant impact on cost reduction in our general tertiary-care teaching hospital after the implementation of antifungal stewardship measures.¹⁰ The use of conventional amphotericin B increased after the intervention; however, the overall use of conventional amphotericin B throughout the study was low (5% of total antifungals used). In conclusion, a multifaceted ASP contributed to a reduction in the use of antifungals in hospitalized patients. This study provides evidence supporting the efficacy of ASPs to optimize the use of antifungal agents in hospitals, and our findings emphasize the need to promote antifungal stewardship alongside antibiotic stewardship.

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To err is human, to forget is device-related: A cautionary note for endoscopists

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To the Editor—More than 5 million endoscopies are performed annually in the United States, and ~1 in 1.8 million procedures is associated with a healthcare-related infection.^{1–3} However, the true rate of infection transmission during endoscopy is largely unrecognized because of the late onset of clinical symptoms after the procedure, underreporting, and other surveillance challenges.^{1–4}

Risk factors for gastrointestinal (GI) infections after endoscopy include bacterial biofilm formation, inadequate decontamination, immunocompromised patients, presence of infective foci in the operating field, and equipment malfunction. Procedural endoscopies, such as variceal ligation, are associated with significantly higher infection transmission than diagnostic GI procedures.^{5–8}

The disinfection of endoscopes involves a complicated, multistep process, and any retained object in one of its narrow channels, such as a sheath, could increase the microbial burden and the chance of an endoscopy-related infection, as illustrated by the following example.^{1,9,10} During a routine colonoscopy, the operator noticed resistance while advancing a vascular clipping wire through the channel. A sheath of a balloon-tipped catheter (M00558470 Boston Scientific CRE Wire-guided Esophageal/pyloric balloon dilation) was then extruded into the colonic lumen. The sheath and endoscope were withdrawn, and the procedure was completed with a different endoscope.

A standardized protocol for exposure investigation after a breach of disinfection procedure was followed.³ The last time that type of balloon-tipped catheter was used occurred 20 days prior, resulting in 20 patients having potentially been exposed. However, a tracking system linking the serial number of any endoscope in the clinic to every patient it is/was used on had been implemented 1 year previously. This procedure revealed that the involved endoscope was used on only 2 subsequent patients. Review of patient records who had endoscopies in that 20-day period reconfirmed the number of patients potentially exposed ($n = 2$).

Interrogation of the endoscope with various inserts revealed that the presence of a retained sheath would allow passage of all types of guide wires, (snips, snares, etc), including the cleaning

brush. The only device whose passage would have been prevented by a retained sheath was a vascular clipping device. Such clippings were performed as recently as 2 days prior to the incident, further confirming number of potentially exposed patients. Notably, this explained why the sheath had not been extruded by the cleaning brushes during the preparatory steps of reprocessing.

Exposed patients were notified and offered free testing for blood-borne and enteric pathogens. The county and state health departments were notified, and a MAUDE (Manufacturer and User Device Experience) report was filed with the US Food and Drug Administration. A search of the MAUDE database and PubMed revealed 2 similar incidents in the MAUDE database describing the failure of removal of the sheaths, which led to it being lodged in the endoscope compromising the disinfection process in one (June 14, 2019), and in the other, leading to detachment of the exit marker (February 18, 2017). No similar cases were found in PubMed.

The root cause analysis revealed that 4 factors contributed to this incident. First, the assisting technologist was newly trained and inexperienced. Second, the rapid turnover of patients, insufficient number of endoscopes, and different models of catheters stocked heightened risk of reprocessing breakdown. Third, there was no count and verification for the number of removable components (similar to an operating-room sponge count). Last, there were 2 important design flaws. The first flaw pertains to the sheath design, having a size that allows it to enter the channel. Additionally, this brand lacks a large warning flag that also precludes channel sheath entry (Fig. 1). The second flaw pertains to the cleaning brushes that are not large enough to extrude a lodged sheath because they pass through the lumen of the embedded sheath. This permits the sheath to remain, undetected, in the endoscope during the preparatory steps of reprocessing.

The Boston Scientific sheath covering the balloon is flared at each end. However, there is no tag on the sheath stating to remove it prior to use the balloon. In contrast, the sheath of the Cook Medical balloon has a tag indicating its removal prior to insertion of the balloon, and it is also large enough that the provider would not be able to advance the balloon unless the sheath were removed (Fig. 1). Additionally, because sheaths are not conventionally counted after the procedure, there is a risk of them being left unnoticed within the lumen of the endoscope channel.

The following measures would help prevent the recurrence of this process breakdown. First, manufacturers should consider modifying the design of balloon sheaths and cleaning brushes. Sheaths should

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