ORIGINAL RESEARCH

Assessment of prescription patterns of systemic antifungal medications in critically ill patients

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ABSTRACT
Background: systemic fungal infections are superficial, cutaneous, and subcutaneous infections. These infections gravely threaten the healthcare system. The present study was conducted to assess prescription patterns of systemic antifungal medications in critically ill patients. **Materials & Methods:** This study was conducted on 145 patients in the Department of Pharmacology in collaboration with the Department of Critical care Medicine and the Department of Medicine of King George's Medical University (KGMU). Clinical symptoms and investigations were recorded. Prescription patterns of systemic antifungal medications was recorded. **Results:** The majority of the patients were 12-31 years old [63(43.45%)], followed by 52-71 years old [34(23.45%)], where the mean age was recorded [43.11±20.09] years. Statistically, a significant difference was observed. Most of the patients were males [74(51.03%)], followed by females [71(48.97%)]. Out of 160 comorbidities diagnosed, the majority of the patients had no comorbidities [96(60.00%)], followed by patients who had diabetes [22(13.75%)], peptic ulcer disease [11(6.88%)] and so on. The Charlson Comorbidity Index showed that the majority of the patients had mild comorbidities [42(65.63%)], followed by moderate comorbidities [16(25.00%)], and this difference was statistically significant. The majority of the patients were referred from trauma [118(83.10%)], followed by referred from department of medicine [8(5.63%)], QMH [7(4.93%)] and so on. The majority of the patients were prescribed Inj Caspofungin [82(56.55%)], followed by Inj. Fluconazole [44(30.34%)], Inj Anidulafungin [12(8.28%)]. Statistically, a significant difference was observed in antifungal agent prescription to patients. Charlson comorbidity index, Apache score, Sofa score and duration of antifungal prescription shows a significant positive correlation with each other. **Conclusion:** Caspofungin was the most often used antifungal medication. The usage of more modern antifungal drugs is also growing. It was observed that most patients in were age group 12-31 years; have systemic antifungal medications, especially in males.
Key words: Anidulafungin, fungal infections, Caspofungin

INTRODUCTION
Included in systemic fungal infections are superficial, cutaneous, and subcutaneous infections. These infections gravely threaten the healthcare system.[1] IFI prevalence has increased markedly in patients with acquired immunodeficiency syndrome (AIDS), those receiving immunosuppressive therapy, those undergoing hematopoietic stem cell transplants (HSCT), cancers, the elderly, and those receiving critical care.[2] Candida and Aspergillus species are the most commonly reported fungal pathogens; Zygomycetes, Fusarium, Scedosporium, and black moulds are also frequently observed.[3]

Antifungal resistance represents a major clinical challenge in the treatment of IFIs. The problem of growing antifungal resistance is exacerbated by the emergence of resistant fungal species and a paucity of new antifungal agents in development with unique mechanisms of action.[4] In addition, the utility of current antifungal drugs may be limited by drug–drug interactions and serious adverse effects/toxicities that prevent their prolonged use or dosage escalation. The data on systemic antifungal prescribing patterns in Indian patients is scarce.[5]
Several physiological alterations, such as third spacing, hypoalbuminemia, renal or hepatic failure,

and common ICU interventions, such as renal replacement therapy and extracorporeal membrane oxygenation, can affect the pharmacokinetics of antifungal drugs.[6] Moreover, many ICU patients are in a septic state, in which the endothelial dysfunction secondary to the inflammation seen in sepsis and the septic shock causes capillary leakage, which in turn causes an expansion of the interstitial space and can increase the volume of distribution (Vd) of a drug, particularly for hydrosoluble compounds.[7] Hypoalbuminemia in critically ill patients may also contribute to an increase in Vd and substantially affect agents with a high protein-binding capacity, resulting in a greater amount of unbound drug, resulting in a greater distribution.[8] The present study was conducted to assess prescription patterns of systemic antifungal medications in critically ill patients.

MATERIALS & METHODS

The present work was conducted on 145 patients in the Department of Pharmacology in collaboration with the Department of Critical care Medicine and the Department of Medicine of King George's Medical University (KGMU). Ethical clearance was taken from the institutional ethical committee of KGMU. Consent for participation in the project was obtained, and they were enrolled on the project study.

Data such as name, age, gender etc. was recorded. Clinical symptoms and investigations were recorded. Prescription patterns of systemic antifungal medications was recorded. Data thus obtained were subjected to statistical analysis. P value < 0.05 was considered significant.

RESULTS

Table-1: Age-wise distribution of patients admitted to ICU

Age Distribution (YEARS)	No.	%	P- Value
12-31	63	43.45%	X=12.65 p=0.0055*
32-51	27	18.62%	
52-71	34	23.45%	
72-91	21	14.48%	
Grand Total	145	100.00%	
MEAN±SD	43.11±20.09		--

The majority of the patients were 12-31 years old [63(43.45%)], followed by 52-71 years old [34(23.45%)], where the mean age was recorded [43.11±20.09] years. Statistically, a significant difference was observed in the age-wise distribution of enrolled patients [p=0.0055*].

Table-2: Gender of patients admitted to ICU

Gender	No.	%
Female	71	48.97%
Male	74	51.03%
Grand Total	145	100.00%

Most of the patients were males [74(51.03%)], followed by females [71(48.97%)].

Table-3: Comorbidities in patients admitted to ICU

|	Comorbidities	No.	%	P-Value
	NONE	96	60.00%	X=115.0 p<0.0001*
YES	Cerebrovascular event (hemiplegia)	4	2.50%	
	CHF	3	1.88%	
	CPD	3	1.88%	
	Diabetes	22	13.75%	
	Dementia	3	1.88%	
	CAD	3	1.88%	
	HTN	3	1.88%	
	CKD	3	1.88%	
	CLD	3	1.88%	
	Liver disease	3	1.88%	
	Peptic Ulcer Disease	11	6.88%	
	Peripheral vascular disease	3	1.88%	
	Grand Total	160	100.00%	

Out of 160 comorbidities diagnosed, the majority of the patients had no comorbidities [96(60.00%)], followed by patients who had diabetes [22(13.75%)], peptic ulcer disease [11(6.88%)] and so on. Statistically, a significant difference was observed in the comorbidities of patients [p<0.0001*].

Table-4: Charlson Comorbidity Index of patients admitted to ICU

| Charlson comorbidity index	No.	%	P-value
Mild (1-2)	42	65.63%	
Moderate (3-4)	16	25.00%	X=16.00
Severe (≥5)	6	9.38%	p=0.0003*
Grand Total	64	100.00%	

The Charlson Comorbidity Index showed that the majority of the patients had mild comorbidities [42(65.63%)], followed by moderate comorbidities [16(25.00%)], and this difference was statistically significant [p=0.0003*].

Graph I Referred patients admitted to ICU
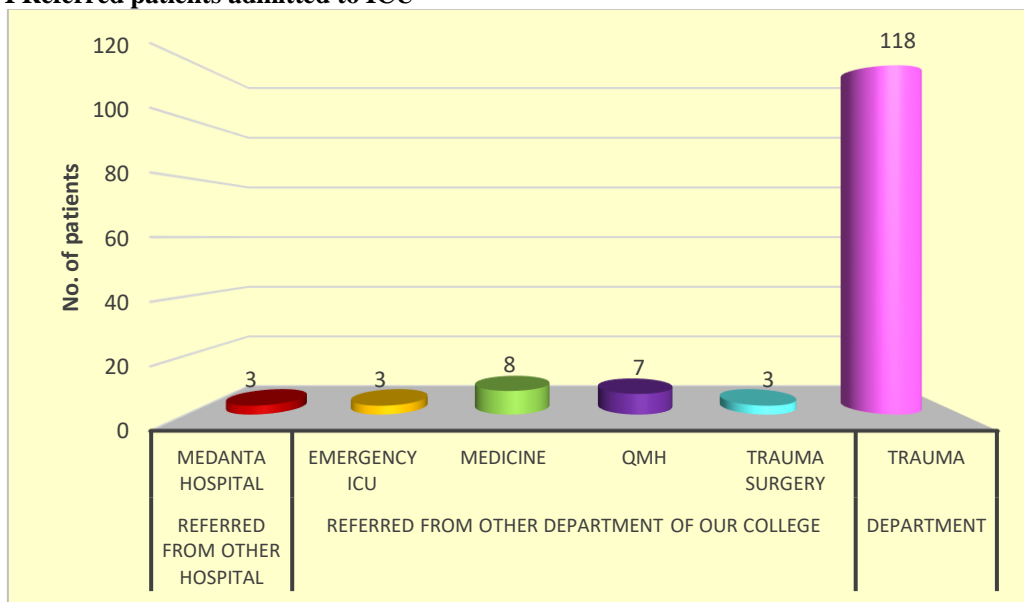
The majority of the patients were referred from trauma [118(83.10%)], followed by referred from department of medicine [8(5.63%)], QMH [7(4.93%)] and so on.

Graph II Antifungal agents prescribed to patients admitted to ICU
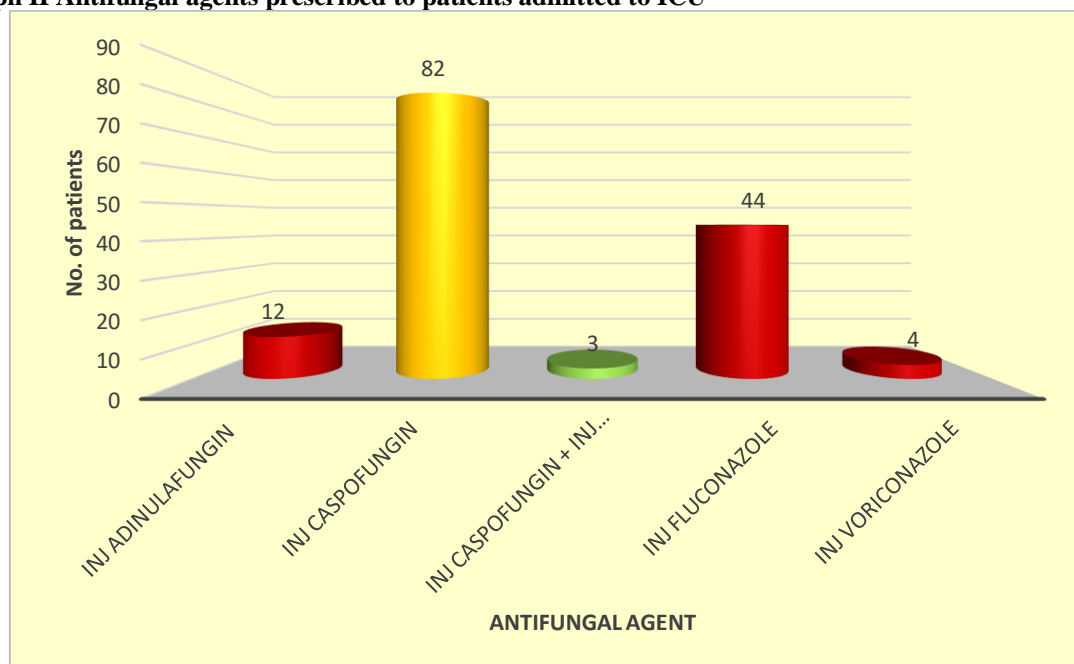
The majority of the patients were prescribed Inj Caspofungin [82(56.55%)], followed by Inj Fluconazole [44(30.34%)], Inj Anidulafungin [12(8.28%)]. Statistically, a significant difference was observed in antifungal agent prescription to patients.

Table-5: Correlation matrix of the different variable with each other

Correlation Matrix Of The Different Variables	Age	Charlson Comorbidity Index	Apache Scoring	Sofa Score	Duration Of Antifungal Prescribed (Days)	Epinephrine Or Norepinephrine Use	Dialysis Or Haemofiltration
Age	1.000						
Charlson comorbidity index	0.110	1.000					
Apache scoring	0.096	**0.393***	1.000				
Sofa score	0.121	**0.257***	**0.485***	1.000			
Duration of antifungal prescribed (days)	0.049	0.364	**0.582***	**0.490***	1.000		
Epinephrine or norepinephrine use	0.168	0.039	0.023	0.159	-0.006	1.000	
Dialysis or haemofiltration	-0.109	0.071	0.208	**0.297***	0.205	0.147	1.000
Parenteral nutrition	0.064	-0.018	0.143	0.061	0.160	**-0.329***	-0.117

After applying spearman correlation matrix of each individual variable with each individual, Charlson comorbidity index, Apache score, Sofa score and duration of antifungal prescription shows a significant positive correlation with each other. In implies that the change in any of the variable does the positive effect on the other variable means if one's variable characteristics related to mortality increases so that other variables characteristics also increases.

DISCUSSION

Triazoles, echinocandins, polyenes, and fluoropyrimidines are the four classes of antifungal agents typically administered systemically to critically ailing patients.[9] They all exhibit clinically significant pharmacokinetic (PK) and pharmacodynamic (PD) alterations in critical states, which may account for decreased drug exposure in critically ill patients and treatment failure.[10] The present study was conducted to assess prescription patterns of systemic antifungal medications in critically ill patients.

We found that the majority of the patients were 12-31 years old [63(43.45%)], followed by 52-71 years old [34(23.45%)], where the mean age was recorded [43.11±20.09] years. Naaz, R et al[11] found that over fifty percent of the patients were between 21 to forty years. More men (51.8%) than women (48%) were present. Sixty-four percent of all recommended medications were topical. The most common fungal infection was tinea corporis. Most antifungal prescriptions were for the Azoles class.

Al-Shayyab et al[12] included 600 Jordanian dentists. The questionnaire collected practitioners' personal information, as well as their attitude toward and prescription of antifungal treatment for oral candidiasis. Only 330 of the 423 questionnaires that were returned were considered. The respondents' attitudes were strongly impacted by their experience (OR = 0.14; P<0.001) and workplace (OR = 4.70; P<0.001). The most often prescribed antifungal agent was Nystatin (78.2%), followed by miconazole (62.4%), which was administered for topical use. The prescribing of systemic antifungals by 21.2% of respondents had a statistically significant (P<0.05) correlation with the country in which they acquired their degree. Private-practice dentists with the least amount of expertise have a significantly more positive outlook on the treatment of oral candidiasis. The most commonly used antifungal agents among Jordanian dentists are nystatin and miconazole.

We found that most of the patients were males [74(51.03%)], followed by females [71(48.97%)]. Out of 160 comorbidities diagnosed, the majority of the patients had no comorbidities [96(60.00%)], followed by patients who had diabetes [22(13.75%)], peptic ulcer disease [11(6.88%)] and so on. The Charlson Comorbidity Index showed that the majority of the patients had mild comorbidities [42(65.63%)], followed by moderate comorbidities [16(25.00%)]. The majority of the patients were referred from trauma [118(83.10%)], followed by referred from department of medicine [8(5.63%)], QMH [7(4.93%)] and so on.

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positive correlation with each other. In implies that the change in any of the variable does the positive effect on the other variable means if one's variable characteristics related to mortality increases so that other variables characteristics also increases.

Björnsdottir, S et al[13] identified 1305 patients with both a diagnosis of AD and treatment with a combination of hydrocortisone/cortisone acetate and fludrocortisone. Overall, Alzheimer's disease (AD) patients in Sweden were prescribed more prescriptions than controls, and 59.3% of AD patients had medications indicating autoimmune illness. Patients used more gastrointestinal medications, anti-anemic preparations, lipid-modifying agents, antibiotics for systemic use, hypnotics and sedatives, and treatments for obstructive airway disease both before and after the diagnosis of AD. Notably, some hypertension medications including high-ceiling diuretics were prescribed more frequently after the diagnosis of AD. The presence of gastrointestinal symptoms and anaemia, particularly when accompanied by autoimmune illnesses, should alert the clinician to the likelihood of AD. The increased usage of cardiovascular medications by AD patients following diagnosis raises questions regarding the efficacy of the replacement therapy.

CONCLUSION

Authors found that Caspofungin was the most often used antifungal medication. The usage of more modern antifungal drugs is also growing. It was observed that most patients in were age group 12-31 years; have systemic antifungal medications, especially in males.

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