Infection and Drug Resistance

Dovepress
open access to scientific and medical research

Open Access Full Text Article

ORIGINAL RESEARCH

Impact of Obesity on Echinocandin Effectiveness in Treating Candida Infections: A Retrospective Observational Cohort Study

Ahmad Aljohani[1,2,*], Saeed Alqahtani[3,*]

[1]Pharmaceutical Care Services, King Fahd General Hospital, Ministry of Health, Jeddah, Saudi Arabia; [2]Department of Pharmacy, College of Pharmacy, Nursing and Medical Sciences, Riyadh Elm University, Riyadh, Saudi Arabia; [3]Department of Clinical Pharmacy, College of Pharmacy, King Saud University, Riyadh, Saudi Arabia

*These authors contributed equally to this work

Correspondence: Saeed Alqahtani, Department of Clinical Pharmacy, College of Pharmacy, King Saud University, P. O. Box2457, Riyadh, Saudi Arabia, Tel +966114677471, Fax +966114677486, Email saeed@ksu.edu.sa

Introduction: Echinocandins are used to treat invasive candidiasis (IC), with FDA-approved doses indicated for both obese and non-obese patients. Pharmacokinetic (PK) studies have identified subtherapeutic exposure in obese patients receiving standard doses (SDs) of echinocandins. However, research on clinical outcome differences of echinocandins' SDs between obese and non-obese patients is lacking. Therefore, this study aimed to evaluate the effectiveness of echinocandins' SDs in obese compared to normal-weight patients with IC.

Patients and Methods: This retrospective cohort study was conducted at King Saud University Medical City (KSUMC) from Jan 2017 to Feb 2023. The study included adult patients diagnosed with *Candida* infections who received ≥ 4 doses of echinocandins. Patients with body mass index (BMI) less than 18 kg/m^2 were excluded from the study. The primary and secondary outcomes included the total length of stay (LOS), IC duration, frequency of clinical resolution and all-cause mortality.

Results: This study included 132 patients (47 obese; 85 non-obese) with a median age of 61 years. The median BMI and weight were different between the obese (34.5 kg/m^2, 88 kg) and non-obese (24 kg/m^2, 65 kg) groups (P= 0.01). Micafungin and caspofungin were used in 63.6% and 36.4% of patients, respectively. The total LOS and length of IC infections were similar between both groups, with median values of 29.5 days (P= 0.896) and 18 days (P = 0.160), respectively. The clinical improvement percentages were 68.1% for obese and 65.9% for non-obese patients (P= 0.797), with all-cause mortality rates at 44.7% and 42.4%, respectively (P= 0.796).

Conclusion: The study found no clinical outcome differences between obese and non-obese patients, with Similar effectiveness of the echinocandins' SDs in both groups. Further research in multi-centre settings is recommended to detect any potential differences between the two groups.

Keywords: echinocandins, *candida*, obesity, effectiveness

Introduction

Fungal infections caused by *Candida* species could lead to invasive infections associated with serious medical complications. These infections are very common in healthcare environments and are considered one of the leading causes of infection-related morbidity and mortality.[1] The cornerstone of the treatment of IC infections is echinocandins including anidulafungin, caspofungin and micafungin.[2] The dosing regimens of echinocandins approved by the FDA are indicated for adult patients as follows: anidulafungin at a 200 mg loading dose followed by a maintenance dose of 100 mg; caspofungin at a 70 mg loading dose, followed by 50 or 70 mg as maintenance; and micafungin 100 or 150 mg without loading dose. These SDs are fixed across all BMI categories, including morbidly obese patients.[3]

Obese patients have unique PK parameters that are characterised by alterations in the volume of distribution (VD) and clearance (CL) compared to normal-weight patients.[4,5] These differences in PK parameters have resulted in several PK

Received: 31 January 2024
Accepted: 20 June 2024
Published: 9 July 2024

studies recommending the dose adjustment of echinocandins in obese patients to achieve the required minimum inhibitory concentration (MIC) and to avoid therapeutic failure.[6–8] Furthermore, there have been few studies investigating the clinical outcome variations between obese and non-obese patients receiving the SDs of echinocandins.[9,10] However, these studies have shown conflicting data regarding the clinical outcomes difference in the effectiveness of SDs of echinocandins in treating *Candida* infections in obese compared to non-obese patients. Therefore, due to the lack of clinical studies in the current literature and conflicting data regarding the effectiveness of SDs of echinocandins in obese patients, our study aims to evaluate the clinical outcomes in obese and non-obese patients who received SDs of one of the echinocandins during treatment for IC.

Materials and Methods

Study Design, Setting, and Patient Population

An observational retrospective cohort study was conducted from the 1st of January 2017 until the 1st of February 2023 at KSUMC. The study was approved by the institutional review board at KSUMC on 14/05/2023 with Ref. No. 23/0325/IRB. The study included hospitalised adult obese and non-obese patients who received more than four consecutive doses of SDs of one of the echinocandin agents mentioned previously. Also, only patients with a confirmed diagnosis of *Candida* infection were included. Diagnosis of *Candida* infection was confirmed by a positive culture of any type of *Candida spp* and clear documentation of diagnosis from an infectious disease physician. The study excluded patients with BMI < 18 Kg/m^2 and those who did not complete the course of the treatment in the hospital. Additionally, Figure 1 shows all the inclusion and exclusion criteria applied during the study period from 2017 – until the 1st of February 2023.

Variables and Definitions

Obese patients were defined as patients with BMI ≥ 30 kg/m^2, based on the definition of the Centers for Disease Control and Prevention (CDC) and World Health Organisation (WHO).[11,12] Demographic and comorbidity variables were collected from the 1st day of admission. Microbiological data, including the type of *Candida spp* and type of *Candida* infections, were collected from the 1st day of confirmed diagnosis. Subsequently, the types of *Candida* infections were classified into candidemia and non-candidemia infections, which included intra-abdominal, abdominal, wound, lung and any IC infections other than candidemia. Treatment data, including the name of the medication and its dose, were collected from the date of initiation.

Outcomes and Definitions

The primary outcomes include the total LOS, the duration of *Candida* infection and the incidence of clinical resolution. We calculated the LOS from the 1st day of echinocandin treatment until the date of discharge, while the duration of *Candida* infection was calculated from the date of diagnosis with *Candida* infection until the last day of echinocandin treatment. In addition, clinical resolution outcomes were determined from a physician's documentation in the patient's medical records, indicating no need for continued or additional antifungal therapy due to clinical resolution. The secondary outcome included all-cause mortality in the hospital.

Data Collection and Analysis

We extracted the data from electronic medical records using the Cerner Millennium System (eSIHI) used in KSUMC. Data were collected in Microsoft Excel sheets and appropriately revised. Revised data were then moved to the Statistical Package for Social Sciences (SPSS) version 26 for statistical analysis. In descriptive statistics, normally distributed variables are presented as the mean and standard deviation (SD), while non-normally distributed data are presented as the median and interquartile range (IQR). Categorical variables are described as frequencies and percentages. Associations between categorical variables were tested using Pearson's Chi-square statistical test. Means of normally distributed scale data between obese and non-obese patients were compared using the independent-samples *t*-test while non-normally distributed continuous data were tested using the Mann–Whitney *U*-test. In addition, logistic regression and multivariate

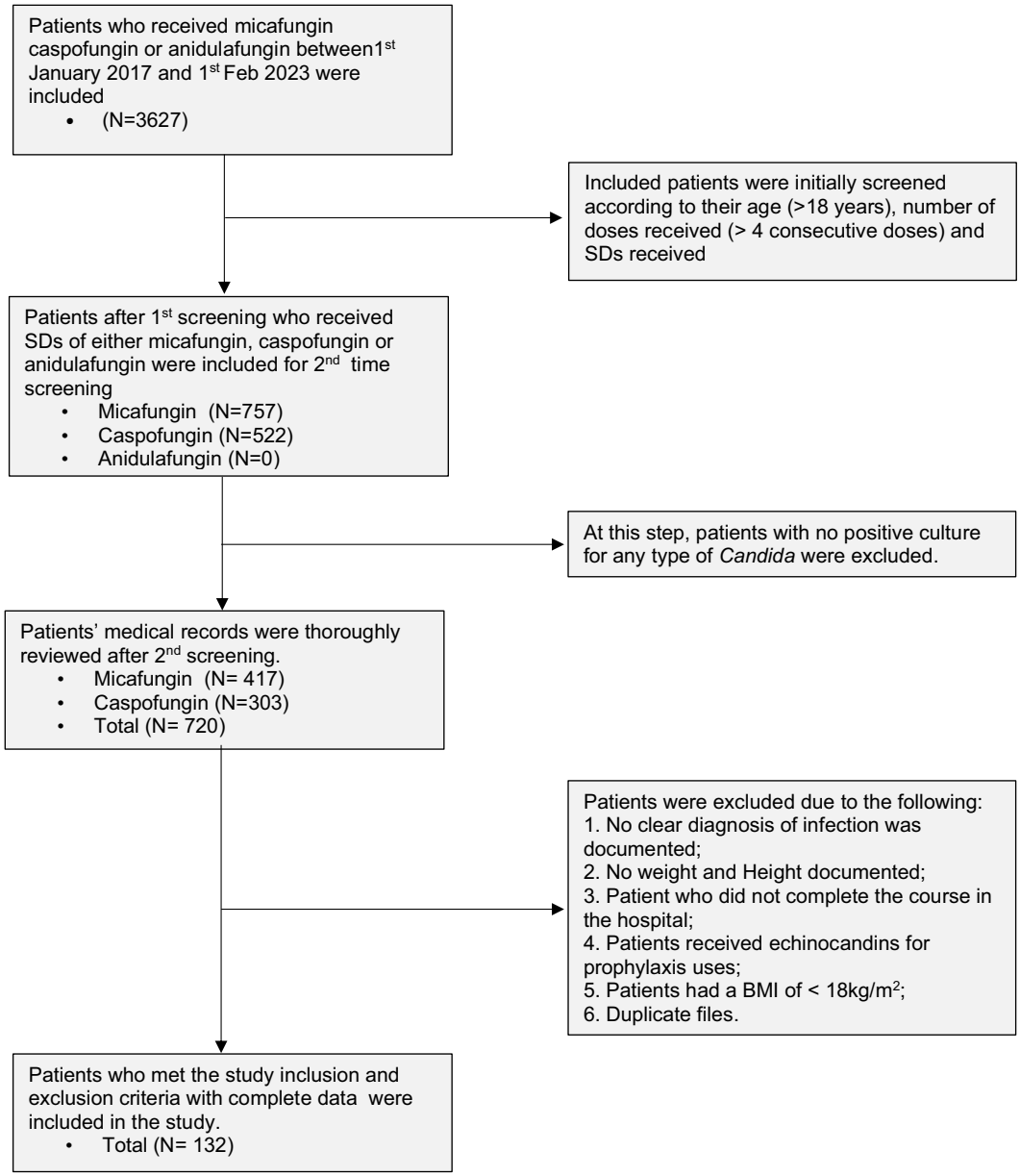

Figure 1 The patient inclusion process.

analysis were used for primary outcomes, with adjustments made for potential confounders. A P value less than 0.05 was considered to indicate statistical significance.

Results

After screening the medical records by applying the inclusion and exclusion criteria (as shown in Figure 1), we included 132 patients for the final analysis 47 obese and 85 non-obese. The patient characteristics are presented in Table 1. The median age was 61 (IQR 45–68) with no significant difference between the obese and non-obese groups (P= 0.4). There were differences in weight, height and BMI between the groups (P< 0.05). The median BMI was 34.5 (IQR 32–37.40) kg/m^2 for obese patients and 24 (IQR 21.90–26.50) kg/m^2 for non-obese patients. In total, 67 (50.8%) of the included patients were male and 65 (49.2%) were female. Male patients were more frequent in the non-obese group (50 (58.8%)) compared with the obese patients group (17 (36.2%)).

Table 1 Basic Characteristics of All Patients with Candida Infections Treated with the SDs of Echinocandins

Baseline Characteristics		Total	Obese	Non-Obese	P value
		132	47	85	
Age (Years, Median (IQR))		61 (45–68)	62 (46–69)	60 (43.5–67)	0.411
BMI [Kg/m^2, Median (IQR)]		27 (22.5–32.5)	34.5 (32–37.4)	24 (21.9–26.5)	0.001[a]
Weight [Kg, Median (IQR)]		71.5 (62–84)	88 (80–102)	65 (58–71)	0.001[a]
Height [cm, Median (IQR)]		162.5 (155–168)	159 (153–166)	165 (157–169)	0.016[a]
Gender	Male	67 (50.8%)	17 (36.2%)	50 (58.8%)	0.0124[a]
	Female	65 (49.2%)	30 (63.8%)	35 (41.2%)	0.0124[a]
Co-morbidities	Diabetes	64 (48.5%)	27 (57.4%)	37 (43.5%)	0.126
	Cardiovascular	71 (53.8%)	27 (57.4%)	44 (51.8%)	0.531
	ICU Admission	66 (50%)	25 (53.2%)	41 (48.2%)	0.586
	Major surgery	56 (42.4%)	21 (44.7%)	35 (41.2%)	0.696
	Immunocompromised	51 (38.6%)	11 (23.4%)	40 (47.1%)	0.008[a]
	Malignancy	47 (35.6%)	11 (23.4%)	36 (42.4%)	0.029[a]
Medication	Caspofungin	48 (36.4%)	14 (29.8%)	34 (40%)	0.243
	Micafungin	84 (63.6%)	33 (70.2%)	51 (60%)	
Type of infection	Candidemia	71 (53.8%)	27 (57.4%)	44 (51.8%)	0.531
	Non-Candidemia	61 (46.2%)	20 (42.6%)	41 (48.2%)	
Type of *Candida*	*C. albicans*	45 (34.1%)	12 (25.5%)	33 (38.8%)	0.413
	C. glabrata	41 (31.1%)	16 (34%)	25 (29.4%)	
	C. tropicalis	15 (11.4%)	4 (8.5%)	11 (12.9%)	
	C. parapsilosis	8 (6.1%)	4 (8.5%)	4 (4.7%)	
	C. krusei	16 (12.1%)	7 (14.9%)	9 (10.6%)	
	C. dubliniensis	7 (5.3%)	4 (8.5%)	3 (3.5%)	

Notes: [a]P value less than 0.05 indicates a statistically significant difference; Data presented as the frequency (%) or median (IQR).

Additionally, the comorbidity frequency was comparable between the groups, except that immunocompromised and malignant patients were noted more frequently in the non-obese patient group. The type of *Candida* infections (candidemia vs non-candidemia) did not show a statistically significant difference between the two groups, with *C. albicans and C. glabrata* being the most common causes of these infections. In total, 63.3% of patients were treated with SDs of micafungin, while 36.4% were treated with caspofungin. The treatment selection was found to be similar for both obese and non-obese patients.

The median length of *Candida* infections in both obese and non-obese patients was 20 days (IQR 16.25–28.5) and 17 days (IQR 14–30), respectively; with no statistically significant difference between the two groups (P= 0.160). In addition, the median LOS duration was found for obese (29.5 days (IQR 19.25–57.5)) and for non-obese (29.5 days (IQR 18.5–42.25)) patients with no significant differences between the groups (P= 0.896). Clinical improvements among obese and non-obese patients were noted in 32 cases (68.1%) and 56 cases (65.9%) respectively with no significant differences between the two groups (P= 0.797). In addition, the all-cause mortality rates among obese and non-obese patients with *Candida* infections were 21 (44.7%) and 36 (42.4%), respectively, with a P value of 0.796 (see Table 2).

A subgroup analysis was conducted on patients based on the type of infection: either candidemia or non-candidemia infections. In patients with candidemia (a total of 71 patients; 27 obese and 44 non-obese), no significant difference was observed in the primary and secondary outcomes between the two groups (P> 0.05). In addition, the primary and secondary outcomes presented no significant differences in the groups diagnosed with non-candidemia infections with a P value of > 0.05. (see Table 3). Furthermore, as shown in Table 4, the predictive impact of obesity status on the duration of infection and LOS in patients with invasive *Candida* infections treated with SDs of caspofungin and micafungin was non-statistically significant. This finding was derived from multivariate linear regression analyses that controlled for age, gender, comorbidities, and the type of echinocandin used. Additionally, logistic regression analyses indicated that obesity status did not a have statistically significant impact on clinical improvement in these patients, even after adjusting for the same potential confounders (see Table 4).

Discussion

In recent years, the rate of obesity has increased significantly, leading clinicians to encounter more obese patients with various serious illnesses. Unfortunately, clinical studies or data on dosing regimens in obese patients for various medications are often limited or absent. This can make it challenging for clinicians to ensure that obese patients receive appropriate therapeutic dose regimens, particularly for serious illnesses, such as IC, including candidemia.[13]

Several PK studies have shown lower exposure to the SDs of echinocandins in obese compared to normal-weight patients, recommending dose adjustment to achieve the required PK/PD targets.[7,8,14–16]

Conversely, some studies have found no significant variations in echinocandin exposure in obese compared to normal-weight patients, leading to no dose adjustment recommendations.[17,18] Due to conflicting findings and the limited

Table 2 Clinical Outcomes of Obese and Non-Obese Patients with IC Infections Including Candidemia and Non-Candidemia Infections

Clinical Outcomes	Total 132	Obese 47	Non-Obese 85	P Value	Effect Size	Risk Estimate (95% CI)
Length of infection (days)	18 (15–29.75)	20 (16.3–28.5)	17 (14–30)	0.160	0.0006	
LOS (days)	29.5 (19.5–43.2)	29.5 (19.2–57.5)	29.5 (18.5–42.25)	0.896	0.0026	
Clinical improvement	88 (66.7%)	32 (68.1%)	56 (65.9%)	0.797	0.022	0.9 (0.4–1.9)
All-cause mortality	57 (43.2%)	21 (44.7%)	36 (42.4%)	0.796	0.023	0.9 (0.5–1.9)

Notes: Data presented as the frequency (%) or median (IQR).
Abbreviation: CI, Confidence Interval.

Table 3 Clinical Outcomes of Obese and Non-Obese Patients with Candidemia and Non-Candidemia Infections

Candidemia patients						
Clinical Outcomes	**Total**	**Obese**	**Non-Obese**	**P Value**	**Effect Size**	**Risk Estimate (95% CI)**
	71	**27**	**44**			
Length of infection (days)	18 (15–23)	19 (16.5–28.5)	17 (15–20.25)	0.226	0.000072	
LOS (days)	28 (20–44)	28.5 (17.75–59.5)	28 (20–44)	0.889	0.0016	
Clinical improvement	43 (60.6%)	17 (63%)	26 (59.1%)	0.746	0.038	0.85 (0.32–2.3)
All-cause mortality	40 (56.3%)	15 (55.6%)	25 (56.8%)	0.917	0.012	1.1 (0.4–2.8)
Non-candidemia patients						
	Total	**Obese**	**Non-obese**			
	61	20	41			
Length of infection (days)	20 (14–33.5)	20 (16–40)	18 (14–33.25)	0.392	0.00083	
LOS (days)	31 (18–41)	31.5 (19.25–57.5)	31 (17.50–39)	0.825	0.0043	
Clinical improvement	45 (73.8%)	15 (75%)	30 (73.2%)	0.879	0.020	0.91 (0.27–3.1)
All-cause mortality	17 (27.9%)	6 (30%)	11 (26.8%)	0.795	0.033	0.86 (0.3–2.8)

Notes: Data presented as the frequency (%) or median (IQR).
Abbreviation: CI, Confidence Interval.

Table 4 Regression Analysis of Primary Outcomes with Controlling Potential Confounders

Multivariate Regression Analysis				
Clinical Outcomes	**R Square**	**P Value (R Square)**	**Unstandardized Coefficient B**	**P Value (95% CI (B))**
LOS (days)	0.052	0.744	− 0.484	0.831 (- 4.99–4.02)
Length of infection (days)	0.085	0.440	2.273	0.727 (−10.7–15.22)
Logistic regression analysis				
Clinical outcomes	**COR(95% CI)**	**P value for COR**	**AOR(95% CI)**	**P valuefor AOR**
Clinical improvement rate	1.177 (0.439–3.153)	0.746	3.023 (0.746 −12.257)	0.121

Abbreviations: COR, Crude odd ratio; AOR, Adjusted odd ratio; CI = confidence interval.

research evaluating the variations in clinical outcomes between obese and normal-weight patients treated for IC using SDs of echinocandins, our study was conducted to identify any potential differences in the clinical outcomes between these two groups when treated with the SDs of one of the echinocandins.

Our study found no significant differences in clinical outcomes between obese and non-obese patients treated with SDs of caspofungin or micafungin for IC, including candidemia and non-candidemia infections. Primary and secondary outcomes showed no significant differences, aligning with Results from other studies.

In our findings, all-cause mortality rates were not significantly different between obese and non-obese patients with candidemia. Similar results were noted by Hutton et al (2022) in their study on SDs of anidulafungin, where no significant difference was found in the 30-day all-cause mortality among BMI categories (P= 0.976). Additionally, Barber et al (2020) conducted a study that found no differences in hospital mortality between obese and non-obese groups with candidemia receiving the SDs of micafungin (P= 0.36).

In addition, Hutton et al (2022) found no significant differences in the clinical response across BMI categories in patients who received SDs of anidulafungin to treat candidemia. These results are in accordance with our findings, which showed no difference in the clinical improvement outcomes between obese and non-obese patients with candidemia infections (P= 085). Furthermore, a post hoc analysis of nine clinical trials on caspofungin's SDs regimen showed similar clinical success rates (71% to 77%) across BMI categories.[13] Our study also observed similar clinical improvement percentages among our included both obese and non-obese patients (60%, 66.6% and 73% in patients with candidemia, IC, and non-candidemia infections, respectively). Notably, these results, showing the effectiveness of SDs of echinocandins across various BMI categories, support other findings that showed successful treatment in a critically ill obese patient (BMI >40 kg/m²) treated with SDs of micafungin for a urinary tract infection, despite the lower serum drug concentration noted in this patient.[19]

Moreover, our study found a total median LOS of 29 days for IC patients, consistent with a similar study on obese patients with IC treated with a high dose of micafungin (around 300 mg daily, median BMI 37 kg/m²) in which the median LOS was 27 days.[20] Despite the high dose used in this study, the duration of total LOS is comparable with our findings for IC patients treated with SDs of either micafungin or caspofungin.

However, a study conducted in 2020 to evaluate the impact of obesity on candidemia patients treated with micafungin, fluconazole and posaconazole, found that the obese group had a longer infection-related LOS by 7 days compared to the non-obese group.[10] In contrast, our study found no significant difference in the total hospital LOS between the two groups (P= 0.889). This difference in LOS between our study and that of Barber et al (2020) could be due to differences in the study population; our study included only those treated with the SDs of echinocandins, while theirs included patients treated with micafungin, representing 73% of the total patients, with the others receiving either fluconazole or posaconazole.

Additionally, Barber et al (2020), found a significant difference in the median duration of candidemia resolution between obese and non-obese groups (P= 0.02), whereas our study showed no significant difference (P= 0.226). However, this variation in results may be attributed to differences in how the resolution duration was calculated; Barber et al (2020) counted from the first positive to the first negative culture, while we calculated from the first confirmed diagnosis day until the discontinuation of medication due to clinical resolution.

Moreover, our study identified *C. albicans and C. glabrata* as the most prevalent *Candida* types causing IC, including both candidemia and non-candidemia infections. This aligns with findings from other epidemiological studies, showing that these two *Candida* pathogens are commonly associated with most IC infections.[21–23]

Nevertheless, retrospective studies are susceptible to selection bias and confounder effects. In this study, efforts to mitigate bias included strict adherence to inclusion and exclusion criteria for both obese and non-obese patients, consistent application of clear outcomes and variable definitions for both groups and ensuring comparable data between the two groups. However, no study is without limitations, and our study has some that should be taken into account. Firstly, the weight distribution among the obese patients included in our study may not represent the broader obese population due to the limited range of obese and morbidly obese patients included in our study. Thus, further studies to include large numbers of patients with high and extremely high weights are required. Secondly, the retrospective single-centre design may have limited the sample size and, therefore, the generalisability of the results. To overcome such limitations, future studies should be conducted in multicentre settings in order to generate a more representative sample and more generalisable results.

Conclusion

This research study examined the relationship between obesity and the effectiveness of SDs of echinocandins in treating IC. No significant differences were found in clinical outcomes between the obese and non-obese patients, indicating that factors such as BMI and its related PK variations may not significantly affect the therapeutic efficacy of echinocandins in particular caspofungin and micafungin. However, further research is required to investigate the clinical outcomes of SDs of echinocandins in obese patients to ensure safe pharmacotherapy.

Abbreviations

IC, Invasive candidiasis; FDA, U.S Food and Drug Administration; PK, Pharmacokinetic; SDs, Standard doses; BMI, Body Mass Index; LOS, Length of Stay; VD, Volume of Distribution; CL, Clearance; MIC, Minimum Inhibitory Concentration; CDC, Centers for Disease Control and Prevention; WHO, World Health Organisation; SD, Standard Deviation; IQR, Interquartile Range; PD, Pharmacodynamics.

Data Sharing Statement

The datasets utilised and analysed in this study are available from the corresponding author upon reasonable request.

Ethics Statement

This study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the Institutional Review Board at KSUMC on 14/05/2023 with Ref. No. 23/0325/IRB. The informed consent of this study was waived by the Institutional Review Board at KSUMC. However, all patient data was confidentially maintained and kept anonymous.

Acknowledgments

The authors extend their appreciation to the Researchers Supporting Project (Number: RSP2024R2), King Saud University, Riyadh, Saudi Arabia.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Disclosure

The authors declare that they have no conflicts of interest related to this work.

References

1. McCarty TP, White CM, Pappas PG. Candidemia and invasive candidiasis. *Infect Dis Clin North Am*. 2021;35(2):389–413. doi:10.1016/j.idc.2021.03.007
2. Pappas PG, Kauffman CA, Andes DR, et al. Clinical practice guideline for the management of candidiasis: 2016 update by the infectious diseases society of America. *Clinl Infect Dis*. 2016;62(4):e1–50. doi:10.1093/cid/civ933
3. Liu X, Liu D, Pan Y, Li Y. Pharmacokinetic/pharmacodynamics variability of echinocandins in critically ill patients: a systematic review and meta-analysis. *J Clin Pharm Therapeutics*. 2020;45(6):1207–1217. doi:10.1111/jcpt.13211
4. Meng L, Mui E, Holubar MK, Deresinski SC. Comprehensive guidance for antibiotic dosing in obese adults. *Pharmacotherapy*. 2017;37(11):1415–1431. doi:10.1002/phar.2023
5. Barras M, Legg A. Drug dosing in obese adults. *Austr Prescr*. 2017;40(5):189–193. doi:10.18773/austprescr.2017.053
6. Lempers VJC, Rongen A, Dongen EPV, et al. Does weight impact anidulafungin pharmacokinetics? *Clin. Pharmacokinet.* 2016;55(10):1289–1294. doi:10.1007/s40262-016-0401-8
7. Yang Q, Zhang T, Zhang Y, et al. The recommended dosage regimen for caspofungin in patients with higher body weight or hypoalbuminaemia will result in low exposure: 5 years of data based on a population pharmacokinetic model and Monte-Carlo simulations. *Front Pharmacol*. 2022;13(3):4601. doi:10.3389/fphar.2022.993330

8. Wasmann RE, Smit C, Ter Heine R, et al. Pharmacokinetics and probability of target attainment for micafungin in normal-weight and morbidly obese adults. *J Antimicrob Chemother*. 2019;74(4):978–985. doi:10.1093/jac/dky554
9. Hutton M, Kenney RM, Vazquez JA, Davis SL. Influence of body weight category on outcomes in candidemia patients treated with anidulafungin. *J Pharm Pract*. 2022;35(1):20–25. doi:10.1177/0897190020938219
10. Barber KE, Wagner JL, Miller JM, Lewis EA, Stover KR. Impact of obesity in patients with candida bloodstream infections: a retrospective cohort study. *Infect Dis Ther*. 2020;9(1):175–183. doi:10.1007/s40121-020-00285-7
11. Centers For Disease Control and Prevention [homepage on the Internet]. Atalanta: About Adult BMI; 2022. Available from: https://www.cdc.gov/healthyweight/assessing/bmi/adult_bmi/index.html. Accessed August 11, 2023.
12. World Health Organisation. *The WHO acceleration plan to stop obesity*. 2023 July: 1–20. Available from: https://www.who.int/publications/i/item/97892400756343/07/2023. Accessed August 11, 2023.
13. Ryan DM, Lupinacci RJ, Kartsonis NA. Efficacy and safety of caspofungin in obese patients. *Med Mycol*. 2011;49(7):748–754. doi:10.3109/13693786.2011.571293
14. Muilwijk EW, Schouten JA, van Leeuwen HJ, et al. Pharmacokinetics of caspofungin in ICU patients. *J Antimicrob Chemother*. 2014;69(12):3294–3299. doi:10.1093/jac/dku313
15. Märtson AG, van der Elst KCM, Veringa A, et al. Caspofungin weight-based dosing supported by a population pharmacokinetic model in critically Ill patients. *Antimicrob. Agents Chemother.* 2020;64(9):e00905–20. doi:10.1128/AAC.00905-20
16. Wasmann RE, Ter Heine R, van Dongen EP, et al. Pharmacokinetics of anidulafungin in obese and normal-weight adults. *Antimicrob. Agents Chemother.* 2018;62(7):e00063–18. doi:10.1128/AAC.00063-18
17. Maseda E, Grau S, Luque S, et al. Population pharmacokinetics/pharmacodynamics of micafungin against Candida species in obese, critically ill, and morbidly obese critically ill patients. *Critical Care*. 2018;22(1):1–9. doi:10.1186/s13054-018-2019-8
18. Lempers VJ, Schouten JA, Hunfeld NG, et al. Altered micafungin pharmacokinetics in intensive care unit patients. *Antimicrob. Agents Chemother.* 2015;59(8):4403–4409. doi:10.1128/aac.00623-15
19. Zomp A, Bookstaver PB, Ahmed Y, Turner JE, King C. Micafungin therapy in a critically ill, morbidly obese patient. *J Antimicrob Chemother*. 2011;66(11):2678–2680. doi:10.1093/jac/dkr323
20. Grant VC, Nguyen K, Rodriguez S, Zhou AY, Abdul-Mutakabbir JC, Tan KK. Characterizing safety and clinical outcomes associated with high-dose micafungin utilization in patients with proven invasive candidiasis. *Trop Med Infect Dis*. 2022;7(2):23. doi:10.3390/tropicalmed7020023
21. Tukenmez Tigen E, Bilgin H, Perk Gurun H, et al. Risk factors, characteristics, and outcomes of candidemia in an adult intensive care unit in Turkey. *Am J Infect Control*. 2017;45(6):e61–e63. doi:10.1016/j.ajic.2017.02.022
22. Cretella D, Barber KE, King ST, Stover KR. Comparison of susceptibility patterns using commercially available susceptibility testing methods performed on prevalent Candida spp. *J Med Microbiol*. 2016;65(12):1445–1451. doi:10.1099/jmm.0.000383
23. Pfaller MA, Andes DR, Diekema DJ, et al. Epidemiology and outcomes of invasive candidiasis due to non-albicans species of candida in 2496 patients: data from the prospective antifungal therapy (PATH) registry 2004-2008. *PLoS One*. 2014;9(7):e101510. doi:10.1371/journal.pone.0101510