Jornal de Assistência Farmacêutica e Farmacoeconomia
v.11, n.1, 2026.
Original Article

Anidulafungin Usage Profile and its Economic Impact: A Practical Assessment

Perfil de uso de anidulafungina e seu impacto econômico: uma avaliação prática

Bruna Brazeiro Brum[1]; Sandrine Comparsi Wagner[2]; Riciéli Pacheco Crestani[3]; Helena Schirmer[4]

[1] Intensive Care Attention Program - Universidade Federal de Ciências da Saúde de Porto Alegre; Porto Alegre, Rio Grande do Sul, Brasil.
[2] Department of Diagnostic Methods - Universidade Federal de Ciências da Saúde de Porto Alegre; Porto Alegre, Rio Grande do Sul, Brasil.
[3] Pharmacy Service - Santa Casa Brotherhood Porto Alegre; Porto Alegre, Rio Grande do Sul, Brasil.
[4] Department of Basic Health Sciences - Universidade Federal de Ciências da Saúde de Porto Alegre; Porto Alegre, Rio Grande do Sul, Brasil.

Corresponding Author:
Bruna Brazeiro Brum; Intensive Care Attention Program - Universidade Federal de Ciências da Saúde de Porto Alegre; Porto Alegre, Rio Grande do Sul, Brasil.
Email: brunabrazeiro@gmail.com

How to cite:
Brum, BB; Wagner, SC; Schirmer, H; Crestani, RP. Perfil de uso de anidulafungina e seu impacto econômico: uma avaliação prática. JAFF [Internet];11(1). Available from: https://ojs.jaff.org.br/

Received in: 04/04/2025

Accepted for publication on: 11/26/2025

ABSTRACT

Introduction: Candidemia is a systemic fungal infection associated with healthcare, related to high mortality rates, prolonged hospitalization, and increased healthcare system costs. Therapeutic recommendations include initiating treatment with echinocandins, performing blood cultures, and, for azole-susceptible isolates such as *Candida albicans*, therapy with fluconazole. Strategies involving antifungal de-escalation are important for therapeutic optimization, aiming to reduce fungal resistance, promote patient safety, and apply the concept of pharmacoeconomics within healthcare institutions. **Objective:** To characterize the profile of anidulafungin use in Intensive Care Units (ICUs) and to estimate the resource savings generated by its de-escalation. **Methods:** Descriptive retrospective study including adult patients admitted to ICUs, from the Brazilian Unified Health System (SUS), who received anidulafungin prescriptions. **Results:** A total of 106 patients were analyzed, of whom only 21 (20.4%) had mycological diagnosis, with *Candida albicans* being the most frequent isolate (47.6%). De-escalation was performed in 6 patients (28.6%), resulting in savings of R$12,378.29. It is estimated that this amount could have increased by R$5,412.84 if de-escalation had been applied in all cases with indication. **Conclusions:** The de-escalation strategy demonstrated potential to optimize therapy based on mycological diagnosis, reduce institutional costs, and contribute to the rational use of antifungals, avoiding unnecessary exposure to broad-spectrum agents.
Keywords: Anidulafungin; Pharmacoeconomics; Antimicrobial Stewardship.

RESUMO

Introdução: A candidemia é uma infecção fúngica sistêmica, associada à assistência à saúde, relacionando-se à alta taxa de mortalidade, prolongamento no tempo de hospitalização e aumento nos custos do sistema de saúde. A recomendação terapêutica inclui início de tratamento com fármacos da classe das equinocandinas, realização de hemoculturas, e para isolados suscetíveis a azóis, como *Candida albicans*, terapia com fluconazol. Estratégias envolvendo ações de descalonamento antifúngico, são importantes na otimização terapêutica, visando reduzir a resistência fúngica, promover segurança ao paciente e aplicar o conceito de farmacoeconomia para a instituição. **Objetivo:** Caracterizar o perfil de uso de anidulafungina em Unidades de Terapia Intensiva (UTIs) e estimar a economia de recursos gerada pelo descalonamento deste antifúngico. **Métodos:** Estudo descritivo retrospectivo que incluiu pacientes adultos internados em UTIs, provenientes do Sistema Único de Saúde (SUS), com prescrição de anidulafungina. **Resultados:** Foram analisados 106 pacientes, dos quais apenas 21 (20,4%) apresentaram diagnóstico micológico, sendo *Candida albicans* o isolado mais frequente (47,6%). O descalonamento foi realizado em 6 pacientes (28,6%), resultando em uma economia de R$12.378,29. Estima-se que esse valor poderia ser acrescido em R$5.412,84 caso o descalonamento tivesse sido aplicado em todos os casos com indicação. **Conclusões:** A estratégia de descalonamento demonstrou potencial para otimizar a terapêutica baseada no diagnóstico micológico, reduzir os custos institucionais e contribuir para o uso racional de antifúngicos, evitando a exposição desnecessária a agentes de amplo espectro.
Palavras-chave: Anidulafungina; Farmacoeconomia; Gestão de Antimicrobianos.

Introduction

Candidemia results from hematogenous dissemination and/or establishment of the yeast in deep tissues, and is associated with a high mortality rate, prolonged length of hospital stay and, consequently, increased healthcare costs.[12] Immunocompromised patients, such as those with hematologic malignancies, transplant recipients and individuals admitted to intensive care units (ICUs), constitute risk groups for invasive fungal infections.[1] Mortality related to this infection ranges from 30 to 60%, and the time to disease manifestation is variable, occurring more frequently between 10 and 50 days after hospital admission.[3] Risk factors for candidemia include diabetes mellitus, abdominal surgery, prior use of broad-spectrum antibiotics, use of central venous catheters, immunosuppression, prophylactic antifungal therapy, as well as hematologic patients.[45]

More than 17 *Candida* species have been described as causative agents of candidemia in humans. However, the majority of cases are attributed to a few predominant species such as *C. albicans*, *Nakaseomyces glabratus* (*C. glabrata*), *C. tropicalis*, *C. parapsilosis*, *Pichia kudriavzevii* (*C. krusei*) and *C. auris*.[6] Candidemia presents multiple clinical challenges, among which are delayed initiation of treatment due to difficulties in establishing early diagnosis, rapid clinical deterioration of patients, the risk of developing antifungal resistance and the emergence of multidrug-resistant species, such as *Candida auris*.[7]

Currently, three classes of antifungal agents are available for the treatment of candidemia, namely polyenes (amphotericin B), azoles (fluconazole and voriconazole) and echinocandins (anidulafungin, micafungin and caspofungin). Until the mid-2000s, fluconazole was the first-line therapeutic option.[8,9] Due to the increasing incidence of non-*albicans* isolates and resistance to this antifungal agent, the Infectious Diseases Society of America (IDSA) and the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) began to recommend echinocandins as first-line therapy for the initial management of candidemia, with subsequent transition to fluconazole 200 to 400 mg in non-neutropenic patients who are clinically stable and have isolates susceptible to this antifungal agent, such as *C. albicans*. In cases of infection caused by *N. glabratus* (*C. glabrata*), de-escalation with higher doses of fluconazole 800 mg per day or voriconazole 200 to 300 mg twice daily is recommended. In infections caused by *P. kudriavzevii* (*C. krusei*), the use of voriconazole is recommended for sequential oral therapy. The recommendation for the use of amphotericin B applies to cases involving isolates resistant to the previously mentioned classes. Treatment duration is two weeks when patients present with negative blood cultures and clinical stability.[10]

It is important to highlight the possibility of acquiring resistance to echinocandins during therapy, as well as reports of cross-resistance to azoles in isolates of *N. glabratus* (*C. glabrata*). Consequently, the indiscriminate use of echinocandins as empirical therapy and azoles, for prophylaxis has led to epidemiological changes, with an increase in multidrug-resistant strains of *N. glabratus* (*C. glabrata*).[11]

The term de-escalation emerged in the 1990s within the context of antimicrobial stewardship strategies , in studies aimed at reducing the indiscriminate use of broad-spectrum antimicrobial agents.[12] Subsequently, the concept was expanded to the practice of antifungal stewardship strategies, which aim to optimize the use of these agents, primarily through the selection of the most appropriate therapeutic regimen.[13,14] One of the main approaches is antifungal therapy de-escalation, which consists of replacing a broad-spectrum agent with another agent with a narrower spectrum, lower toxicity and reduced cost, based on pathogen identification and its susceptibility profile.[15] As a positive example of de-escalation practice, de-escalation from an echinocandin to agents of the azole class is highlighted when a susceptible isolate is identified. This strategy reduces costs, minimizes toxicity and exposure to broad-spectrum agents and maintains

similar clinical outcomes in terms of mortality when compared with continuous echinocandin therapy.[15,16] Conversely, among negative examples, therapeutic failure resulting from premature de-escalation prior to diagnostic confirmation is noteworthy, leading to persistent candidemia and resulting in fatal outcomes.[17] Another relevant risk is increased mortality in patients with hemodynamic instability if the substitution reduces antifungal coverage.[18] Therefore, de-escalation should be performed cautiously, based on reliable mycological diagnosis, guided by institutional protocols and associated with careful clinical assessment.[19]

In addition to preserving therapeutic effectiveness, the de-escalation strategy reduces unnecessary exposure to broader-spectrum antifungal agents, minimizes the risk of resistance development and contributes to the optimization of institutional resources.[20] In a study conducted in 2018, Jaffal et al. evaluated patients in intensive care units and observed that de-escalation occurred in only 20% of cases of candidemia initially treated with broad-spectrum antifungal agents. In these patients, treatment duration was shorter when narrower-spectrum agents were used; however, there was no significant difference in intensive care unit length of stay or one-year mortality, demonstrating the safety of this strategy in critically ill patients.[21]

Antifungal therapy stewardship strategies involving de-escalation from anidulafungin to fluconazole in candidemia have proven to be an effective monitoring measure. In addition, this approach promotes patient safety by reducing the indiscriminate use of antimicrobial agents and contributes to the promotion of econom.[22] The aim of this study was to characterize the profile of anidulafungin use in intensive care units and to estimate the resource savings generated by the de-escalation of this antifungal agent.

Methods

This is a descriptive and retrospective prevalence study, in which the profile of patients receiving anidulafungin in the year 2023 was characterized among those admitted to intensive care units of a philanthropic hospital complex in southern Brazil, originating from the Unified Health System (SUS). Adult patients admitted to intensive care units, covered by the SUS and with prescriptions for anidulafungin were included. Patients with prescriptions for anidulafungin for prophylactic use, as reported in medical records, such as neutropenic patients, were excluded.

Data collection was performed using the institutional Tasy® system. To characterize the antifungal use profile and determine study eligibility, the following data were obtained from medical records: sex, age, use of central venous access devices, use of antimicrobial agents and their prescribed classes, use of vasoactive drugs, primary disease and comorbidities, clinical outcome and mycological diagnosis with identification of the causative agent at the genus and species levels.

For the assessment of cost savings, the identified *Candida* spp. species and the indication for de-escalation in accordance with the Infectious Diseases Society of America (IDSA) recommendations for the management of candidemia[10] were taken into consideration. For cost calculations, the number of days of fluconazole use was considered. In cases in which de-escalation of antifungal therapy was recommended but not performed, the potential economy benefit was estimated based on switching to fluconazole from the fifth day of treatment, in accordance with IDSA recommendations[10].

The results were expressed in terms of frequency, median, and interquartile range. The costs of medications and supplies required for drug administration are described as mean values (Table 1), considering values from June 2024, according to data provided by the hospital complex.

The study was approved by the Research Ethics Committee of Irmandade Santa Casa de Porto Alegre (ISCPA), Opinion No. 6,837,180, in accordance with the guidelines and regulatory standards for research involving human beings (Resolution No. 466/2012) and the Brazilian General Data Protection Law (LGPD No. 13,709/2018).

Table 1. Mean cost of medications and supplies used in June 2024.

Medications and supplies	Mean cost per unit (R$)
Fluconazole injectable solution, bag 2 mg/mL, 100 mL	7,67
Fluconazole hard gelatin capsule 150 mg	1,15
Anidulafungin lyophilized powder for injection 100 mg	146,94
Disposable syringe 20 mL	1,16
Disposable needle	0,13
Water for injection 10 mL	0,23
Prefilled syringe of sodium chloride 0.9% 10 mL	2,06
Sodium chloride injectable solution 0.9%, bag 100 mL	3,31
Sodium chloride injectable solution 0.9%, bag 250 mL	3,83

Source: Prepared by the author.

Results

A total of 163 adult patients admitted to the ICU who received a prescription for anidulafungin in 2023 were analyzed. Of these, 106 (65%) were patients from the Brazilian Unified Health System (SUS) and met the inclusion criteria. A total of 57 patients were excluded from the study for not being treated under the SUS and/or for having an anidulafungin prescription for prophylactic use.

Information regarding the sample, such as sex, median age, most prevalent comorbidities, and antimicrobial use, is described in Table 2.

Approximately 80 different comorbidities were identified, such as ischemic stroke, hypothyroidism, dyslipidemia, and neoplasms. Regarding patient age, the median was 63.5 years, with an interquartile range of 22. Of the 106 patients included in the study, only 2 (1.9%) were not receiving antimicrobial therapy at the time of anidulafungin prescription. With respect to mycological diagnosis, among the 106 patients included, culture was not requested in only 3 (2.8%). Of the remaining 103 (97.2%) patients, *Candida* spp. growth was identified in at least one biological sample in 21 (20.4%) cases (Table 3), which were considered for the economy analysis.

Table 2. Profile of patients admitted to ICUs with anidulafungin prescription in 2023.

Characteristic	N	Frequency (%))
Sex		
Male	68	64,1
Female	38	35,9
Median age (years)	63,5	
Interquartile range (years)	22	
Use of central venous access devices	103	97,2
Immunosuppression	61	57,5
Use of vasoactive drugs	61	57,5
Mycological examination	103	97,2
Positive culture for *Candida* spp.	21	20,4
Deaths	67	63,2
Comorbidities[a]	241	
Systemic arterial hypertension	25	23,6
Type 2 diabetes mellitus	19	17,9
Cirrhosis	19	17,9
Liver transplantation	15	14,1
Chronic kidney disease	10	9,4
Chronic obstructive pulmonary disease	7	6,6
Antimicrobials		
Use of antimicrobials	104	98,1
Most frequently prescribed combination: meropenem and vancomycin	30	28,8

[a]The most frequent comorbidities are presented.
Source: Prepared by the author.

Table 3. *Candida* species isolated from ICU patients with anidulafungin prescription in 2023.

Species	N	Frequency (%)
C. albicans	10	47,6
C. tropicalis	3	14,3
C. orthopsilosis	2	9,5
C. parapsilosis	2	9,5
P. kudriavzevii (C. krusei)	2	9,5
C. dubliniensis	1	4,8
N. glabratus (C. glabrata)	1	4,8
Total	21	100

Source: Prepared by the author.

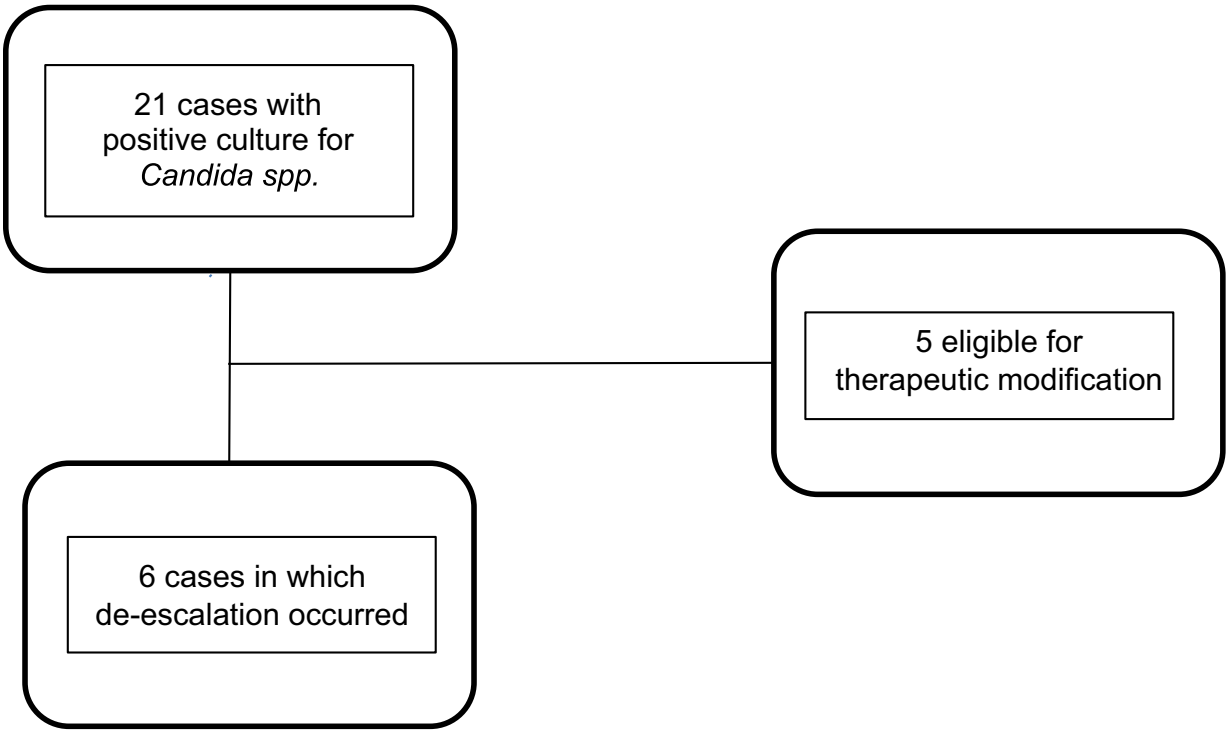
The estimated cost savings for one day of treatment with each drug are described in Table 4. Of the 21 cases with positive culture for yeast, de-escalation to fluconazole occurred in only 6 (28.6%), as shown in Figure 1.

Table 4. Daily cost savings generated by treatment de-escalation.

Initial therapy	De-escalation	Daily cost savings (R$)[a]
Anidulafungin 100 mg IV	Fluconazole 200mg IV	144,10
Anidulafungin 100 mg IV	Fluconazole 400mg IV	136,43
Anidulafungin 100 mg IV	Fluconazole 800mg IV	121,09
Anidulafungin 100 mg IV	Fluconazole 150mg capsule	154,74
Anidulafungin 100 mg IV	Fluconazole 300mg capsule	153,59

[a]Mean costs referring to June 2024..
IV: intravenous. **Source:** Prepared by the author.

Figure 1. Patients with positive yeast culture and the occurrence of switching to fluconazole.



Source: Prepared by the author.

Table 5 presents the economy savings achieved in cases in which de-escalation was performed, whereas Table 6 shows the estimated potential savings that could have been achieved with the adoption of step-down therapy, considering the intravenous formulation of fluconazole 200 mg. Of the 21 mycological diagnoses, *Candida albicans* isolates were identified in 10 samples. Among these cases, de-escalation from anidulafungin to fluconazole was performed in 4 patients, while this strategy was not adopted in another 4 patients. In one case, the isolate was obtained from pericardial fluid, a condition in which the therapeutic recommendation is to maintain anidulafungin 200 mg[1]. Another patient died before the release of the mycological result, making de-escalation impossible. In addition to *C. albicans* isolates, Table 5 also describes cases of de-escalation from anidulafungin to higher doses of fluconazole, referring to isolates of *C. tropicalis* and *C. parapsilosis*.

Table 5. Cost savings obtained from de-escalation of anidulafungin to fluconazole.

Patient	Isolate	*Step down therapy*	Duration of use (days)	Reduction in direct costs (R$)
1	*C. albicans*	Fluconazole 200mg IV	15	- 2.161,50
2	*C. albicans*	Fluconazole 300mg capsule	15	- 2.303,85
3	*C. albicans*	Fluconazole 400mg IV	7	- 955,01
4	*C. albicans*	Fluconazole 400mg IV	7	- 955,01
5	C. tropicalis	Fluconazole 400mg IV	7	- 955,01
6	C. parapsilosis	Fluconazole 400mg IV	37	- 5.047,91
Total				- 12.378,29

IV: intravenous.
Source: Prepared by the author.

Table 6. Estimated cost savings in the event of de-escalation from anidulafungin to fluconazole in the sample, according to IDSA recommendations.

Patient	Isolate	Alternative treatment	Duration of use (days)	Reduction in direst costs (R$)
1	C. albicans	Fluconazole 200mg IV	13	- 1.873,33
2	C. albicans	Fluconazole 200mg IV	11	- 1.585, 10
3	C. albicans	Fluconazole 200mg IV	4	- 576,40
4	C. albicans	Fluconazole 200mg IV	2	- 288,20
5	N. glabratus (C. glabrata)	Fluconazole 800mg IV	9	- 1.089,81
Total				- 5.412,84

IV: intravenous. **Source:** Prepared by the author.

The cost savings achieved through the de-escalation performed amounted to R$12,378.29. The additional potential savings, if therapeutic modification of antifungal agents had been implemented, are estimated at approximately R$5,412.84, which would result in a total direct cost reduction of R$17,791.13, considering the intravenous formulation of fluconazole 200 mg.

Discussion

Candida spp. is a commensal microorganism of the human intestine. However, the transition to a pathogenic state may occur under different circumstances, such as alterations in the gastrointestinal microbiota caused by the use of broad-spectrum antimicrobials, use of central venous catheter devices, immunological impairment of the patient, contamination of internal devices due to handling by health care professionals, and biofilm formation[23]. Other risk factors include chronic liver disease, chronic kidney disease, diabetes, multiple transfusions of blood components, pancreatitis, and prolonged hospitalization[27,28]. Correlating these factors with the results of this study, as observed in Table 1, the characterized population had at least one risk factor for candidemia.

For the treatment of fungal infections, there is a limited number of therapeutic options, which is further aggravated by antifungal resistance, whether intrinsic or acquired[24-26]. Therefore, the use of faster diagnostic techniques, such as serological assays and molecular biology tests, may shorten the time to diagnosis[27,28], directly impacting the reduction of broad-spectrum empirical therapies, as well as improving treatment targeting[24]. Data analysis revealed that, although mycological examinations were requested, *Candida* spp. detection occurred in only 21 cases. Of these, de-escalation was implemented in 16. The lack of adherence to de-escalation

in indicated cases may be related to the prolonged time required to obtain diagnostic results, variability in the clinical criteria adopted by medical teams, and low adherence to institutional protocols. These findings reinforce the need for faster diagnostic tests with greater sensitivity, in order to reduce the indiscriminate use of broad-spectrum antifungals and promote optimization of therapies and available resources.

Drug safety and toxicity are crucial factors to be considered in therapeutic decision-making, constituting an essential pillar in the management of infections. In the context of antifungal agents, Yang et al.[29] demonstrated that adverse effects related to the use of these drugs may lead to therapy discontinuation. Echinocandins and azoles, in particular, show lower discontinuation rates when compared with polyenes. The most common adverse effects include cardiac, gastrointestinal, hepatic, renal, and cutaneous disorders. Kyriakidis et al.[30] highlight that antifungal therapy may cause outcomes ranging from mild enzymatic alterations to fulminant hepatic failure, in addition to presenting a high potential for drug–drug interactions due to hepatic metabolism, which increases the risk of adverse effects. Koch et al.[31] reported that anidulafungin and caspofungin may influence patient hemodynamics, causing hypotension and increasing the need for vasopressors during therapy. Thus, beyond cost reduction, therapy de-escalation is necessary to promote patient safety. In this study, de-escalation to fluconazole could have been performed in five patients, as fluconazole is an antifungal agent with a favorable safety profile and fewer adverse effects. Although the present study did not assess the occurrence of adverse reactions to therapy, this aspect represents another important factor in therapeutic selection and switching.

In 1985, the World Health Organization (WHO) defined the concept of rational use of medicines as the situation in which "patients receive medications appropriate to their clinical needs, in doses that meet their individual requirements, for an adequate period of time, and at the lowest cost to them and their community"[32]. To apply this concept, the presence of a pharmacist is required. In 2017, Ioannidis et al. evaluated the application of step-down therapy in patients with candidemia and its economic impact. Of the 157 patients included, 51 met the criteria for de-escalation to fluconazole, however, this occurred in only 23 cases, generating additional costs to the health care system of €211,837. In addition, echinocandin-resistant strains of C. albicans and C. glabrata were identified. The use of echinocandins may result in higher costs for the health care system. According to Gebretekle et al.,[34] the use of caspofungin as first-line treatment for candidemia generated higher costs (US$7,714) compared with treatment with fluconazole (US$3,217) or amphotericin B (US$2,781) as second-line therapy. Studies indicate that treatments with micafungin and caspofungin for candidemia caused by albicans and non-albicans species are more costly and less effective than fluconazole, whereas anidulafungin is more effective but has a higher cost[35]. In our study, we observed cost savings of R$12,378.29 and estimated a possible additional savings of R$5,412.84 if de-escalation had been applied. The avoided expenditures were not as substantial as those reported in other studies. [14,35] However, as a positive aspect of the present study, the rationalization of hospital resources stands out, which may contribute to investments in equipment and process improvements, especially those related to diagnostics. Moreover, this practice helps prevent the development of antifungal resistance, reinforcing the relevance of implementing stewardship programs.

However, some limitations of the present study should be considered, such as its retrospective design, which is limited by the quality of medical record documentation and may generate biases in data collection. In addition, the study being conducted at a single institution hinders the generalizability of the findings.

As a perspective for continuity, the integration of pharmaceutical intervention with sequential oral therapy is highlighted, with the aim of facilitating dehospitalization or the transition of patients from the ICU to inpatient units. It is relevant to evaluate the impact of this practice on clinical outcomes, including length of hospital stay and occurrence of complications, as well as the economic impact through the reduction in the use of intravenous antifungals. Furthermore, this approach may strengthen

the role of the clinical pharmacist in decision-making and expand antifungal stewardship strategies.

Conclusion

The present study demonstrated that antifungal management strategies, when directed toward therapeutic optimization based on mycological diagnosis, can contribute to the reduction of institutional costs, in addition to minimizing the indiscriminate use of antifungal agents.

Ethics approval

Approved by the Research Ethics Committee of Irmandade da Santa Casa de Misericórdia de Porto Alegre (ISCMPA) under Opinion No. 6,837,180.

Authors' contributions

BBB, SCW, HS, RPC: Conception and design or analysis and interpretation of data; drafting of the article or critical revision of important intellectual content; responsibility for all aspects of the work in ensuring the accuracy and integrity of any part of the manuscript. SCW, HS, RPC: Final approval of the version to be published.

Conflicts of interest

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

Funding

Ministry of Health, through the Multiprofessional Residency Program.

Data Availability Statement

The underlying contents of the research text are contained in the manuscript.

Handling editor

Lindemberg Assunção Costa

References

1. Pagano L, Mayor S. Invasive fungal infections in high-risk patients: report from TIMM-8 2017. Future Sci OA [Internet]. 2018 Jun 14 [cited 2023 Aug 11];4(6). Available from: https://www.future-science.com/doi/10.4155/fsoa-2018-00192.
2. Bassetti M, Giacobbe DR, Vena A, Wolff M. Diagnosis and Treatment of Candidemia in the Intensive Care Unit. Semin Respir Crit Care Med [Internet]. 2019 [cited 2023 Aug 9];40(4):524–39. Available from: https://pubmed.ncbi.nlm.nih.gov/31585478/.
3. Cavling Arendrup M, Patterson TF. Multidrug-Resistant Candida: Epidemiology, Molecular Mechanisms, and Treatment. The Journal of Infectious Diseases The Journal of Infectious Diseases ®. 2017;216(S3):445–51. Available from: https://pubmed.ncbi.nlm.nih.gov/28911043/.
4. Chowdhary A, Voss A, Meis JF. Multidrug-resistant Candida auris: "new kid on the block" in hospital-associated infections? J Hosp Infect [Internet]. 2016 Nov 1 [cited 2023 Nov 5];94(3):209–12. Available from: https://pubmed.ncbi.nlm.nih.gov/27634564/.
5. Kimura S, Kameda K, Harada K, Saburi M, Okinaka K, Shinohara A, et al. Risk and Predictive Factors for Candidemia After Allogeneic Hematopoietic Cell Transplantation: JSTCT Transplant Complications Working Group. Transplant Cell Ther. 2022 Apr 1;28(4):209.e1-209.e9.
6. McCarty TP, White CM, Pappas PG. Candidemia and Invasive Candidiasis. Infect Dis Clin North Am [Internet]. 2021 Jun 1 [cited 2023 Aug 6];35(2):389–413. Available from: https://pubmed.ncbi.nlm.nih.gov/34016283/.
7. Epelbaum O, Chasan R. Candidemia in the Intensive Care Unit. Clin Chest Med [Internet]. 2017 Sep 1 [cited 2023 Aug 9];38(3):493–509. Available from: https://pubmed.ncbi.nlm.nih.gov/28797491/.
8. Asai N, Sakanashi D, Suematsu H, Kato H, Hagihara M, Shiota A, et al. To what degree could clinical trials in evidence based medicine reflect reality in the treatment of candidemia? Journal of Microbiology, Immunology and Infection. 2022 Feb 1;55(1):147–53. Available from: https://pubmed.ncbi.nlm.nih.gov/33339744/.
9. Eschenauer GA, Nguyen MH, Clancy CJ. Is Fluconazole or an Echinocandin the Agent of Choice for Candidemia. Annals of Pharmacotherapy. 2015 Sep 24;49(9):1068–74. Available from: https://pubmed.ncbi.nlm.nih.gov/26104051/.

10. Pappas PG, Kauffman CA, Andes DR, Clancy CJ, Marr KA, Ostrosky-Zeichner L, et al. Clinical Practice Guideline for the Management of Candidiasis: 2016 Update by the Infectious Diseases Society of America. 2015; Available from: https://academic.oup.com/cid/article/62/4/e1/2462830.
11. Pham CD, Iqbal N, Bolden CB, Kuykendall RJ, Harrison LH, Farley MM, et al. Role of FKS mutations in Candida glabrata: MIC values, echinocandin resistance, and multidrug resistance. Antimicrob Agents Chemother. 2014;58(8):4690–6. Availabke from: https://pubmed.ncbi.nlm.nih.gov/24890592/.
12. Leone M, Garcin F, Bouadma L, et al. De-escalation versus continuation of empirical antimicrobial treatment in severe sepsis: a multicenter non-blinded randomized noninferiority trial. Intensive Care Med. 2003;29(8):1254–1261. Available from: https://hal.umontpellier.fr/hal-01945691v1.
13. Chen D, Wan X, Kruger E, Chen C, Yue X, Wang L, et al. Cost-effectiveness of de-escalation from micafungin versus escalation from fluconazole for invasive candidiasis in China. J Med Econ. 2018 Mar 4;21(3):301–7. Available from: https://pubmed.ncbi.nlm.nih.gov/29303621/.
14. de Mello Vianna CM, Mosegui GBG, da Silva Rodrigues MP. Cost-effectiveness analysis and budgetary impact of anidulafungin treatment for patients with candidemia and other forms of invasive candidiasis in Brazil. Rev Inst Med Trop Sao Paulo. 2023;65. DOI: 10.1590/S1678-9946202365009.
15. Albanell-Fernández M, Salazar González F, Montero Pérez O, Aniyar V, Carrera Hueso FJ, Soriano A, et al. Clinical evaluation of antifungal de-escalation in Candida infections: a systematic review and meta-analysis. Int J Infect Dis. 2024;143:107020. Available from: https://pubmed.ncbi.nlm.nih.gov/38548167/.
16. Pappas PG, Kauffman CA, Andes DR, et al. Clinical Practice Guideline for the Management of Candidiasis: 2016 Update by the IDSA. Clin Infect Dis. 2016;62(4):e1–e50. Available from: https://pubmed.ncbi.nlm.nih.gov/26679628/.
17. Farmakiotis D, Kontoyiannis DP. Failure of early antifungal de-escalation in Candida glabrata bloodstream infection. Mycoses. 2020;63(8):776–784.
18. Andes DR, et al. Timing of antifungal therapy and mortality in candidemia: a global cohort analysis. Clin Infect Dis. 2022;75(1):e142–e151.
19. Bassetti M, Peghin M, Carnelutti A. Antifungal de-escalation: balancing safety and stewardship. Curr Opin Infect Dis. 2020;33(6):591–598.
20. Fisher MC, Alastruey-Izquierdo A, Berman J, Bicanic T, Bignell EM, Bowyer P, et al. Tackling the emerging threat of antifungal resistance to human health. Nat Rev Microbiol. 2022;20(9):557-71. Available from: https://pubmed.ncbi.nlm.nih.gov/35352028/.
21. Jaffal K, Poissy J, Rouzé A, Préau S, Sendid B, Cornu M, Nseir S. De-escalation of antifungal treatment in critically ill patients with suspected invasive Candida infection: incidence, associated factors, and safety. Ann Intensive Care. 2018;8:49. Available from: https://pubmed.ncbi.nlm.nih.gov/29675561/.
22. Khanina A, Yen Tio S, Ananda-Rajah MR, Kidd SE, Williams E, Chee L, et al. Consensus guidelines for antifungal stewardship, surveillance and infection prevention, 2021. 2021; Available from: https://onlinelibrary.wiley.com/doi/10.1111/imj.15586.
23. Neville BA, d'Enfert C, Bougnoux ME. Candida albicans commensalism in the gastrointestinal tract. Vol. 15, FEMS yeast research. 2015. Available from: https://pubmed.ncbi.nlm.nih.gov/26347504/.
24. Arendrup MC, Patterson TF. Multidrug-resistant candida: Epidemiology, molecular mechanisms, and treatment. Journal of Infectious Diseases. 2017 Jan 15;216:S445–51. Available from: https://pubmed.ncbi.nlm.nih.gov/28911043/.
25. Garcia-Rubio R, Cuenca-Estrella M, Mellado E. Triazole Resistance in Aspergillus Species: An Emerging Problem. Drugs. 2017 Apr 1;77(6):599–613.
26. Arikan-Akdagli S, Ghannoum M, Meis JF. Antifungal resistance: specific focus on multidrug resistance in candida auris and secondary azole resistance in aspergillus fumigatus. Vol. 4,

Journal of Fungi. MDPI AG; 2018. Available from: https://www.frontiersin.org/journals/microbiology/articles/10.3389/fmicb.2016.02173/full?gad_source=1&gad_campaignid=23251497049&gbraid=0AAAAAC_sJ7n9vVWDXgbwNJ7KBmJRP4TvE&gclid=Cj0KCQiA_8TJBhDNARIsAPX5qxRrWymMpCYxHbEXRwQMuYT0dEuaruvOLTFVOw7_6Is9TFoulc-5gvoaAtnzEALw_wcB.

27. Fang W, Wu J, Cheng M, Zhu X, Du M, Chen C, et al. Diagnosis of invasive fungal infections: challenges and recent developments. Vol. 30, Journal of Biomedical Science. 2023. Available from: https://pubmed.ncbi.nlm.nih.gov/37337179/.
28. Ahmed A, Baronia AK, Azim A, Marak RSK, Yadav R, Sharma P, et al. External validation of risk prediction scores for invasive candidiasis in a medical/surgical intensive care unit: An observational study. Indian Journal of Critical Care Medicine. 2017;21(8). Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC5588486/.
29. Yang YL, Xiang ZJ, Yang JH, Wang WJ, Xu ZC, Xiang RL. Adverse Effects Associated With Currently Commonly Used Antifungal Agents: A Network Meta-Analysis and Systematic Review. Vol. 12, Frontiers in Pharmacology. Frontiers Media S.A.; 2021. Available from: https://www.frontiersin.org/journals/pharmacology/articles/10.3389/fphar.2021.697330/full.
30. Kyriakidis I, Tragiannidis A, Munchen S, Groll AH. Clinical hepatotoxicity associated with antifungal agents. Vol. 16, Expert Opinion on Drug Safety. Taylor and Francis Ltd; 2017. p. 149–65. Available from: https://pubmed.ncbi.nlm.nih.gov/27927037/.
31. Koch C, Schneck E, Arens C, Markmann M, Sander M, Henrich M, et al. Hemodynamic changes in surgical intensive care unit patients undergoing echinocandin treatment. Int J Clin Pharm. 2020 Feb 1;42(1):72–9. Available from: https://pubmed.ncbi.nlm.nih.gov/31748967/.
32. Organização Mundial da Saúde. Uso racional de medicamentos. Genebra; 1985.
33. Ioannidis K, Papachristos A, Skarlatinis I, Kiospe F, Sotiriou S, Papadogeorgaki E, et al. Do we need to adopt antifungal stewardship programmes? European Journal of Hospital Pharmacy . 2020 Jan 1;27(1):14–8. Available from: https://pubmed.ncbi.nlm.nih.gov/32064083/.
34. Gebretekle GB, Fentie AM, Gebremariam GT, Ali EE, Erku DA, Alemayehu T, et al. Cost-utility analysis of caspofungin and fluconazole for primary treatment of invasive candidiasis and candidemia in Ethiopia. BMC Health Serv Res. 2022 Dec 1;22(1). Available from: https://link.springer.com/article/10.1186/s12913-022-08662-3.
35. Ou HT, Lee TY, Chen YC, Charbonneau C. Pharmacoeconomic analysis of antifungal therapy for primary treatment of invasive candidiasis caused by Candida albicans and non-albicans Candida species. BMC Infect Dis. 2017 Jul 10;17(1). Available from: https://pubmed.ncbi.nlm.nih.gov/28693479/.