Kentucky Antimicrobial Stewardship Innovation Consortium

Educational Pearl

Empiric Antifungals In the ICU

Critically ill patients with prolonged ICU length of stays are at risk for developing invasive candidiasis. Other risk factors include recent history of immunosuppression, organ failure, intra-abdominal surgery, receipt of total parenteral nutrition, presence of a central line, necrotizing pancreatitis, exposure to broad spectrum antibiotics, and non-sterile site candida colonization (e.g. urine, respiratory culture).[1] Detecting invasive candidiasis can be difficult as blood cultures have low sensitivity and candidiasis signs and symptoms are non-specific. When should empiric antifungals be started in critically ill patients in the ICU?

What do guidelines recommend?

The 2016 Infectious Diseases Society of America (IDSA) Candidiasis guideline recommends that empiric antifungal therapy be considered in nonneutropenic, critically ill patients with risk factors for invasive candidiasis and no other known causes of fever. It is further recommended that antifungal therapy should be promptly started as soon as possible in patients with septic shock and risk factor(s)**.**[1]

In a 2025 American Thoracic Society (ATS) guideline, routine empiric antifungal therapy is not suggested in nonneutropenic patients without a history of solid organ transplantation.[2] In a 2025 guideline from the European Conference for Medical Mycology, it is not recommended to start empiric antifungal solely due to fever, but it is recommended to start empiric antifungals in patients with risk factors and with either septic shock or deteriorating health.[3]

What is the evidence?

In the EMPIRCUS randomized controlled trial that was published after the 2016 IDSA guidelines, empiric micafungin was not found to improve fungal-infection free survival by day 28 when compared with placebo. Approximately 60% of patients received vasopressors at randomization and median number of colonized candida sites was 3 (IQR 2-4). In a subgroup of those with SOFA score > 8, micafungin had a numerical, non-statistically significant improvement in fungal infection free survival.[4]

In a meta-analysis included in the 2025 ATS guideline, mortality was similar between those who received empiric antifungals and those who did not (RR 1.07 95% CI 0.81-1.41).[2]

Key Takeaway: In the ICU, empiric antifungal therapy should be reserved for patients with substantial risk factors and clinical instability (e.g. septic shock). In more stable patients, hold empiric antifungals and start treatment after a diagnosis is made (e.g. positive cultures for *Candida* spp.).

References:

1. 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. *Clin Infect Dis*. 2016;62(4):e1-e50. doi:10.1093/cid/civ933
2. Epelbaum O, Marinelli T, Haydour Q, et al. Treatment of Invasive Pulmonary Aspergillosis and Preventive and Empirical Therapy for Invasive Candidiasis in Adult Pulmonary and Critical Care Patients: An Official American Thoracic Society Clinical Practice Guideline. *Am J Respir Crit Care Med*. 2025;211(1):34-53. doi:10.1164/rccm.202410-2045ST
3. Cornely OA, Sprute R, Bassetti M, et al. Global guideline for the diagnosis and management of candidiasis: an initiative of the ECMM in cooperation with ISHAM and ASM. *Lancet Infect Dis*. 2025;25(5):e280-e293. doi:10.1016/S1473-3099(24)00749-7
4. Timsit JF, Azoulay E, Schwebel C, et al. Empirical Micafungin Treatment and Survival Without Invasive Fungal Infection in Adults With ICU-Acquired Sepsis, Candida Colonization, and Multiple Organ Failure: The EMPIRICUS Randomized Clinical Trial. *JAMA*. 2016;316(15):1555-1564. doi:10.1001/jama.2016.14655

Created 6.9.26