

Treatment options for resistant fungal infections are limited and new drugs with novel mechanisms of actions are needed. Prevention of resistance through antifungal stewardship programs is of paramount importance” Gamaletsou et al (2018).

Abstract:

Invasive fungal infections caused by drug-resistant organisms, are an emerging threat to heavily immunosuppressed patients with haematological malignancies. Modern early antifungal treatment strategies, such as prophylaxis, empirical and pre-emptive therapy result in long term exposure to antifungal agents, which is a major driving force for the development of resistance.

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The extended use of central venous catheters, the non-linear pharmacokinetics of certain antifungal agents, neutropenia, other forms of intense immunosuppression, and drug toxicities are other contributing factors. The widespread use of agricultural and industrial fungicides, with similar chemical structures and mechanisms of action, has resulted in development of environmental reservoirs for some drug-resistant fungi, especially azole-resistant *Aspergillus* species, which have been reported from four continents. The majority of resistant strains have the mutation TR34/L98H, a finding suggesting that the source of resistance is the environment. The globalemergence of new fungal pathogens with inherent resistance, such as *Candida auris* is a new public health threat. The most common mechanism of antifungal drug resistance is the induction of efflux pumps, which decrease intra-cellular drug concentration. Overexpression, depletion, and alteration of the drug target are other mechanisms of resistance. Mutations in the ERG11 gene alter the protein structure of C-demethylase, reducing the efficacy of antifungal triazoles. *Candida* species become echinocandin-resistant by mutations in FKS genes. A shift in the epidemiology of *Candida* towards resistant non-*albicans* *Candida* spp has emerged among patients with haematological malignancies. There is no definite association between antifungal resistance,

as defined by elevated MICs, and clinical outcomes in this population. Detection of genes or mutations conferring resistance with the use of molecular methods may offer better predictive value in certain cases. Treatment options for resistant fungal infections are limited and new drugs with novel mechanisms of actions are needed. Prevention of resistance through antifungal stewardship programs is of paramount importance.

Full Text

Reference:

Gamaletsou, M.N., Walsh, T.J. and Sipsas, N.V. (2018) Invasive Fungal Infections in Patients with Hematological Malignancies: Emergence of Resistant Pathogens and New Antifungal Therapies. Turkish Journal of Haematology. February 2nd. .

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