PK-PD rationale and efficacy of isavuconazole treatment after failure of amphotericin B and posaconazole for COVID-19 associated cranial Mucormycosis

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Objective: This case series describes our experience of using isavuconazole (ISVCZ), along with TDM, after the failure of treatment with Amphotericin B (AmB) and Posaconazole (PCZ) due to the better PK-PD properties of ISVCZ.

Patients and methods: There were 6 patients with ROCM who had disease progression despite surgical debridement and adequate treatment with AmB and PCZ. Anti-fungal treatment was switched to ISVCZ which achieves levels in brain (1.86xR) and in bone-marrow (3xR) as compared to serum levels.

Results: PK-PD considerations for ISVCZ treatment considering the likely levels in brain and bone-marrow and the MIC of majority of Mucoralean molds as ≤4R.

Table 1
Table 2

Results of treatment
Conclusion: Treatment with ISVCZ may mitigate some of the challenges in ROCM due to its PK-PD properties. TDM for ISVCZ is not routinely recommended, but could be used to ensure high plasma exposures and enhanced penetration to the site of infection. Our results are encouraging although there are several limitations of a case series, confounding variables involved, and the use of ISVCZ as salvage after failure of previous treatment.

Clinical success in this series suggests that extrapolative PK-PD considerations in using ISVCZ for such ‘difficult to treat’ patients may be justified.
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Prevalence and outcomes of patients with COVID - associated muromycosis (CAM): A case series

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Background and objective: Coronavirus disease-19 (COVID-19) pandemic caused by the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) virus has been associated with increased secondary bacterial and fungal infections. A few centers from India have reported a high number of cases of COVID-associated mucormycosis (CAM). Depending on the anatomical site of infection, mucormycosis is classified as rhino-orbital-cerebral, pulmonary, gastrointestinal, cutaneous, renal, and disseminated-mucormycosis. Several risk factors such as uncontrolled diabetes mellitus, hematologic malignancies, renal disease, organ transplant, and corticosteroid therapy administered for COVID-19 are implicated in CAM. In this study, we report a case series of CAM, presenting its prevalence, clinical features, risk factors, etiological agent, site of infection, and outcomes in a single center.

Methods: A retrospective data analysis of all proven mucormycosis cases among COVID-19 infected patients from September 1, 2020 to December 31, 2020, was carried out after approval from the institutional ethics committee. All proven cases of mucormycosis (either by culture from sterile site or histopathology), along with compatible clinical and radiological findings, in patients with positive real-time polymerase chain reaction (RT-PCR) for SARS-CoV2 within 2 months of the diagnosis of mucormycosis were included in the study. All patients received treatment for COVID-19 and mucormycosis as per the institutional protocol. Data was collected in a predefined case records form developed for the study which included demographic characteristics, risk factors, days to the diagnosis of mucormycosis after COVID-19, site of involvement by mucormycosis along with microscopy, culture and histopathology, treatment details and outcomes at 6 and 12 weeks.

Results: During the study period, a total of 19 patients were diagnosed with CAM. The major risk factors of the patients were: type 2 diabetes mellitus (DM) (n = 11, 78.9%) and steroid therapy (n = 14, 94.7%). The other co-morbidities included hypertension (n = 7, 47.3%), chronic kidney disease (CKD) (n = 4, 22.2%) and chronic liver disease (n = 1, 5.2%). Rhino orbital mucormycosis (ROM) was the most common form (n = 9, 47.3%). The prevalence of CAM (as calculated by the total number of cases of CAM divided by the number of COVID-19 cases treated) was 5.47/1000 COVID patients during the study period. Majority (11, 57.9%) of the patients were successfully treated and discharged whereas three patients succumbed to infection and one left against medical advice. The mortality in this cohort (n = 4) was 21.05% as compared with 13.9% among all COVID patients (n = 9) admitted during the same time period in 2020.

Conclusion: Though sample size is small, the findings in our study suggest that the mortality from COVID-associated mucormycosis is high, though the risk factors remain the same. The incidence of mucormycosis was twice that in non-pandemic period. Early diagnosis is crucial as despite aggressive surgical medical therapy, mortality continues to be high.

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Baiádolobo meristosporum — anew species on the block!

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Objective: Entomophthorales, including genus Baiádolobo, and Conidiobolus are well-recognised cause of subcutaneous infections in immunocompetent hosts. genus Baiádolobo is ubiquitous. All human infections except one reported so far have been due to R. meristosporum.

Here we present a case of an immunocompetent 5-year-old girl with a soft tissue swelling on the right upper buttock caused by R. meristosporum.