

## $\beta$ -Glucan in the diagnosis of invasive fungal disease

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It is common sense that better noninvasive diagnostic methods are needed for the detection of invasive fungal diseases (IFDs). This is particularly true for immunocompromised patients in whom the performance of invasive medical procedures is not always feasible (1).

The 1,3- $\beta$ -D-glucan (BG) antigenemia is a method for the early diagnosis of invasive aspergillosis (IA) and candidiasis (IC) in neutropenic patients (2). Because of the morbidity and mortality of these infections, early antifungal therapy is critical. A noninvasive monitoring tool that detects both *Aspergillus* and *Candida* species is an attractive approach. A positive result of the screening test may trigger further investigations and preemptive antifungal therapy. The results suggest that BG may fulfill this goal. Although BG does not differentiate IA from IC, combination of BG data with imaging culture, and histopathologic data allows an etiological diagnosis in most cases. Moreover, in patients with positive screening results for BG, genus-specific fungal markers (ie, galactomannan for *Aspergillus* species (3) and mannan/ antimannan for *Candida* species (4) may contribute to the differentiation of IA from IC. Because several treatment options that are active against both fungi are now available, therapeutic

decisions are less dependent on an immediate etiological diagnosis (5). A positive BG result may trigger the initiation of antifungal therapy. The complementary investigations may then allow its adjustment. The similar overall survival rates for patients with IA (93%) and IC (89%) support the efficacy of the initial empirical antifungal strategy.

With regard to the diagnostic performance of BG the observation showed similar sensitivities, specificities, and positive and negative predictive values for IA (0.60, 0.96, 0.64, and 0.95, respectively) and IC (0.59, 0.96, 0.67, and 0.94, respectively). The median time elapsed from fever onset to positive BG result was also similar (median time, 0 days; range: -25 to 19 days for IA, median time, 2 days, range: -1 to 16 days for IC). These results support the efficiency of BG for early detection of both IA and IC. However, as pointed out by Pasqualotto and Sukiennik (1), the median time to the peak BG level in IA (median time, 3 days; range:-25 to 25 days) was possibly shorter than for IC (median time, 12 days; range: 1-46 days). The kinetics of other fungal markers is influenced by the timing of antifungal therapy. Ongoing treatment or prophylaxis may result in early and low peaks, whereas late start is associated with delayed and higher peaks (6). The use of a candida-specific prophylaxis (fluconazole in one-fourth of IA and IC cases) did not result in a higher BG sensitivity in IA than in IC. Moreover, the median time elapsed from fever onset to initiation

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of antifungal therapy was similar for IA (median time, 1 day; range: -13 to 13 days) and IC (median time, 3 days; range: 0-10 days). One might speculate that the early peak in IA and later peak in IC could reflect different pathogeneses. The microbial load may indeed differ: single pulmonary lesions were documented in IA, whereas multiple hepatosplenic lesions suggesting hematogenous dissemination were documented in IC. It remains to be determined whether the concomitance of late BG peak and neutrophil recovery in IC might reflect the reaction induced by the immune restoration typically associated with the radiological appearance of organ abscesses. Because of the small sample size, no firm conclusion can be drawn about the different kinetics of BG in IA and IC.

In Iran, despite significant development in the management and diagnosis of invasive fungal infection in immunocompromised and organ transplant patients, mold infections are much less frequently detected when compared with candida infection. Unavailability of adequate diagnostic facilities including 1,3  $\beta$ -D glucan and genus specific fungal markers like galactomannan for *Aspergillus* species, and advanced culture technique even in most academic centers might complicate patients management (7).

In conclusion, usefulness of  $\beta$ -glucan testing for the detection of invasive fungal infection (IFI) in patients with hematological malignancies demonstrated that  $\beta$ -glucan testing is able to detect IFI at early stages, before major radiological manifestation occurred and the ability of  $\beta$ -glucan testing to detect both invasive aspergillosis (IA) and invasive candidiasis (IC) in patients at high risk is one of the main advantages of this approach.

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