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Evolving therapeutic strategies for fungal infections

VORICONAZOLE IN PRIMARY TREATMENT OF INVASIVE ASPERGILLOSIS - AN OBSERVATIONAL STUDY; CORELLATION OF EFFICACY WITH C-REACTIVE PROTEIN AND PROCALCITONIN LEVELS

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Objective

To assess the efficacy of primary antifungal therapy of invasive aspergillosis (IA) with voriconazole in high-risk immunocompromised patients. Secondary objectives were to evaluate the risk factors, diagnostic procedures and clinical signs as a triggers for antifungal therapy and the role of inflamatory markers - C- reactive protein (CRP) and procalcitonin(PCT) in patients with IA.

Patients and methods

Multicenter observational retrospective study in 8 centers during 2 years period was performed. Patients with proven, probable and possible IA from hematooncology units and ICU were enrolled. EORTC/MSG 2008 criteria for IFD were used for classification and response evaluation. Data regarding risk factors, diagnostic procedures, prophylaxis, response to the therapy with voriconazole and survival were collected and analyzed. Dynamics of CRP and PCT was documented and assessed. Descriptive statistics was used.

Results

86 patients were enrolled with average age of 50 years (range 0-79). The major risk factors were previous ATB therapy (83%), chemotherapy (63%) and neutropenia (58%). According to local investigators 44% possible IA, 43% probable IA and 13% proven IA were documented. Lungs were the most common site of infection (88%). Serum galactomannan (GM) was performed in 73% of patients and was positive in 24%. GM in bronchoalveolar lavage (BAL) was done in 48% of patients with 63% positive results. 76% of patients had positive CT/HRCT scans (halo in 49%, air-crescent sign in 37%). The triggers which lead to antifungal therapy were CT, persistent fever, positive GM in 76%, 71% and 44%. Daily dose 400 mg of voriconazole was administred in 75% of patients and in 50 % of all patients the switch from iv to oral form was possible. Average duration of therapy was 29 days (range 4-116). Response rate (CR+PR) of 59% was shown at the end of treatment (EOT) with 34% mortality rate. Better therapeutic response was achieved in patients with possible IA (69%) than in probable cases (45%). CR+PR was associated with the normal neutrophils level at the EOT and mortality was higher in patients with persistent neutropenia. Overall survival was not affected by previous antifungal prophylaxis. C-reactive protein and procalcitonin levels at the EOT were significantly higher in patients with failure of voriconazole than in patients with succesfull outcome.

Conclusions

Voriconazole documented favourable clinical outcome in 60% of patients with mortality rate of 36%. Normal neutrophil counts correlated with better outcome as well as normalisation of CRP and PCT levels.