

P480

Maintenance antifungal therapy of recurrent esophageal candidiasis in HIV-negative patients

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Objective The efficiency of maintenance antifungal therapy of recurrent esophageal candidiasis (REC) in HIV-negative patients is not well established.

Methods In prospective single-center study (2004–2014) we include 124 HIV-negative patients with REC. Median age was 53 y (46–65), women 91. Endoscopic examination with a biopsy, microscopy and culture was made in all patients. Identification of the pathogen was made with MALDI-TOF Mass Spectrometry. Determination of susceptibility of pathogens to fluconazole and voriconazole was made with the disco-diffusion CLSI M44-A method. Criteria of RCE was ≥ 1 relapse in a year.

Results Risk factors were: thyroid disease (43%) with hypothyroidism (17%), bronchial asthma (12%), diabetes mellitus (9%), smoking (100%), inhaled (90%) and per os (52%) corticosteroids, and very hot food use (67%). The clinical signs were dysphagia (90%), retrosternal discomfort (50%), and odinophagia (18%). Endoscopic features were hyperemia (100%) and contact sensitivity (100%) of esophagus mucosa, and white fibrin plaques (75%). Main etiology agent was *C. albicans* (99%), sensitive *in vitro* to fluconazole and voriconazole (100%). Treatment of relapse fluconazole 150 mg day⁻¹ for 3–4 weeks was effective in 100% patients. The patients were divided into two groups: with or without maintenance antifungal therapy – 50 mg fluconazole once a week for 6 months. If patients did not receive maintenance therapy rate of relapse in 6 months was 57%. All patients with maintenance therapy were in remission of REC in 6 months ($P < 0.005$). No side effects or drug-drug interactions in patients with maintenance antifungal therapy were detected.

Conclusions Maintenance antifungal therapy with 150 mg fluconazole once a week for 6 months is effective and safe in HIV-negative patients with recurrent esophageal candidiasis.

P481

Immunological and immunohistochemical features of recurrent esophageal candidiasis in HIV-negative patients.

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Objectives The immunological and immunohistochemical features of a reNAAAAA current esophageal candidiasis (REC) in HIV-negative patients are not well understood.

Methods We examined immunological and immunohistochemical parameters in 78 patients with REC. The median age of patients was 53 years. Criteria of REC was ≥ 1 relapse in a year. Subpopulations of lymphocytes were determined by immunocytochemical method using a monoclonal antibody «DAKO». Blood cell supernatants were tested for IFN- γ and IL-10 by using an ELISA test 'Cytokine'. The antibodies used for immunohistochemical staining were monoclonal mouse anti-human CD3 +, CD4 +, CD8 +, CD68 + («DAKO»). Statistical analysis was done using Mann-Whitney U-test ($P < 0.05$).

Results Our study showed that in patients with REC was a reduction of the absolute numbers of CD3 + (1.216*10⁹/L), CD4 + (0.735*10⁹/L), CD8 + (0.483*10⁹/L), CD16 + (0.157*10⁹/L) lymphocytes, and the increase the spontaneously secreting IFN- γ (63.0 pg ml⁻¹) and IL-10 (144.0 pg ml⁻¹) ($P < 0.05$).

Immunohistochemical parameters were characterized by a decreased of CD3 + and CD68 + cells and increased CD4 + and CD8 + cells in the epithelium of the esophagus and the underlying tissues.

Conclusions Immunological parameters, identified in this trial may be of interest in the pathogenesis of recurrent esophageal candidiasis in HIV-negative patients.

P482

Validation of the DermaGenius Nail plus multiplex assay, a new commercial PCR assay developed for the detection and identification of dermatophyte and *Candida* in nails

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Objectives Superficial dermatophytosis is the most common fungal infection in humans. Diagnosis of dermatophytosis is currently based on microscopy or histology associated with culture on specific agar media. However, direct microscopy lacks specificity and culturing has a long turn-around-time of 2–4 weeks. These limitations can be prevented by the use of molecular diagnostics. The DermaGenius (DG) multiplex kit (PathoNostics, the Netherlands) is a new commercial realtime-PCR kit, which can differentiate various dermatophytes species including the nail pathogens *T. rubrum*, *T. mentagrophytes*, *T. interdigitale* and 2 *Candida* species (*C. albicans* and *C. parapsilosis*). This study aimed at the validation of the kit on nails clippings. Results were compared with histology and culture data.

Methods A set of 76 nail clippings was collected from 76 patients attending the dermatology consultation at the University Hospital of Liege on suspicion of onychomycosis. All nails were divided in three pieces for histology, culture and the PCR multiplex assay. Histologic preparations were stained with PAS staining. Cultures were performed on 2 different Sabouraud agar medium slants (bioMérieux). The DNA extraction protocol used a proteinase K pre-treatment followed by an automated DNA-extraction (EasyMag, bioMérieux). An Internal Control (IC) was included to monitor for PCR inhibition or manual errors. The realtime-PCR amplification was performed with the DG kit on a Rotor-Gene Q instrument (Qiagen) by using quantitative amplification and melting curve analysis.

Results In total, 35 of 76 cases (46%) were classified as confirmed onychomycosis based on positive microscopy (M+) with or without positive culture (C+) or just by positive culture of a confirmed pathogen. Based on negative microscopy (M-) and negative culture of a confirmed pathogen, 41 cases (54%) were reported as non-fungal onychodystrophy. Agreement between DermaGenius (DG) and culture was found in 52% of the cases while 86% agreement was reported when comparing positive DG with confirmed onychomycosis. Three positive cultures (microscopy negative) were not detected by DG (2 *T. rubrum*, 1 *C. albicans*). However, DG could detect 7 additional infections (9%). Eleven discrepancies DG+/C+ were determined which could be positively confirmed in favour of DG result by ITS sequence analysis. Most discrepancies could be explained by fungal/yeast species overgrowing the agar slant, including species of *Candida*, *Fusarium*, *Trichosporon*, which were not considered as the source of infection.

Conclusion The DermaGenius Nail plus multiplex was able to detect the most prevalent pathogenic dermatophytes species in clinical nail specimens and proved to be more sensitive and specific than culture and direct microscopy. The DNA extraction procedure has been shown to work efficiently in diagnostics which enables the physician in charge of the patient to start a dedicated treatment rapidly.