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Abstract (poster session)

Failure of toxin A/B enzyme immunoassay to detect toxin-producing strains for diagnosis of nosocomial Clostridium difficile-associated diseases

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Introduction: Clostridium difficile is the most frequent cause of nosocomial diarrhoea. In many medical centres diagnosis of C. difficile associated disease (CDAD) is still based on enzyme immunoassay (EIA) detection of fecal toxin A/B alone despite the known low sensitivity of this approach. Objectives: The aim of this study was to compare the sensitivity of the fecal toxin A/B test with toxigenic cultures in different patient populations with CDAD. Methods: At the University Hospital Basel, Switzerland, all stool specimens submitted for C. difficile between 2004 and 2011 were analyzed by two methods: detection of fecal toxin A/B by EIA directly from stool (=group 1) and toxigenic culture when fecal-toxin was negative (=group 2). All inpatients with CDAD were analyzed. CDAD was defined according to international guidelines by: 1) diarrhoea and a positive result for fecal toxin A/B or 2) diarrhoea, a positive C. difficile culture, and fulfilling the ESCMID clinical definition (Clin Microbiol Infect 2009;15:1067) for C. difficile and initiating appropriate therapy. Results: During the study period 12'481 stool specimens were submitted to the laboratory for C. difficile. 559 (4.5%) patients fulfilled the ESCMID criteria of CDAD. The sensitivity of the fecal toxin A/B assay was only 49% (Figure 1). Age (mean 66 years), sex (male: 49.7%), underlying diseases and fever at onset were equally distributed between the two groups. The outcome of CDAD between group 1 and 2 was recurrence in 11.3% vs. 8.3% and mortality in 7.7% vs. 7.8%, respectively ($p=0.27$ and $p=0.97$, respectively). Predictors for negative direct fecal toxin A/B but positivity by toxigenic culture were patients from haematology unit (OR 3.6, CI 95% 1.8-7.7, $p<0.0002$) and patients under corticosteroids (OR 2.6, CI 95% 1.4-5, $p=0.002$). Patients with CDAD and a positive toxigenic culture only were less likely to be treated with adequate antibiotics (OR 6.76, CI 95% 3.3-13.84, $p<0.0001$). Conclusion: The sensitivity of the fecal toxin A/B assay was only 49% in patients with CDAD. Toxigenic culture significantly increases the sensitivity to 86%, particularly in the haematology unit and in immunocompromised patients. Patients with CDAD with negative direct fecal toxin A/B but positive toxigenic culture had a similar clinical presentation and outcome as those with positive fecal toxin A/B. Toxigenic culture, or more recently PCR, should be applied, if fecal toxin EIA results are negative.

Figure 1: Enrollment and results of CDAD patients with fecal toxin A/B EIA and toxigenic culture