Use of intravenous tigecycline in patients with severe Clostridium difficile infection: a retrospective case-control study

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Background: There are only a limited number of possible antimicrobials for the treatment of severe Clostridium difficile infection (sCDI). Tigecycline showes significant in vitro effect against C. difficile and is approved for the treatment of complicated intra-abdominal infections. The current ESCMID guideline recommends tigecycline as an alternative drug for sCDI with low evidence (Grade C-III). Our aim was to analyse the efficacy of tigecyclin compared to the standard therapy (vancomycin±metronidazole) in patients diagnosed and treated with sCDI.

Material/methods: A retrospective matched case-control study of adult patients hospitalized and treated with sCDI at our department between January 1st, 2014 and October 1st, 2015 was performed. Data were collected by reviewing the electronic medical records. Patients receiving tigecycline for ≥48 h were included in the case group. Patients were excluded if tigecycline was given for <48 h. Controls were treated with standard therapy and were matched to cases in 1:1 ratio by identical ATLAS scores. Diagnosis of CDI was based on confirmation of toxigenic C. difficile from unformed stool by enzyme immunoassay detecting GDH, toxins A+B. Disease severity was determined according to the current ESCMID guideline. Primary outcome was clinical cure, secondary outcomes were in-hospital and 90-day all-cause mortality and relapse, rate of colectomy and complications (sepsis, ileus, toxic megacolon). The Mann-Whitney U-test and the Fisher's exact test were used.

Results: Of 359 patients with sCDI, 45 (12.5%) with a mean ATLAS score of 7.8±1.3 were included in the case group (55.6% men, age 75.2±10.1 years). 7 (15.6%) received tigecycline as first anti-CDI treatment, 38 (84.4%) as second or third choice. Mean starting day of treatment from admittance was 8.2±7.1, duration was 10.3±4.5 days. Case patients had hospital-onset episodes more frequently (64.4 vs. 28.9%, p=0.001), longer duration of symptoms prior to treatment (15.9±12.7 vs. 9.6±10.1 days, p=0.001) and detectable ascites on abdominal ultrasound (64.4 vs. 33.3%, p=0.005). Cure rate was significantly higher among patients treated with tigecycline (75.6 vs. 53.3%, p=0.04). Overall and 90-day mortality rates were lower among cases (37.8 vs. 46.7%, p=0.5; 4.4 vs. 11.1%, p=0.4), in-hospital mortality was similar between groups (33.3 vs. 35.6%, p=1.0). In-hospital, 90-day and overall relapse
rates did not differ between cases and controls (6.7 vs. 8.9%, p=1.0; 8.9 vs. 8.9%, p=1.0; 15.6 vs. 17.8%, p=1.0). Colectomy was only needed in the control group (0 vs. 4.4%, p=0.4). Overall complication and sepsis rates were significantly lower among patients treated with tigecycline (28.9 vs. 53.3%, p=0.03; 15.6 vs. 40.0%, p=0.01). Rates of toxic megacolon were equal (6.7 vs. 6.7%, p=1.0), ileus was more frequent in the case group (11.1 vs. 8.9%, p=1.0).

**Conclusions:** Favorable outcomes suggest that tigecyclin could be used effectively as an alternative agent in cases of sCDI refractory to standard therapy.