Tygecycline versus INR increase: more than expected?

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Background: Tigecycline is a glycylcycline antibiotic used for the treatment of complicated-skin and soft tissue infections, complicated-intraabdominal infections and community-acquired bacterial pneumonia. Tigecycline-associated gastrointestinal side effects such as nausea, vomiting and diarrhea related to the tigecycline, are common (>10%). Prolonged prothrombin time / INR and partial thromboplastin time are considered to be among the rare side effects (<2%). However, during clinical practice, we observed that, prolonged INR side effect could be more than 2%. Herein, we aimed to investigate the frequency of coagulation disorder side effect of tigecycline.

Materials/methods: Patients who were hospitalized in the oncology, neurosurgery or infectious diseases clinics between June - September 2016 and treated with tigecycline, were extracted from hospital database and retrospectively reviewed. INR values at the beginning and end of treatment were compared. INR increase was evaluated according to the American National Institute of Allergy and Infectious Diseases Division of Microbiology and Infectious Diseases (DMID) Adult Toxicity criteria (https://www.niaid.nih.gov/sites/default/files/dmidadulttox.pdf).

Results: By analysing the hospital database we identified 79 patients who received tigecycline. Nineteen patients were excluded from the study since INR was not measured at the beginning and/or end of treatment. In 55 of the 60 patients, INR levels were within normal limits (0.9-1.2) at the beginning of treatment while 19 of 55 (34.5%) had prolonged INR after treatment. Prolongation was found to be mild (1.01 - 1.25 x ULN-upper limit of normal) in 12 of 19 patients, moderate (1.26-1.5 x ULN) in six and severe (1.51 -3.0 x ULN) in one. In 10 of 19 patients tigecycline, was stopped, and the INR values returned to normal. One of the patients had comorbidity (liver malignancy/disease) that could cause prolonged INR while two had concurrent use of rifampicin with tigecycline. There was no difference in INR abnormality rate between tigecycline monotherapy (9/27 - 33%) versus combination therapy receiving cases (10/33 – 30%).

Conclusions: Tigecycline is a commonly preferred antibiotic in daily Infectious Diseases practice. Our data show that the side effect of INR prolongation may be as high as 34.6 %. Our findings suggest that regular INR follow-up may be beneficial in cases receiving tigecycline.