Hypofibrinogenaemia associated with the administration of tigecycline

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Poster EP-421

Background

- Tigecycline is a semisynthetic glycylcycline antimicrobial agent with a broad spectrum of in vitro activity against Gram positive and Gram negative pathogens with the exception of *Pseudomonas aeruginosa* [1].
- Off label prescription of tigecycline has been utilized in critically ill patients because of its efficacy against carbapenemase producing *Acinetobacter baumannii* and *Klebsiella pneumoniae,* in combination with the deficit of active antimicrobial for these pathogens[2].
- The most common adverse event are gastrointestinal disorders [1].
- To our knowledge, the first reported cases of alteration in coagulation parameters regarding hypofibrinogenaemia and increase in international normalized ratio (INR) and activated partial thromboplastin time values (aPTT) as adverse event associated with the use of tigecycline are reported.

Material and Methods

- Patients receiving tigecycline at a tertiary hospital from 2012 until 2013 empirically based on colonization or for documented MDR infections were recorded.
- Patients with liver disease, coagulation disorders and severe bleeding were excluded.
- Tigecycline was administered at a dose of 50mg every 12 hours with a loading dose of 100mg.
- Demographics, clinical characteristics and hematology and coagulation variables were recorded during treatment with tigecycline and after cessation of tigecycline therapy.
- Overall differences of the measured parameters at the measurements after the tigecycline initiation and cessation were assessed with the Friedman test of repeated measures, while differences between subsequent measurements and the measurements at initiation and cessation were assessed with Wilcoxon signed ranks matched pairs tests. Statitistical significance was set at 0.05.

Results

- A total of 205 patients received tigecycline during the two year period.
- 23 patients (10%) were found with hypofibrinogenemia during treatment with tigecycline.
- Type of infections where tigecycline was administered were ventilator associated pneumonia (11), intra-abdominal infections (8) and bacteremia (4).

Graph 1. Graphical representation of plasma fibrinogen concentration, INR and aPTT and PLT during treatment and after tigecycline cessation. Boxes represent interquartile ranges and whiskers show ranges. Statitistical significance was set at * $p < 0.05$.

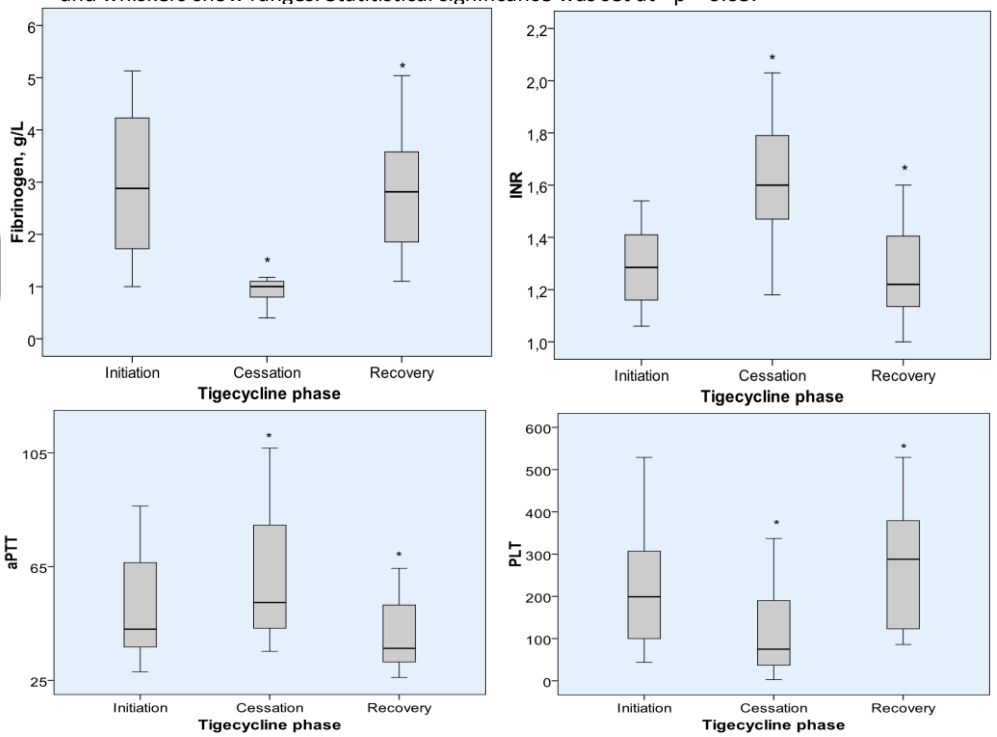

Table 1. Demographic characteristics of patients with hypofibrinogenaemia

Characteristic	
Mean age, years (range)	74 (51 - 80)
Gender	
Male, n	15
Female , n	7
Charslon comorbidity Index, median (range)	6 (3-10)
APACHE II score, median (range)	19 (8-30)

Table 2. Outcome and time of decrease of fibrinogen levels and normalization after termination of tigecycline

Outcome	
Decrease of fibrinogen levels, time after initiation of tigecycline, day median (range)	8 (4-20)
Normalization of fibrinogen levels after termination of tigecycline, day, median (range)	3 (1-6)
Administration of human fibrinogen concentrate due to bleeding disorders, pts	7
Incidence of hypofibrinogenaemia	10%

Conclusions

- Hypofibrinogemaenia is an important adverse effect of tigecycline and occurs after a median period of 8 days of treatment with a incidence of 10%.
- Close monitoring of fibrinogen levels and coagulation parameters are advised during tigecycline treatment in the critically ill patients and discontinuation of tigecycline is obligatory when fibrinogen level declines below 1.2 g/L.

References

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2. Poulakou G et al. J Infect. 2009;58:273-84

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