Poster

[P27-1] P27-1: Anti-infective drugs (6): Anti-MRSA and antifungals

Chair: Yasuhiro Tsuji, Japan

Wed. Sep 27, 2017 12:30 PM - 1:30 PM Annex Hall (1F)

(Wed. Sep 27, 2017 12:30 PM - 1:30 PM Annex Hall)

[P27-1-6] Prediction of thrombocytopenia associated with linezolid based on pharmacokinetic-pharmacodynamic simulation

Tetsushu Onita[1], Noriyuki Ishihara[2], Nobuhiro Nishimura[3], Hiroki Tamaki[4], Kazuro Ikawa[5], Norifumi Morikawa[6], Kohji Naora[7] (1.Shimane University Hospital, 2.Shimane University Hospital, 3.Shimane University Hospital, 4.Shimane University Hospital, 5.Hiroshima University, 6.Hiroshima University, 7.Shimane University Hospital)

Keywords: linezolid, thrombocytopenia, pharmacokinetic-pharmacodynamic simulation

Background

Linezolid is used for the treatment of methicillin-resistant *Staphylococcus aureus* (MRSA) infections. However, linezolid treatment is often discontinued due to the occurrence of its adverse effect, thrombocytopenia. Recent studies have reported that renal dysfunction increased linezolid trough concentration (C_{min}) and that higher drug exposure induced thrombocytopenia. This study investigated the relationship between the incidence of linezolid-induced thrombocytopenia and the safety probability predicted by pharmacokinetic-pharmacodynamic simulation.

Methods

This was a retrospective study of hospitalized patients with MRSA infections in Shimane University Hospital during 2010-2014. Mild and severe thrombocytopenia was defined as a decreased to 70% and 30% in the ratio of platelet counts during linezolid treatment to the baseline levels, respectively. Monte Carlo simulation was performed using two population pharmacokinetic (PPK) parameters with covariates such as renal function (Matsumoto et al. 2014 and Sasaki et al. 2011). The probability of target attainment (%) was determined as the fraction that achieved C_{min} <8 mg/L, and “safety probability achievement” was defined as the probability was 70%.

Results

The age, body weight and creatinine clearance of 32 patients who satis ed the selection criteria were 74.0 ± 12.0 (mean ±standard deviation) years old, 53.2 ±11.1 kg and 50.5 ±41.2 mL/min, respectively. All patients received 600 mg every 12 h linezolid, and 16 of whom developed thrombocytopenia (11 mild cases and 5 severe cases). Using PPK parameters of Matsumoto et al., the incidence of thrombocytopenia was 1.7 times higher in the non-achievement group (13 of 23 [56.5%]) than in the safety-probability-achievement group (3 of 9 [33.3%]). Using PPK parameters of Sasaki et al., the incidence of thrombocytopenia was twice higher in the non-achievement group (15 of 28 [53.6%]) than in the safety-probability-achievement group (1 of 4 [25%]). The severe cases were included almost in the non-achievement group for both Matsumoto parameters (4 of 5 [80%]) and Sasaki parameters (5 of 5 [100%]). These predicted values corresponded well to the incidence rates.

Conclusions

This study suggested that the pharmacokinetic-pharmacodynamic simulation using PPK parameters with covariates such as renal function is useful for predicting the onset of thrombocytopenia associated with linezolid.