Piperacillin/Tazobactam Versus Meropenem for Empirical Treatment of Febrile Neutropenia in Hematological Patients in Siriraj Hospital: A Randomized Controlled Non-Inferiority Trial

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Background: Carbapenems have been widely used as empirical therapy in several situations, including febrile neutropenia, resulting in the increased prevalence of carbapenem-resistant enterobacteriaceae (CRE). Piperacillin/tazobactam, a penicillin derivative with narrower antimicrobial spectrum can be used interchangeably to meropenem in febrile neutropenic patients.

Objective: To investigate whether piperacillin/tazobactam (PT) is non-inferior to meropenem (M) for the empirical treatment of febrile neutropenia in hematological patients.

Methods: An open-label, randomized controlled, non-inferiority study was conducted in Siriraj Hospital between January and December 2017. Adult hematological patients with febrile neutropenia were enrolled with 1:1 randomization into PT and M groups. Primary outcome was clinical response within 14 days. The clinical response difference of 10% margin was considered as non-inferiority.

Results: A total of 109 episodes of febrile neutropenia were assessed and 93 episodes were eligible for the study. Forty-six episodes were randomly assigned to the PT group and 47 episodes to the M group. There were more male patients in the M group (70.2% vs 50%, p = 0.046). Underlying hematological diseases were comparable between the two groups and lymphoma was the most common diagnosis (46.2%), followed by acute myeloid leukemia (41.9%). Approximately, 37% and 31.9% of febrile neutropenic subjects were enrolled during the first chemotherapy in the PT and the M groups, respectively. Categorized by MASCC score of < 21, there were comparable proportion of high risk patients in both groups (30.4% vs 31.9% in PT and M, respectively). Clinical response within 14 days in the PT and the M groups was 78.3% and 68.1%, respectively (difference 10%; 95% confidence interval, -7% to 28%, P = 0.268). Comparing between the PT and the M group, there were similarity in 28-day mortality (4.3% vs 4.3%, P = 1.00), median duration of fever (3 days vs 3 days, P = 0.293), and adverse drug reaction (6.5% vs 12.8%, P = 0.486).

Conclusion: For empirical treatment of febrile neutropenia in hematological patients, piperacillin/tazobactam is non-inferior to meropenem in terms of clinical response with comparable 28-day mortality, duration of fever, and adverse drug reactions.

Keywords: Febrile neutropenia, Piperacillin/tazobactam, Meropenem, Hematologic malignancy