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Empiric piperacillin-tazobactam versus carbapenem in febrile neutropenia : increased incidence of invasive pulmonary aspergillosis

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Background: Febrile neutropenia (FN) is a common complication in cancer patients receiving myelosuppressive chemotherapy and pose a mortality risk. Empiric broad spectrum antimicrobial therapy can be life-saving. Piperacillin-tazobactam and carbapenems are commonly employed in these instances. The objective was to compare the clinical outcomes of piperacillin-tazobactam and carbapenems as empiric therapy in oncology and haematology patients with febrile neutropenia.

Material/methods: In a retrospective analysis, we compared the effects of empiric piperacillin-tazobactam versus carbapenems in the management of febrile neutropenia. We constructed a logistic regression model to estimate a propensity score for each patient's probability of receiving a treatment given pre-treatment characteristics. The propensity score model was estimated using the following variables: age, gender, ethnicity, underlying condition, stem cell transplant recipient, multinational association for supportive care in cancer (MASCC) score and antimicrobial prophylaxis. The outcomes of interest were death, incidence of drug-resistant gram-negative organism, gram-positive organism and invasive pulmonary aspergillosis, length of treatment and hospitalisation.

Results: There were 353 and 370 patients receiving piperacillin-tazobactam and carbapenem respectively before matching, and 234 patients in each group after matching. The all-cause mortality was 6% (43/723) There was no significant difference in the incidence of death for both the matched (4.3% vs 6.8%, p = 0.226) and unmatched (5.1% vs 6.8%, p = 0.346) cohorts.

There was a higher incidence of invasive pulmonary aspergillosis in both the matched (2.6% vs 6.8%, p = 0.029) and unmatched (2.0% vs 8.4%, p = 0.000) cohorts. In the unmatched cohort, there were higher incidences of culture results positive for extended-spectrum beta-lactamase (ESBL)- producing (5.8% vs 23.2%, p = 0.000) and drug-resistant gram-negative organisms in the carbapenem group (9.9% vs 30.8%, p = 0.000). However, those receiving piperacillin-tazobactam were more likely to succumb when confronted with such organisms (20.7% vs 7.0%, p = 0.084). There were few gram-positive organisms (overall <1%) and no difference was found in both group. These differences were not significant in the matched cohort. There were no significant differences in the length of hospitalisation (median: 20 vs 24 days, p = 0.926) and antibiotic treatment (median: 10 vs 10 days, p = 0.612).

Conclusions: In a cohort of oncology and haematology patients, a higher incidence of invasive pulmonary aspergillosis was observed in patients receiving empiric carbapenem therapy for febrile neutropenia. This was observed despite using propensity score matching to adjust for confounders presented by the two treatment group in terms of age, risk of FN complications and stem cell transplant recipient.