A meta-analysis of piperacillin/tazobactam and carbapenems in cancer patients with febrile neutropenia

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Introduction

Survival rates in cancer patients have increased significantly in parallel with the advances in chemotherapy and supportive care. However, febrile neutropenia is one of the major complications during treatment, causing morbidity and even mortality.

Therefore, in case of febrile neutropenia, empiric antimicrobial treatment should be started immediately [1]. Initial antibiotic treatment should have a wide spectrum, bactericidal and anti-pseudomonal activity [2].

Piperacillin is a broad-spectrum ureido-penicillin and tazobactam is a beta-lactamase inhibitor, active against many Gram-positive and most Gram-negative pathogens, including *Pseudomonas aeruginosa* and anaerobic pathogens [3]. Carbapenems are effective for most of the bacteria responsible for infections in neutropenic patients. They are the most common antimicrobials used as monotherapy in these patients [4]. They have excellent microbiological activity against both Gram-negative and Gram-positive bacteria and are the treatment of choice for extended spectrum beta-lactamase (ESBL) producing Gram-negative bacterial infections.

Our objective was to evaluate the risk of treatment failure in cancer patients treated with piperacillin/tazobactam or carbapenems as initial empiric treatment for febrile neutropenia.

Methods

We performed a meta-analysis of randomized controlled trials identified in PubMed and Cochrane library (inception to May 2013). We decided to focus our attention to randomized clinical trials of febrile neutropenia in which at least one treatment arm consisted of piperacillin/tazobactam or a carbapenem. The efficacy outcome was the risk of treatment failure assessed at the test-of-cure visit and expressed as Risk Ratio (RR).

Results

Of 131 articles reviewed, 11 studies, involving 2100 patients, have been included in our meta-analysis. Treatment failure occurred in 20% and in 14% of patients treated with piperacillin/tazobactam and carbapenem monotherapy regimens, respectively. There was no significant difference in treatment failure when cancer patient were treated with piperacillin/tazobactam or carbapenems (RR: 0.75 [0.50 – 1.14]).

Conclusions

The results obtained in this study demonstrate with sufficient evidence that both piperacillin/tazobactam and carbapenems are effective in the treatment of febrile neutropenia in cancer patients, confirming their validity especially in empirical therapy. However, recent studies [5] have shown that carbapenems result in a higher rate of antibiotic and *Clostridium difficile*-associated diarrhea.

References

[1] Hughes WT, Armstrong D, Bodey GP, Bow EJ, Brown AE, Calandra T, Feld R, Pizzo PA, Rolston KV, Shenep JL, Young LS. Guidelines for the use of antimicrobial agents in neutropenico patients with cancer. *Clin Infect Dis* 2002; 34:730–751.

[2] An MM, Zou Z, Shen H, Zhang JD, Chen ML, Liu P, Wang R, Jiang YY. Ertapenem versus piperacillin/tazobactam for the treatment of complicated infections: a meta-analysis of randomized controlled trials. *BMC Infect Dis.* 2009; 9:193-203.

[3] Hamidah A, Rizal AM, Nordiah AJ, Jamal R. Piperacillin–tazobactam plus amikacin as an initial empirical therapy of febrile neutropenia in paediatric cancer patients. *Singapore Med J* 2008; 49:26–30.

[4] Hung KC, Chiu HH, Tseng YC, Wang JH, Lin HC, Tsai FJ, Peng CT. Monotherapy with meropenem versus combination therapy with ceftazidime plus amikacin as empirical therapy for neutropenic fever in children with malignancy. J Microbiol Immunol Infect 2003; 36:254–9.

[5] Paul M, Yahav D, Bivas A, Fraser A, Leibovici L. Anti-pseudomonal beta-lactams for the initial, empirical, treatment of febrile neutropenia: comparison of beta-lactams. Cochrane Database Syst Rev. 2010, Issue 11. Art. No.: CD005197.