Comparison of anti-anaerobic antimicrobial strategies in cancer patients with febrile neutropenia and gastrointestinal symptoms

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Introduction

Empirical therapy using an antipseudomonal, broad-spectrum antibiotic is part of the initial management of febrile neutropenia (FN). Anti-anaerobic coverage is usually recommended by guidelines as part of the initial treatment when gastrointestinal (GI) symptoms (eg, abdominal pain, diarrhea, perianal pain) are present. Unfortunately, only scarce data regarding the optimal anti-anaerobic antimicrobial strategy for patients with FN and GI symptoms are available.

Objective

To compare the mortality rates of hospitalized adult cancer patients with FN and GI symptoms who either underwent monotherapy using an antibiotic with antipseudomonal and anti-anaerobic activity (piperacillin-tazobactam or a carbapenem) or were treated with a combination of cefepime and metronidazole.

Methods

We performed a prospective cohort study in a single tertiary hospital from October 2009 to August 2011. All consecutive adult cancer patients admitted to the hematology ward with FN secondary to intensive chemotherapy and GI symptoms (abdominal pain, diarrhea or perianal pain) were evaluated. Kaplan-Meier curves were used for calculating time-dependent occurence of death. For comparison between groups, the log-rank test was applied.

Results

Table 1. Characteristics of patients with febrile neutropenia (FN) and gastrointestinal symptoms.

Variable	Combination therapy* group (n=22)	Monotherapy† group (n=15)	*P*
Age, years, mean (SD)	44.7 (14.3)	41.2 (11.0)	0.43
Female sex	15 (68.1)	5 (33.3)	0.05
Type of Cancer			0.18 ✦
Acute myeloid leukemia	6 (27.3)	7 (46.7)	
Acute lymphoblastic leukemia	4 (18.2)	2 (13.3)	
Chronic myeloid leukemia	1 (4.5)	2 (13.3)	
Multiple myeloma	6 (27.3)	0 (0)	
Lymphoma	5 (22.7)	3 (20.0)	
Other solid tumors	0 (0)	1 (6.7)	
Relapsing underlying disease	13 (59.0)	12 (80.0)	0.28
Clinical comorbidity	5 (22.7)	7 (46.6)	0.16
High dose chemotherapy regimens	12 (54.5)	9 (60.0)	0.74
Nosocomial-acquired episode of FN	19 (86.3)	13 (86.6)	0.97
ANC at the time of diagnosis of FN, median cells/mm³ (IQR)	80 (160)	130 (360)	0.47
ANC <100 cells/mm³ at the time of diagnosis of FN	13 (59.0)	6 (40.0)	0.32
High-risk MASCC score	8 (36.3)	2 (13.3)	0.15
Neutropenic enterocolitis	1 (4.5)	1 (6.6)	0.99
Pseudomembranous colitis	1 (4.5)	1 (6.6)	0.99
Documented aerobic bacteremia	8 (36.3)	9 (60.0)	0.19
In vitro resistance of aerobic blood isolates to initial antibiotic treatment	1 (4.5)	2 (13.3)	0.55

Data presented as n (%) unless otherwise indicated. *Cefepime + metronidazole; †Piperacillin-tazobactam or imipenem or meropenem. ✦Chi-square test for goodness of fit; ANC Absolute neutrophil count; HSCT Hematopoietic stem cell transplantation; IQR Interquartile range (P75 – P25); MASCC Multinational Association for Supportive Care in Cancer; SD Standard deviation.

Figure 1. Survival curves according to antibiotic strategy in patients with febrile neutropenia and gastrointestinal symptoms.

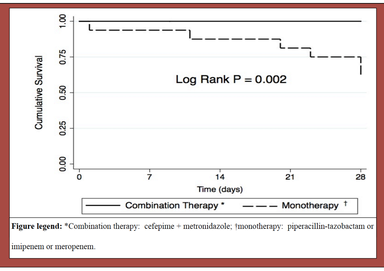

Figure legend: *Combination therapy: cefepime + metronidazole; †monotherapy: piperacillin-tazobactam or imipenem or meropenem.

Conclusions

The present study demonstrated higher survival rates in adult cancer patients with FN who presented with GI symptoms treated with a combination of a fourth-generation cephalosporin plus metronidazole compared with those who underwent monotherapy using a broad-spectrum antibiotic with antipseudomonal and anti-anaerobic activity.

These findings have scientific plausibility as an antimicrobial strategy using a combination of cefepime and metronidazole has better coverage for anaerobic pathogens than a monotherapy strategy (piperacillin-tazobactan or a carbapenem).

Given the scarce data in the literature regarding this important issue, larger randomized trials are required to confirm the superiority of combination cefepime-metronidazole treatment over broad-spectrum monotherapies in patients with FN and GI symptoms.

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