Poster : 1044

Influence of ciprofloxacin prophylaxis on the antimicrobial susceptibility profile of gram-negative bacilli recovered from the bloodstream of patients admitted to a hematology/bone marrow transplant service

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Abstract

Background: Fluoroquinolones are widely prescribed for febrile neutropenia prophylaxis. However, antimicrobial-resistant bacteria can be selected out during their use. The primary objective of this study was to determine the impact of ciprofloxacin (CIP) prophylaxis on the antimicrobial susceptibility profile of gram-negative bacilli isolated from the bloodstream of patients admitted to a hematology/bone marrow transplant (BMT) service.

Methods: Patients admitted to a hematology/BMT service in Winnipeg (Manitoba, Canada) between 2010 and 2015 with gram-negative bacteremia were retrospectively identified from a review of the microbiology laboratory database. Patients could be included more than once in the analysis if at least one week had passed between bacteremia episodes. A chart review was performed for all patients. Abstracted data included patient demographic information, the isolate antimicrobial susceptibility profile, and receipt (or not) of CIP prophylaxis.

Results: In total, 70 episodes of gram-negative bacteremia occurred among 48 patients over the study period (susceptibility profile in the table below). The most common pathogens were *Escherichia coli* (36%), *Pseudomonas aeruginosa* (14%), *Klebsiella pneumoniae* (13%), *Stenotrophomonas maltophila* (9%), and *Acinetobacter* spp. (7%). Twenty isolates were recovered from patients receiving CIP prophylaxis.

	% Susceptible (number susceptible/number tested)			
Antimicrobial	**All isolates**	**Isolates from patients not on CIP prophylaxis**	**Isolates from patients on CIP prophylaxis**	**P value for CIP prophylaxis vs no prophylaxis (chi-square test)**
Ceftazidime	80.9 (55/68)	85.7 (42/49)	68.4 (13/19)	0.10
CIP or levofloxacin	55.1 (38/69)	70.0 (35/50)	15.8 (3/19)	<0.01
Gentamicin	73.9 (51/69)	84.0 (42/50)	47.3 (9/19)	<0.01
Meropenem	88.4 (61/69)	92.0 (46/50)	78.9 (15/19)	0.13
Piperacillin-tazobactam	77.9 (53/68)	81.6 (40/49)	57.8 (11/19)	0.03

Conclusion: Gram-negative bacilli recovered from the bloodstream of patients receiving CIP prophylaxis tended to be more resistant to all antimicrobials evaluated, relative to those isolates recovered from patients not on prophylaxis. Meropenem was the most active antimicrobial, with 88.4% of isolates remaining susceptible in vitro.

Introduction

The use of quinolone prophylaxis in high-risk neutropenic patients is now considered the “standard of care” and is recommended by major societal guidelines.[1,2,3] Prophylaxis with ciprofloxacin (CIP) and levofloxacin has been demonstrated to reduce infections and mortality in high-risk patients.[4,5] However, some data suggest an association between the use of quinolone prophylaxis and infections with fluoroquinolone-resistant bacteria.[3] Only a small number of studies have specifically looked into the effect of fluoroquinolone prophylaxis on antimicrobial resistance in immunocompromised patients. The primary objective of this study was to determine the impact of CIP prophylaxis on the antimicrobial susceptibility profile of gram-negative bacilli isolated from the bloodstream of patients admitted to a hematology/bone marrow transplant (BMT) service.

Methods

Patients admitted to a hematology/BMT service in Winnipeg (Manitoba, Canada) between 2010 and 2015 with gram-negative bacteremia were retrospectively identified from a review of the microbiology laboratory database. Patients could be included more than once in the analysis if at least one week had passed between bacteremia episodes. A chart review was performed for all patients. Abstracted data included patient demographic information, the isolate antimicrobial susceptibility profile, and receipt (or not) of CIP prophylaxis. Patient characteristics related to malignancy, chemotherapy, and stem cell therapy were also recorded. Descriptive statistics were used to analyze the collected data.

Results

Table 1. gram-negative bacilli recovered from the bloodstream of patients on ciprofloxacin prophylaxis

Organism	Frequency
Acinetobacter spp.	1
Brevundimonas spp.	1
Escherichia coli	11
Leptotrichia spp.	1
Pseudomonas aeruginosa	2
Rhizobium spp.	1
Stenotrophomonas maltophilia	3

Table 2. gram-negative bacilli recovered from the bloodstream of patients not on ciprofloxacin prophylaxis

Organism	Frequency
Acinetobacter spp.	4
Brevundimonas spp.	1
Enterobacter cloacae	3
Escherichia coli	14
Fusobacterium spp.	1
Klebsiella pneumoniae	9
Moraxella spp.	1
Pseudomonas aeruginosa	8
Pseudomonas oryzyhabitans	3
Pseudomonas putida	2
Stenotrophomonas maltophilia	3
Sphingomonas spp.	1

Table 3. Antimicrobial susceptibility profile of gram-negative bacilli recovered from patients on a hematology/BMT ward, stratified by the presence or absence of CIP prophylaxis

	% Susceptible (number susceptible/number tested)			
Antimicrobial	**All isolates**	**Isolates from patients not on CIP prophylaxis**	**Isolates from patients on CIP prophylaxis**	**P value for CIP prophylaxis vs no prophylaxis (chi-square test)**
Ceftazidime	80.9 (55/68)	85.7 (42/49)	68.4 (13/19)	0.10
CIP or levofloxacin	55.1 (38/69)	70.0 (35/50)	15.8 (3/19)	<0.01
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Piperacillin-tazobactam	77.9 (53/68)	81.6 (40/49)	57.8 (11/19)	0.03

In total, 70 episodes of gram-negative bacteremia occurred among 48 patients over the study period. Twenty isolates were recovered from patients receiving CIP prophylaxis (Table 1). The most common pathogens were *Escherichia coli* (36%), *Pseudomonas aeruginosa* (14%), *Klebsiella pneumoniae* (13%), *Stenotrophomonas maltophila* (9%), and *Acinetobacter* spp. (7%) (Table 1, Table 2). The aggregate isolate susceptibility profile is presented in Table 3.

Limitations

- Only a small number of isolates were included in the study.
- Clinical and Laboratory Standards Institute breakpoints for certain antimicrobials changed over the study period. All data presented here reflects categorical interpretations based on breakpoints at the time that testing was performed.
- Fluoroquinolone susceptibility generally reflects susceptibility to ciprofloxacin for all organisms except *Stenotrophomonas* (for which levofloxacin was tested).,
- Patients could be included more than once in the study.
- Susceptibility testing was performed by a variety of different methods.

Conclusions

- Gram-negative bacilli recovered from the bloodstream of patients receiving CIP prophylaxis tended to be more resistant to all antimicrobials evaluated, relative to those isolates recovered from patients not on prophylaxis.
- Meropenem was the most active antimicrobial, with 88.4% of isolates remaining susceptible in vitro.

References

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ID WEEK, New Orleans, LA, October 26 to 30, 2016