#2331

Comparison of Ciprofloxacin versus Levofloxacin and Rate of Breakthrough Infection in Hematopoietic Stem Cell Transplant Patients

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Abstract

Background: Infection is a serious complication of hematopoietic stem cell transplantation and guidelines recommend fluoroquinolone prophylaxis. Ciprofloxacin was recently replaced by levofloxacin as the preferred agent on the Northwestern Memorial Hospital (NMH) formulary. The study objective is to compare differences in rate of breakthrough infections for ciprofloxacin versus levofloxacin prophylaxis in an autologous stem cell transplant population.

Methods: This is a retrospective, cohort study comparing consecutive patients that received ciprofloxacin (1/2007-5/2008) prophylaxis vs. levofloxacin (1-12/2015) prophylaxis for adult autologous HSCT with multiple myeloma who received high-dose melphalan. Endpoints include: differences in rectal colonization with VRE, time to engraftment, length of treatment, *Clostridium difficile* infection, rate of febrile neutropenia, incidence of breakthrough infections, and inpatient mortality. This study was IRB approved by Northwestern University.

Results: 164 ciprofloxacin and 155 levofloxacin patients were included. There was no difference in baseline characteristics, length of treatment, *Clostridium difficile* infection, or febrile neutropenia between the study groups. There was a significantly higher incidence of bloodstream infections in the ciprofloxacin group (24/154) compared to levofloxacin group (10/143) p=0.03, primarily caused by a statistically higher incidence of gram positive bloodstream infections (ciprofloxacin (21/154) versus levofloxacin (8/143); p<0.01). Significantly higher rates of VRE rectal colonization were seen in ciprofloxacin-treated patients (p<0.01). There was no difference in inpatient mortality.

Conclusion: Ciprofloxacin prophylaxis was associated with a significantly higher rate of breakthrough bloodstream infections during HSCT compared to levofloxacin, with no difference in inpatient mortality.

Introduction

- Due to several risk factors for infection (e.g. neutropenia, chemotherapy damage to GI mucosa, central venous access) many autologous hematopoietic stem cell transplant (HSCT) patients develop infections
- ASBMT/IDSA/CDC guidelines recommend fluoroquinolone prophylaxis
- Many institutions utilize different fluoroquinolones
- Ciprofloxacin was replaced by levofloxacin as the preferred agent on the Northwestern Memorial Hospital (NMH) formulary

Objective

- To compare differences in rate of breakthrough infections for ciprofloxacin versus levofloxacin prophylaxis in an autologous stem cell transplant population

Methods

Study Design
- Retrospective, cohort study
- Study Period: Jan 2015 to Dec 2015 for levofloxacin patients compared to a historical control of consecutive ciprofloxacin patients from Jan 2007 to May 2008

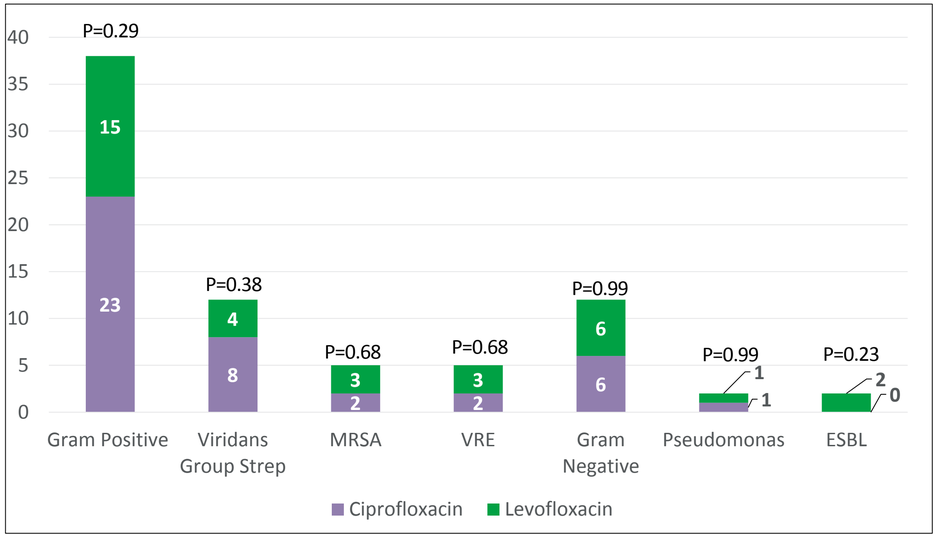
Patient Selection
- Inclusion Criteria: Patients ≥ 18 y/o that received autologous stem cell transplant for multiple myeloma with a high-dose melphalan regimen (140-200mg/m^2), received prophylaxis with a fluoroquinolone, and were treated during initial hospitalization for transplant
- Exclusion Criteria: Fluoroquinolone allergy or contraindication to fluoroquinolone therapy

Endpoints
- Primary: Comparison of all microbiologically documented infections for patients receiving levofloxacin prophylaxis versus ciprofloxacin prophylaxis
- Secondary endpoints: Differences with colonization with MRSA and VRE, rate of febrile neutropenia, time to engraftment, rate of *Clostridium difficile* infections, differences in site of infection, differences in organism isolated

Statistical Analysis
- Chi-square, Fisher's exact, Student's T-test, and Wilcoxon Rank-sum were used in analyses as appropriate
- All statistical analyses were performed with Intercooled Stata, version 13 (Statacorp, College Station, TX)

Results

Figure 1. Comparison of Organisms Isolated for Ciprofloxacin vs. Levofloxacin



Results (continued)

Table 1. Patient Demographics

	Ciprofloxacin n=154	Levofloxacin n=143	p-value
Age, years (median, IQR)	59 (53-64)	60 (55-67)	0.02
Gender, female (n,%)	69 (44.8)	64 (44.8)	0.99
MRSA Surveillance (n,%)	3 (2)	0 (0)	0.25
VRE Surveillance (n,%)			
Negative	131 (85)	132 (93.6)	0.61
Prior to admission	8 (5.2)	6 (4.3)	0.79

Table 2. Breakthrough Infections and Transplant Outcomes

	Ciprofloxacin n=154	Levofloxacin n=143	p-value
Breakthrough infections (n,%)	35 (22.7)	27 (18.9)	0.42
Breakthrough Infections-bacteremia (n,%)	24 (15.6)	10 (7.0)	0.03
Days to positive culture post transplant (median, IQR)	9 (7-11) n=34	8 (6-9) n=27	0.12
Number of positive cultures (median, IQR)	1 (1-2) n=35	1 (1-2) n=27	0.97
Neutropenic when cultured (n,%)	21 (61.8) n=34	21 (77.8) n=27	0.18
C diff culture positive (n,%)	8 (5.2) n=154	14 (11.1) n=126	0.07
C diff toxin positive (n,%)	8 (5.2) n=154	14 (11.6) n=121	0.053
VRE Screen Changed – to + while on FQ prophylaxis (n,%)	15 (9.7)	3 (2.1)	<0.01
Infection Source			
Blood (n, %)	24 (15.6)	10 (7.0)	0.03
Urine (n, %)	3 (1.9)	8 (5.6)	0.13
C Diff (n,%)	8 (5.2)	14 (9.7)	0.18
Lung (n,%)	3 (1.9)	2 (1.4)	0.99
Days to Engraftment (median, IQR)	12 (11-12) Range: 9-21	12 (11-13) Range: 10-19	<0.01
Neutropenic Fever (n,%)	85 (55.2)	85 (59.4)	0.46
Mortality	1	0	---

Conclusions

- Statistically significant difference (p=0.03) between ciprofloxacin and levofloxacin for blood stream infections, with no apparent difference in overall mortality between the two treatment arms
- Statistically significant difference in VRE surveillance conversion in the ciprofloxacin group compared to the levofloxacin group (p<0.01)