

Impact of Ciprofloxacin Prophylaxis on Antimicrobial Resistance in Neutropenic Leukemia/Stem Cell Transplant Patients at a Major Canadian Teaching Hospital

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Background

- Fluoroquinolone (FQ) prophylaxis is known to reduce risk of febrile neutropenia, bacteremia, and infection-related mortality
- FQ prophylaxis is hypothesized to promote gut colonization with FQ-resistant organisms
- Clinical significance of FQ-resistant bacteria in fecal flora of patients receiving prophylaxis during neutropenia has not been well studied
- At the Leukemia/Bone Marrow Transplant Unit (L/BMT), ciprofloxacin (CIP) prophylaxis is administered to acute myelogenous leukemia (AML) patients to prevent febrile neutropenia during consolidation chemotherapy
- Emergence of FQ-resistant bacteremia is of particular concern in this patient population

Objectives

- Primary:** To determine the prevalence of CIP-resistant bacteria in fecal flora before and after FQ prophylaxis
- Secondary:** To determine the relationship between CIP-resistant fecal colonization and the incidence of CIP-resistant bacteremia

Methods

- Design:** Single-centre, prospective, observational study
- Inclusion:** All AML patients admitted to L/BMT undergoing induction chemotherapy between May 2013 and August 2014
- Intervention:** Perirectal swabs were collected before induction and first consolidation chemotherapy (i.e. prior to FQ prophylaxis) and prior to each subsequent consolidation, pre BMT, and at completion of any curative chemotherapy
 - Perirectal samples were cultured for antibiotic sensitivities
 - Patients were administered CIP-based prophylaxis (500 mg PO BID); prophylaxis commenced during neutropenia with consolidation chemotherapy and was discontinued when empiric antibiotics were initiated for febrile neutropenia
- Endpoints:**
 - Incidence of CIP-resistant fecal colonization prior to and after FQ prophylaxis
 - Risk of CIP-resistant bacteremia in patients with CIP-resistant fecal colonization
 - Bacteria isolated from positive perirectal swabs

Table 1: Baseline characteristics of patients

Age, median years (range)	56 (24-74)
Male, sex (%)	44 (54)
No. of patients receiving cycles	
Consolidation 1	61
Consolidation 2	51
Consolidation 3	24
BMT	28
No. of patients with bacteremia (%)	
Induction (no prophylaxis)	32 (39)
Consolidation 1 (CIP prophylaxis)	3 (5)
Consolidation 2 (CIP prophylaxis)	8 (16)
Consolidation 3 (CIP prophylaxis)	4 (17)
BMT (no prophylaxis)	6 (21)
Duration of CIP prophylaxis, median days	9.5

Table 2: Incidence of positive perirectal swabs prior to and after prophylaxis

Chemotherapy cycle	No. of perirectal swabs collected	No. of perirectal swabs with growth (%)	Before CIP-Prophylaxis	After CIP-Prophylaxis
			No. of perirectal swabs with CIP-resistance (%)	No. of perirectal swabs with CIP-resistance (%)
Induction	81	12 (15)	11/12 (92)	-
Consolidation 1	45	9 (20)	7/9 (78)	-
Consolidation 2	36	4 (11)	-	4/4 (100)
Consolidation 3	21	3 (14)	-	3/3 (100)
Pre-BMT	24	3 (13)	-	2/3 (67)
End of therapy	15	4 (27)	-	4/4 (100)

Table 3: Prevalence of C-resistant bacteremia

Perirectal swab	CIP-resistant bacteremia	No CIP-resistant bacteremia
CIP-resistant	2	9
No CIP-resistant or no growth	1	68

Fisher's exact test, two-tailed P value = 0.0482

Results

- Eight patients received a FQ up to 14 months prior to admission; one patient grew a CIP-resistant organism on perirectal swab; two patients developed FQ-resistant bacteremia
- The majority of perirectal swabs grew *E. coli* (83%), all but one were CIP-resistant however only 8/53 (15%) of bacteremias were due to *E. coli* and 3/8 (38%) were CIP-resistant
- 92% of positive perirectal swabs grew CIP-resistant organisms before initiation of CIP-prophylaxis
- Rates of CIP-resistant stool isolates before and after prophylaxis did not appear different
- CIP-resistant bacteremia developed in 3 patients (all *E. coli* during induction); 1 developed intermediate sensitivity bacteremia (*Klebsiella*) during BMT; no patients had CIP-resistant bacteremia during consolidation cycles (while receiving CIP prophylaxis)
- Probability of CIP-resistant bacteremia in a patient colonized with a CIP-resistant organism is 20%
- Probability of bacteremia with a CIP-resistant organism in a patient not colonized with a CIP-resistant organism is 1%
- Incidence of gram-negative bacteremias were 37% at induction (i.e. no CIP prophylaxis) vs. 0-25% during consolidation (i.e. CIP prophylaxis)
- For gram-positive bacteremias, the incidence was 50% at induction vs. 75-100% during consolidation

Conclusions

- The majority of patients were colonized with CIP-resistant organisms prior to CIP prophylaxis
- CIP-resistant bacteremia can occur in patients with CIP-resistant fecal colonization
- Limitation:** A low number of perirectal swabs grew bacteria; this may have been due to poor sampling technique
- Acknowledgements:** We thank the L/BMT Program staff who collected perirectal samples
- CIP-resistant bacteremia was unlikely during CIP prophylaxis