Colonization with Ceftriaxone-Resistant Enterobacteriaceae and Risk of Bacteremia in Patients Receiving Induction Chemotherapy for Acute Leukemia

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ABSTRACT

Background: Bacteremia caused by ceftriaxone-resistant Enterobacteriaceae (CRO-R-E) is associated with ineffective empirical therapy and high mortality in neutropenic patients with leukemia. Increased knowledge of rates of CRO-R-E colonization and risk of bacteremia in these patients is needed.

Methods: From Nov 2015 – Aug 2017, we collected stool or perianal swabs from patients with acute leukemia upon initiation of induction chemotherapy and weekly thereafter during neutropenia. Only patients with acute lymphoblastic leukemia received empirical ceftriaxone prophylaxis. Patients with <7 days of neutropenia during their inpatient admission were excluded. We plated samples onto ESBL screening agar, identified isolated bacteria, performed antimicrobial susceptibility testing, and screened CRO-R-E for β-lactamase genes by PCR. We then determined the prevalence of CRO-R-E colonization at the onset of chemotherapy and the incidence of acquiring CRO-R-E or detecting bacteremia during the hospitalization.

Results: We analyzed 100 patients. Their median age was 64 years, 71% had acute myeloid leukemia, and the median duration of neutropenia was 20 days. Nineteen patients (20%) were initially colonized with CRO-R-E, including 13 (61%) of 81 patients with newly diagnosed leukemia and 6 (32%) of 19 patients with relapsed or refractory disease. There were 23 colonizing CRO-R-E isolates from 23 patients (11 E. coli, 4 Klebsiella pneumoniae, 13 Citrobacter spp.). Of 54 patients not initially colonized with CRO-R-E who had weekly samples collected, 7 (13%) acquired CRO-R-E during their admission. Two (11%) of the 19 patients colonized with CRO-R-E developed CRO-R-E bacteremia (one CTX-M-producing E. coli and one KPC-producing K. pneumoniae), compared to only one (1%) of 81 patients not initially colonized with CRO-R-E (P=0.09).

Conclusions: Patients with acute leukemia have high rates of colonization with CRO-R-E upon initiation of chemotherapy. In a setting where a minority of patients receive prophylaxis, competent empirical therapy is urgently needed. We would like to acknowledge the patients who volunteered for this study, NIAID for funding this study (K23 AI114994), and Hardy Diagnostics for providing HardyCHROM™ ESBL agar plates.

INTRODUCTION

• Ceftriaxone-resistant Enterobacteriaceae (CRO-R-E), including ESBL, AmpC, and carbapenemase-producing organisms, are increasingly common causes of bacteremia in neutropenic patients with leukemia.
• Many first-line agents for fever and neutropenia have limited activity vs. CRO-R-E, and thus neutropenic patients with CRO-R-E bacteremia often receive inadequate empirical therapy.
• This inadequate empirical therapy translates into worse clinical outcomes in neutropenic patients with CRO-R-E bacteremia.
• We hypothesize that screening patients with acute leukemia to detect gastrointestinal colonization with CRO-R-E will identify patients at high risk of developing CRO-R-E bacteremia during neutropenia.
• Primary Objective: Determine the prevalence of CRO-R-E colonization in patients receiving induction chemotherapy for acute leukemia and compare the incidence and etiologies of bacteremia in patients who are and are not colonized with CRO-R-E.

METHODS

• We collected perianal swabs or stool samples from consenting patients with acute leukemia at NewYork-Presbyterian Hospital/Weill Cornell within 5 days of initiating induction chemotherapy and weekly thereafter from November 2015 – August 2017.
• Patients were on a dedicated oncology unit with double-occupancy rooms.
• Samples were plated directly onto HardyCHROM™ ESBL agar plates without a broth enrichment step.
• Inclusion criteria: ≥7 days of neutropenia during their inpatient admission
• Exclusion criteria: 1st sample ≥5 days after starting chemotherapy

METHODS

Antimicrobial susceptibilities of colonizing CRO-R-E

RESULTS

Patient Characteristics N (out of 100 patients)
Age, years, median (IQR) 64 (47-72)
Acute leukemia type
AML 71
ALL (only patients who received levofloxacin prophylaxis) 21
Other 8
Disease status
New diagnosis 81
Relapsed or refractory 19
Chemotherapy
7-1 (cyclophosphamide + doxorubicin) 34
CTX-M (positional cyclophosphamide + doxorubicin) 11
Decitabine 10
HyperCVID 9
Other 26
Duration of neutropenia, days, median (IQR) 20 (13-26)

Colonization with CRO-R-E upon initiating chemotherapy for acute leukemia

13/81 (16%) patients with newly diagnosed leukemia were colonized with CRO-R-E
6/19 (32%) patients with relapsed or refractory leukemia were colonized with CRO-R-E

CONCLUSIONS

1) Nearly 20% of patients with acute leukemia initiating induction chemotherapy are colonized with CRO-R-E, and CTX-M-producing E. coli are most common.
2) Patients with acute leukemia receiving induction chemotherapy who are colonized with CRO-R-E are at increased risk of bacteremia while neutropenic.
3) However, in the absence of routine levofloxacin prophylaxis, the vast majority of bacteremias in colonized patients are caused by CRO-susceptible organisms, and the risk of CRO-R-E bacteremia is modest.
4) In the setting of double-occupancy rooms, >10% of patients with acute leukemia receiving induction chemotherapy acquire CRO-R-E during their hospitalization.

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