RISK OF BACTERIAL INFECTIONS IS NOT INCREASED IN CHILDREN RECEIVING ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION WITHOUT QUINOLONE PROPHYLAXIS

Abstract # 2325

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Revised Abstract

Background
The use of quinolone prophylaxis in children receiving allogenic hematopoietic stem cell transplantation (allo-HSCT) is controversial. We evaluated whether use of the prophylaxis alters the risk of developing fever or bacterial infections in this population.

Methods
Retrospective chart review of patients <18 years of age receiving HSCT at Centro Médico Imbanaco in Cali, Colombia. Two cohorts of patients were compared: Cohort 1 (2012–2014) received quinolone prophylaxis from day –3 until engraftment and cohort 2 (2015-May–2016) did not receive prophylaxis. Episodes of fever and infection between day –3 and engraftment were documented and adjusted according to duration of neutropenia.

Results
Thirty-seven children received quinolone prophylaxis and 26 did not. Median age was 10.1 years (0.7 to 18); 67% were male. The incidence rate ratio per 100 patient-days (IRR) of febrile episodes and bacterial infections in the quinolone prophylaxis group vs. no prophylaxis was 0.66 (95% CI 0.44, 0.99), p = 0.043 and 1.34 (95% CI 0.84, 2.16), p = 0.216, respectively. The rate of microbiologically documented infections per 100 patient-days was 2.47 in the prophylaxis group and 2.86 in the no prophylaxis group (IRR = 0.81 (IC 95% 0.43; 1.54), p = 0.53.
Among patients in the prophylaxis group, 11 infections (50% of the microbiologically documented infections) were caused by multiresistant gram-negative bacteria, compared to 5 (28%) in the no prophylaxis group (p = 0.15).

Conclusions
While quinolone prophylaxis reduced the risk of fever, it did not affect the risk of bacterial infections. The use of quinolone prophylaxis was associated with a non-statistically significant increase in infections due to multiresistant gram-negative bacteria. Understanding the risks and benefits of using quinolone prophylaxis promotes antimicrobial stewardship in this at-risk population.

Background

- Hematopoietic stem cell transplant can cure illnesses that are otherwise irreversible.
- Bacterial infections are major contributors to morbidity and mortality during the period of neutropenia preceding engraftment of donor stem cells.
- The use of quinolone prophylaxis during this period is controversial in children.

Objective

- To determine whether the use of quinolone prophylaxis alters the risk of developing fever or bacterial infections in pediatric patients receiving HSCT during the neutropenic period.

Methodology

- Retrospective chart review of children and adolescents (0–18 years) receiving allo-HSCT for conditions other than aplastic anemia at Centro Medico Imbanaco, in Cali, Colombia.
- Two cohorts of patients were compared. Cohort 1 (1 January 2012 to 31 December 2015) received universal quinolone prophylaxis starting 3 days before the infusion of stem cells, continuing until engraftment. Cohort 2 (1 January 2015 to 1 May 2015) received no quinolone or other antibiotic prophylaxis. Episodes of fever and bacterial infections (clinically and microbiologically documented) were recorded from 3 days before stem cell infusion until the 3rd consecutive day of absolute neutrophil count > 500 cell/uL.
- Incident rates of fever and infections were estimated and compared using risk ratios. Results were adjusted by neutropenia duration.

Results

- Thirty-seven (37) patients received prophylaxis and 26 patients received no prophylaxis.
- Demographic characteristics are shown in Table 1.

Table 1 . Demographic characteristics and pre-trasplant diagnosis of study population

Variable	No prophylaxis (n = 26)	Quinolone prophylaxis (n = 37)	P-value	Total (n = 63)
Age in years Mean ± SD	9.4 ± 4.6	10.7 ± 4.6	0.300	10.1 ± 4.6
Sex n (%)				
Male	17 (65.4)	25 (67.6)	0.856	42 (66.7)
Female	9 (34.6)	12 (32.4)		21 (33.3)
Pre-transplant diagnosis n (%)				
Acute lymphoblastic leukemia	9 (35)	27 (73)		36 (57)
Myeloid leukemia	8 (31)	3 (8)		11 (17)
Hemoglobinopathies	4 (15)	3 (8)	0.02	7 (11)
Primary immunodeficiencies	2 (8)	1 (3)		3 (5)
Metabolic disorders	1 (4)	0		1 (2)
Others	2 (8)	3 (3)		5 (8)
Days with neutropenia Median (IQR)	18.0 (13.0–21.0)	20.0 (16.0–24.0)	0.229	19.0 (14.0–23.0)
Follow-up time in days Median (IQR)	22.5 (20.0–25.0)	22.0 (20.0–26.0)	0.899	22.0 (20.0–25.0)

- Use of quinolone as prophylaxis reduced the proportion of patients with fever and duration of febrile episodes (Table 2).

Table 2. Number of patients with fever and episodes of febrile illness

Outcomes	No prophylaxis* (n = 26)	Quinolone prophylaxis (n = 37)	Incidence rate ratio [95% CI][a]	P-value[a]	Total (n = 63)
Patients with fever n (%)	26 (100)	28 (76)	NA	0.008	54 (86%)
Days with fever Median (IQR)	7 (4–10)	3 (2–7)	NA	0.042	5 (3–8)
Febrile episodes					
# of episodes	51	49			100
Rate per 100 person-days	8.11	5.52	0.66 [0.44; 0.99]	0.043	6.59

*Reference group; [a]Adjusted for days of neutropenia

- A larger proportion of patients without quinolone prophylaxis developed bacterial infection although the rate per 100 patient-days was similar (Table 3).
- Microbiologically documented infections were similar in both groups (Table 3).

Table 3. Number of patients with infections and episodes of infections

Outcomes	No Prophylaxis* (n = 26)	Quinolone prophylaxis (n = 37)	Incidence risk ratio [95% CI][a]	P-value[a]	Total (n = 63)
Patients with bacterial infections n (%)	24 (92)	26 (70)	NA	0.013	50 (79)
Episodes of bacterial infections[b]					
# of episodes	31	40			71
Rate per 100 person-days	4.92	4.50	1.34 [0.84; 2.16]	0.216	4.68
Patients with microbiologically documented Infections n (%)	14 (54)	16 (43)	NA	0.169	30 (48)
Microbiologically documented infections					
# of episodes	18	22			40
Rate per 100 person-days	2.86	2.47	0.81 [0.43; 1.54]	0.53	2.63

*Reference group; [a]Adjusted for days of neutropenia; [b]Clinically and microbiologically documented infections

- There was a non-significant trend towards increasing multidrug-resistant gram negative infections in the prophylaxis group (Table 4).

Table 4. Antimicrobial resistance of microbiologically documented infections

Outcomes	No prophylaxis*	Quinolone prophylaxis	P-value[a]
Microbiologically documented infections # of episodes	18	22	
MDR gram – infection[c] # of episodes (%)	5 (28)	11 (50)	0.15
Gram + or susceptible gram negative infection[d] # of episodes (%)	13 (72)	11 (50)	0.06

*Reference group; [a]Adjusted for days of neutropenia
[c] MDR = Multidrug resistant. *Enterobacteriacea*, n = 8; *Pseudomonas*, n = 5; other, n = 3
[d] *Staphylococci*, n = 9; *Streptococci*, n = 6; *Enterococci*, n = 3; *Enterobacteriaceae*, n = 6

Conclusion

- Quinolone prophylaxis reduced the risk of fever.
- The overall risk of bacterial infections was not affected.
- In patients receiving quinolone prophylaxis, a higher proportion of microbiologically documented infections are due to MDR gram negative infections.
- Understanding the risks and benefits of using quinolone prophylaxis may be useful in developing strategies to offer a more judicious use of antibiotics to this fragile population.

*The authors declare no conflicts of interest.