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Bacteremia during Induction Phase of Treatment for Acute Lymphoblastic Leukemia Treatment in Children: Interest of an Antibiotic Prophylaxis

Katell Michaux MD[1], Clement Legeay PharmD[2], Jean Marie Leclerc MD[3], Diane Laroque PharmD[2], Caroline Laverdière MD[3], Celine Laferrière MD[4], Bruce Tapiéro MD[1], Philippe Ovetchkine MD MSc[1]

1) Division of Infectious Diseases, Department of Pediatrics; 2) Department of Pharmacy; 3) Division of Oncology and Hematology, Department of Pediatrics; 4) Department of Microbiology and Immunology, CHU Sainte Justine-University of Montreal, Montreal, Canada

Introduction

➢ Infections are a major complication of neutropenia in children with Acute Lymphoblastic Leukemia (ALL)

➢ The use of systematic prophylaxis, in order to reduce bacterial infections during this period of treatment for ALL, remains questionable in children

Objectives

➢ To describe characteristics of bacteremia in children with ALL during the induction phase of treatment

➢ To identify risk factors for bacteremia

Methods

Study design and population
- Retrospective study
- Inclusion criteria: All children (ages 0-18) who completed the induction phase of BOSTON 2005 protocol of treatment for ALL, between 2006 and 2012
- Exclusion criteria: Re-induction

Definitions
- Neutropenia = Neutrophil count < 500 /mm3
- Induction = Period from the day of admission until day 32 after the onset of chemotherapy
- **Bacteremia**
  - Any positive blood culture, from day of admission to day 32 after the onset of chemotherapy
  - The following were considered seperate episodes of bacteremia:
    - Positive blood cultures with more than one organism
    - Second positive blood culture with the same organism, after a 7-day period of treatment with adequate antibiotics, and a previous negative blood culture

Data were systematically collected from the Departments of Pharmacy and Microbiology databases, for the following characteristics :
- Demographical (age, gender)
- Clinical (risk level, type of leukemia, antibiotic therapy, outcome)
- Biological (neutrophil count)
- Microbiological (micro-organisms, timing of bacteremia)

Statistical analysis
- SPSS software v 20.0
- p value <0.05

Results

Figure 1: Annual rate of bacteremia

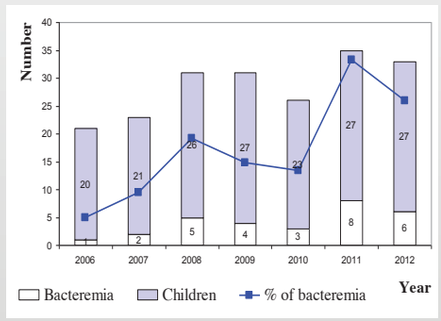


Table 1. Population characteristics

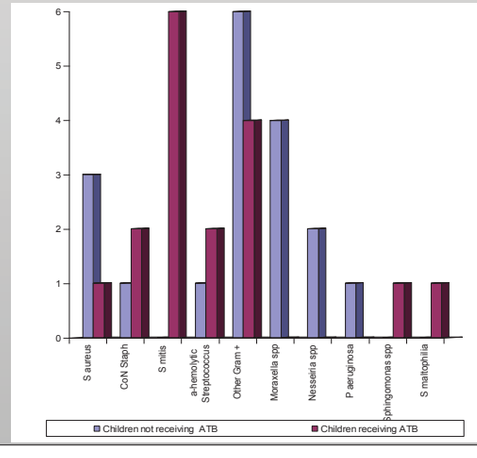
		Overall population N=171 (%)	Bacteremia N=29 (18 %)	No Bacteremia N=142 (82 %)	*P* value
Age (years)	≥ 5 years	82 (48.0)	11 (38.0)	71 (50.0)	0.26
	< 5 years	89 (52.0)	18 (62.0)	71 (50.0)	
Gender	Female	71 (41.5)	15 (51.7)	56 (39.4)	0.21
	Male	100 (58.5)	14 (48.3)	86 (60.6)	
Leukemia Phenotype	T cell	23 (13.5)	2 (6.9)	21 (14.8)	0.26
	B cell	148 (86.5)	27 (93.1)	121 (85.2)	
Risk group*	VHR	12 (7.0)	3 (10.4)	9 (6.3)	0.72
	HR	76 (44.5)	13 (44.8)	63 (44.4)	
	SR	83 (48.5)	13 (44.8)	70 (49.3)	
Neutrophil count at admission (/mm3)	Mean (± SD)	395 (100–1430)	100 (0-450)	420 (140-1740)	0.08
Neutropenia duration (days)	Mean (± SD)	25.8 (11.8)	27.2 (8.9)	25.5 (11.6)	0.47
Fatal outcome		11 (6.4)	0	11 (7.7%)	

* VHR = Very High Risk, HR = High Risk, SR = Standard Risk

Table 2. Characteristics of bacteremia according to antibiotic exposure

	Overall population N = 171	Patients not receiving antibiotics N = 30 (17.5 %)	Patients receiving antibiotics N = 141 (82.5 %)	*P* value
Bacteremia	31 (18.1 %)	14 (46.7%)	17 (12.0 %)	< 0.001
Timing of bacteremia Mean (days)	13.1 (SD 8.3)	8.9 (SD 8.6)	17.0 (SD 6.0)	< 0.01

Figure 2: Characteristics of bacteremia according to antibiotic exposure



Results

➢ Over the 7 years of the study period, 171 children were included (Table 1)
- Median age = 4.7 years (Range: 2.8-10.7)
- Neutropenia was present at admission in 57% of children (98/171)
- 31 episodes of bacteremia in 29 children
- The overall incidence of bacteremia was 18.1 %, with an increase from 5 % in 2006 to 33.3% in 2011

➢ Broad spectrum antibiotics were administered in 82.5 % of the children (141/171)

➢ In patients already receiving antibiotics (Table 2):
- Bacteremia was significantly less frequently observed:
  12.0 % vs 46.7%, $p < 0.001$
  OR = 0.13 CI95%: 0.05-0.31
- Mean time of onset of bacteremia was significantly delayed:
  17.0 day ± 6.0 vs 8.9 days ± 8.7, $p < 0.01$
- No clinical or biological characteristics were found to be associated with an increased risk of bacteremia
- Micro-organisms responsible for bacteremia seem to be different (Fig. 2)

Conclusion

➢ The incidence of bacteremia remains high in children with ALL children during induction phase of chemotherapy, particularly in those who are not exposed to antibiotics

➢ Given that no other predisposing factors for bacteremia were found, antibiotic prophylaxis could be considered during the induction phase of treatment for ALL in children

➢ Careful monitoring for the emergence of resistant pathogens is necessary

Contact information

Katell Michaux, MD
Katell.michaux@umontreal.ca

Phillipe Ovetchkine MD,MSc
Philippe.ovetchkine.hsj@ssss.gouv.qc.ca