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Antibiotic discontinuation in febrile neutropenic patients with acute myeloid leukemia (AML) and acute lymphoblastic leukemia (ALL)

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Background: The aim of this study was to evaluate the possibility of early antibiotic cessation in neutropenic patients with acute leukemia on different chemotherapy cycles.

Material/methods: Single-center, prospective observational study in adults with newly diagnosed ALL and AML was performed in 2013-2015. Patients were followed up for 180 days.

Results:

Study included 110 patients (50-male, 60-female; median age-32 years) from them 66 were with AML and 44—with ALL. These patients had 480 chemotherapy cycles (145-induction, 335-consolidation). Antibiotics were administered in 50% (n=242) of them (83% in induction vs 36% in consolidation; p<0.0001). The indications for antibiotics were clinically and microbiologically documented infections (CMDI) in 63% of febrile neutropenia episodes (FNE), including pneumonia (n=61), cellulitis (n=47) and bacteremia (n=45); and fever of unknown origin (FUO) - in 37% of FNE.

Antibiotic discontinuation was performed in 32% (77/242) of FNE, regardless of type of leukemia (31% in AML vs 37% in ALL, p=0.5). Antibiotic cessation prevailed in induction compared to consolidation chemotherapy cycles (46% vs 18%, OR 3.8, p<0.0001). Median time from defervescence till antibiotic discontinuation was 3 (1–16) days in FUO and 4 (1-19) days in CMDI. The median time from antibiotic discontinuation till neutrophil recovery was 12 (1–41) days in induction and 5 (1-22) days in consolidation (p=0.0001).

Fever recurrence after antibiotic cessation was in 32% (25/77) of chemotherapy cycles and prevailed in induction compared to consolidation (46% vs 18%, p=0.11). Median time from antibiotic cessation till fever relapse was 5 (1-14) days. At the time of antibiotic discontinuation median white blood cells (WBC) count was 0.4x10⁹/L in patients with recurrent fever versus 0.7x10⁹/L in patients without fever relapse (p=0.0006) (Table). Median time from antibiotic cessation till recovery from neutropenia was 15 (7-41) days in patients with recurrent fever versus 7 (1-28) days in patients without fever relapse (p<0.0001). Indications for antibiotic restart (n=25) were FUO in 28% and CMDI in 72% (cellulitis-9,

pneumonia-4, bacteremia-4, invasive aspergillosis-1). All patients became afebrile after the start of appropriate antibiotics. Median duration of antibiotic treatment in patients with recurrent fever was 10 (2-23) days. Nobody was admitted to intensive care unit and all survived.

Table. Factors associated with recurrent fever after antibiotic discontinuation in FNE

	Fever recurrence		p
	Yes n=25	No n=52	
WBC ($10^9/L$) at antibiotic discontinuation, median	0.4 (0.1–0.9)	0.7 (0.1–0.9)	0.0006
Days from antibiotic discontinuation till neutrophil recovery, median	15 (7–41)	7 (1–28)	<0.0001
Mortality	0	0	-

Conclusions:

The antibiotic therapy may be stopped in persistently neutropenic patients with acute leukemia. Relapse of fever was observed in 32% of patients with prolonged neutropenia but did not affect mortality.