

A comparative study of bloodstream infections in acute myeloid leukemia according to different phases of treatment: Can we predict the organism?

Preetam Kalaskar, Asha Anand, Harsha Panchal, Apurva Patel, Sonia Parikh, Sandip Shah

Abstract

Introduction: The treatment of acute myeloid leukemia (AML) consists of induction therapy with anthracyclines and cytarabine followed by two to four cycles of consolidation therapy with high-dose cytarabine after achieving remission. There have been very few studies comparing infections during induction and consolidation. We have analyzed blood cultures of patients with AML during episodes of fever occurring during induction and consolidation, for comparing the bloodstream infections in both the phases. **Materials and Methods:** Blood cultures of patients during febrile episodes were collected from central venous catheters and peripheral blood, both during induction and consolidation therapy of AML. **Results:** The study population included 52 AML patients. During induction, there were 52 episodes of fever and 25 (48%) blood cultures were positive, 15 of these blood cultures reported Gram-negative organisms, 9 reported Gram-positive organisms and 1 as yeast. During consolidation, 47 episodes of fever were recorded and blood cultures were positive in 12, of which 7 were Gram-negative, 5 were Gram-positive. **Conclusion:** The incidence of blood culture positive infections during therapy of AML at our center was higher. The predominant organism isolated was Gram-negative both during induction and consolidation. The incidence of blood culture positive infections had decreased by 50% during consolidation.

Key words: Acute myeloid leukemia, consolidation, induction

Introduction

Treatment of acute myeloid leukemia (AML) consists of induction therapy with anthracyclines and cytarabine followed by two to four cycles of consolidation therapy with high-dose cytarabine after achieving remission.^[1] The induction and consolidation therapies are known to be complicated with infections during neutropenia. Till the late 1960s, Gram-negative infections were predominant infection during therapy of AML. Over the next two to three decades, the predominant infection during therapy changed from Gram-negative to -positive organisms. Recent bloodstream infection rates during induction have been 27.8% and during consolidation phase has been around 25%. The predominant organisms during induction were Gram-positive (80%); those during consolidation were Gram-negative (72%).^[2] There have been very few Indian studies comparing infections during induction and consolidation. We have analyzed blood cultures of patients with AML during episodes of fever occurring during induction and consolidation therapy at our institute during the years 2014–2015 to compare the infective organisms during induction and consolidation.

Materials and Methods

This is a retrospective analysis carried out at our institute from June 2014 to July 2015. Patients with AML were treated at our institute with induction therapy of daunorubicin 60 mg/m² (days 1–3) and cytarabine (100–200 mg/m²) continuous infusion over 24 h (days 1–7).^[1] When the patients developed fever defined as 101°F single-episode or 100.4°F continues for 1 h or more, blood cultures from central venous catheter and peripheral blood were collected along other investigation. Infective episodes were treated as per generally accepted guidelines.^[3] Those in remission,^[4] postconsolidation (defined as <5% blast without hypocellularity, no extramedullary disease) were started on

consolidation therapy. Consolidation therapy consisted of high-dose cytarabine (1.5 mg to 3 mg/m²)^[5] over 2–3 h 12 hourly on days 1, 3, and 5. During consolidation, protocol for treating febrile episodes and culture collections were same as per induction.

Patients of AML, other than therapy-related AML, acute promyeloid leukemia, and myelodysplasia-related features, between age group of 18–60 years who achieved induction remission were included in the study.

Investigations

On treatment, febrile episodes were investigated with chest X-rays, blood cultures from central catheter, peripheral blood, and urine routine microscopy. Antimicrobial treatment was prescribed as per IDSA recommendations.^[3]

Results

The study population included 52 AML patients. There were 27 males and 25 females. During induction, there were 52 episodes of fever and 25 (48%) blood cultures were positive. Fifteen of these blood cultures reported Gram-negative organisms, nine reported Gram-positive organisms, and one as yeast. During consolidation, 47 episodes of fever were recorded and blood cultures were positive in 12 (25.53%), of which 7 were Gram-negative, 5 were Gram-positive [Table 1].

Discussion

Blood culture positive infections are noted in 65% of patients during AML therapy in India^[6] and this leads to increase in morbidity, mortality, and cost of therapy by a great margin. The lack of studies on the comparison of organisms during induction and consolidation led to this observational study. Our study shows that the incidence of blood culture-positive infection varied during induction and consolidation. The strength of the study is the detection of organisms with respect to the different

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How to cite this article: Kalaskar P, Anand A, Panchal H, Patel A, Parikh S, Shah S. A comparative study of bloodstream infections in acute myeloid leukemia according to different phases of treatment: Can we predict the organism?. *South Asian J Cancer* 2017;6:132-3.

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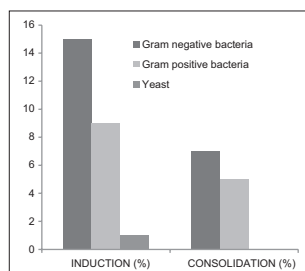
DOI: 10.4103/2278-330X.214584

Department of Medical and Pediatric Oncology,
Gujarat Cancer and Research Institute Regional
Cancer Center, B.J. Medical College, Ahmedabad,
Gujarat, India

Correspondence to: Dr. Asha Anand,
E-mail: ashaanand1757@yahoo.com

Table 1: The distribution of different Gram-positive and Gram-negative infection during induction and consolidation

	Number of culture positive (%)	
	Induction	Consolidation
Gram-negative bacteria	15 (28.8)	7 (14.89)
<i>Escherichia coli</i>	7	3
<i>Klebsiella pneumoniae</i>	4	3
<i>Pseudomonas aeruginosa</i>	2	1
<i>Burkholderia cepacia</i>	2	-
Gram-positive bacteria	9 (17)	5 (10.6)
Coagulase negative staphylococci	4	3
Coagulase positive staphylococci	3	1
<i>Enterococcus</i>	2	1
Yeast	1	-
Total	25/52 (48)	12/47 (25.53)

**Figure 1: Graphical representation of the distribution of organisms in induction and consolidation**

phases of treatment of AML therapy. We had 52 AML patients, who did not receive prophylactic antibiotics during therapy except antifungal in the form of fluconazole. The incidence of blood culture-positive infections during induction was 48%, which is higher compared with studies from the West where it is reported to be 29.6%^[7] while it is lower compared to data reported from India of 65%.^[6] During the last few years, there has been a shift from Gram-negative infections to Gram-positive infections during acute leukemia therapy probably related to increased use of intravascular catheters, fluoroquinolone prophylaxis. However, in our study, the incidence of culture positive infections during induction was 48%, of which 60% were caused by Gram-negative organisms, 36% by Gram-positive organisms, and 4% yeast [Figure 1]. During consolidation, the culture positive infections were 25.5%, of which the Gram-negative infections constituted 50%, Gram-positive infections were 41.66%, and polymicrobial infection were reported in only 1 (8.33%) patient, both were gram-negative organisms [Figure 1]. On analyzing the bloodstream infection,

the incidence of blood culture-positive infection was almost double during induction compared to consolidation. Contrary to our assumption, the consolidation would have more of Gram-negative infections compared to induction in view of increased gastrointestinal toxicity of high-dose cytarabine. This could probably be explained by the active disease during induction compared to consolidation. Our result correlates with Indian studies showing predominant Gram-negative infection in cancer patients.^[8]

Conclusion

The incidence of blood culture-positive infections during therapy of AML at our center was higher. The predominant organism isolated was Gram-negative during both induction and consolidation. The incidence of blood culture-positive infections had decreased by 50% during consolidation.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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