Mortality Review of Children with Acute Lymphoblastic Leukemia: Single Center Experience from a Limited Resource Country

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Background

Hue Central Hospital plays a key role in treating childhood Acute Lymphoblastic Leukemia (ALL) in the central zone of Vietnam which covers a geographically wide area.
The purpose of this study was to review the causes of death in children with ALL to improve their treatment outcomes.

Methods

Medical records of children with ALL who died at HCH between January 2009 and December 2015 were retrospectively reviewed.
Data regarding causes of death were collected.
ALL patients were treated according to the modified Children Cancer Group protocol.

Results

- A total of 70 patients died during a 7-year period. The median age was 6 years.
- The male to female ratio was 2.4 to 1.
- There were 23 (32.9%) standard risk (SR) group patients and 47(67.1%) High risk (HR) patients according to NCI criteria.
- Immunophenotype confirmed that 49 (68.1%) had B cell and 20(28.6%) had T cell and one case was unable to confirm.
- The complete remission (CR) rate after induction therapy was 87.5 %.
- The cause of death is shown in Chart 1. Infection was the number one cause of death (44.3%). Most cases was bacterial infection (94%). HR patients had higher rate of infection than SR patients.
- Time of death is shown in Chart 2 that 33% of the 70 cases died during the maintenance phase.
- Tables 1 to 3 shows the cause of death depending on treatment phases.

Chart 1. Cause of Death

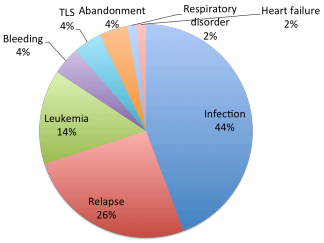

Chart 2.Time of Death

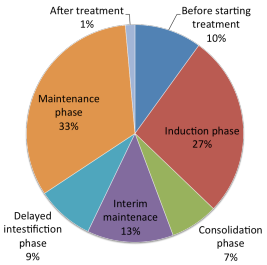

Table 1. Cause of death during an initial term of treatment: Before starting treatment and Induction phase

Cause of death	N (%)	SR	HR
Total	26 (100.0)	6	20
Leukemia	10 (38.0)	1	9
Infection	8 (31.0)	3	5
TLS	3 (11.5)	1	2
Abandonment	3 (11.5)	1	2
Bleeding	2 (8.0)	0	2

Table 2 .Cause of death during the middle term of treatment: Consolidation and Interim maintenance phase

Cause of death	N (%)	SR	HR
Total	11 (100.0)	4	7
Infection	7 (64.0)	3	4
Relapse	1(9.0)	0	1
Heart failure	1 (9.0)	1	0
Respiratory disorder	1 (9.0)	0	1
Bleeding	1 (9.0)	0	1

Table 3. Cause of death during the late phase of treatment: Delayed Intensification, Maintenance phase and After treatment

Cause of death	N (%)	SR	HR
Total	33 (100.0)	13	20
Infection	16 (48.0)	4	12
Relapse	17 (52.0)	9	8

- Regarding social aspects, More than half (65.7%) of the patients were referred from provincial areas.
- Most of the families (94.3%) were low-income and only 15.7% were well educated.
- Of 70 cases, 31 (44.3%) patients had good nutrition and 39 (55.7%) had poor nutrition status.
- There were 6 (9.2%) cases who had insufficient supply of medication such as chemotherapy drugs.

Conclusions / Discussion

Our results showed that the most common cause of death of childhood ALL was infection and one third of the cases died during the maintenance therapy phase although they had achieved complete remission. In order to improve the survival rate it is necessary to improve the supportive care especially such as infection control and might need to adjust the treatment strength such as considering the dose reduction of Mercaptopurine. Recent reports (Yang, et al) show that some patients of East Asian genetic ancestry require reduced doses of Mercaptopurine [1) 2)]. It is important to continue maintenance therapy avoiding severe immunosuppression, which might become a risk for infection.
The results of this review suggest that it is necessary to make basic adjustments to treatment standards. There were fewer treatment abandonment cases, but most of the death cases were from poor families from rural areas. We need to re-investigate whether there were difficulties in accessing medical institutions, delays in visiting doctors, or lack of understanding of the disease by the patient and family. Also there were some cases who passed away before the treatment, such that early detection of disease and prompt referrals to paediatric haematology oncology division are essential. Better training for rural doctors is necessary and should be promoted.

References :

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2) Moriyama T, Yang JJ, et al , NUDT15 polymorphisms alter Thiopurine metabolism and hematopoietic toxicity. Nat Genet. 2016 Apr;48(4):367-73