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Relationship between the general condition of acute lymphoblastic leukemia patients with remission rate and convulsion as an adverse effect chemotherapy

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ABSTRACT A retrospective study on the relationship between the general condition of acute lymphoblastic leukemia patients with remission rate and convulsion as an adverse effect of chemotherapy was conducted in leukemia patients of the hematology-oncology subdivision, Department of Child Health, Medical School, University of North Sumatra, Medan. Of 114 children with acute lymphoblastic leukemia, 81 (71.05%) received chemotherapy, 31 patients among them was in good general condition. Remission rate of the 31 patients was 80.6% (25 children). Whereas in the remaining 50 patients, the remission rate among them was 84% (42 patients). There was no significant relationship between their general condition to the recurrence rate of Acute Lymphoblastic Leukemia patients who had been administered chemotherapy during induction phase. Convulsion was found in 2 cases, due to CNS leukemia. **[Paediatr Indones 2001;41:33-37]**

Keywords: acute leukemia, remission rate, adverse reactions

ACUTE LYMPHOBLASTIC LEUKEMIA (ALL) IS A hemopoietic malignancy with predominantly pathologic lymphoblast.[1] This disease may be curable;[1,2] by modern chemotherapy and supportive care, 97-98% of patients achieve complete remission,[3] which is defined as disappearance of clinical signs and symptoms of disease, normalization of peripheral blood value, and lymphoblast in bone marrow less than 5%.[3-5] The increased remission rate is related by improvement in chemotherapy treatment, recognition of risk factors, and improvement of supportive care.[6] Certain clinical appearances and laboratory findings correlate to the prognosis of ALL patients. These include initial white blood cell count, age at diagnosis, gender, cytogenesis, immuno-phenotype, FAB morphology, mediastinal mass, the presence of organomegaly, lymphadenopathy, hemoglobin level, race, platelet count, serum immunoglobulin, cyto-reduction rapidness, myeloid antigen findings in leukemic cell.[5] Based on these prognostic factors, ALL may be categorized into low risk and high risk groups, which are frequently used as the basis of ALL treatment.[3-10] High risk patients are generally treated more aggressively to achieve remission, while children in the standard or low risk group are treated with unequal effectiveness but less intensively to avoid adverse effect caused by chemotherapy.[3,5] The combination of 3 cytostatic drugs is administered in the induction phase to achieve a good result for remission rate in ALL patients.[3,6,9]

Convulsion is one of the adverse effects that may occur during the remission of the induction phase in ALL patients. It may be due to intracerebral hemorrhage, leukemic cell infiltration into the central ner-

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vous system, cerebral edema, infection, electrolyte or metabolic disorders, and acute neurotoxic reaction caused by drugs.[11] Certain cytostatic drugs such as vincristine and L-asparaginase are known to have neurotoxic effect and may lead to convulsion.[11-13] In this study we reviewed the remission rate of ALL patients with good general condition and bad general condition, and to find the incidence of convulsion as an adverse effect of chemotherapy during induction phase.

Methods

This study was conducted retrospectively by collecting data from medical records of ALL patients in Hematology-Oncology Division of the Department of Child Health, Medical School, University of North Sumatra, Medan, Indonesia, from January 1984 until December 1994 period.

From the data, 144 ALL patients were obtained but 33 patients of them were excluded from the study because they did not receive cytostatic treatment. Eighty-one patients were eligible in the study and were classified into 2 groups, one group with those in good general condition and another group in bad general condition. Separation of the clinical condition was based on prognostic factors such as age of less than 2 years or older than 10 years, initial white blood cell count of less than 100.000/µl, central nervous system leukemia, hepatosplenomegaly, lymphadenopathy, mediastinal mass.[5] Bad general condition was concluded if there was one or more prognostic factor encountered.[5]

The same treatment was given to all patients in both groups, i.e., the combination of 3 cytostatic drugs; prednisolone, vincristine, and L-asparaginase during induction for 4 weeks. Thereafter, all patients underwent thorough clinical examination, blood and bone marrow evaluation to define the occurrence of remission. The criteria of remission were disappearance of clinical signs and symptoms, normal peripheral blood values, and less than 5% of lymphoblast in bone marrow.[3,4,5]

All relevant data were collected in a special form. Statistical analysis was performed using the Chi-squared test to find out the difference of remission rate between the two groups with the significance level of 95% ($p<0.05$).

Results

The prognostic related factors of ALL patients were age, initial white blood cell count, sex, FAB morphology, hepatosplenomegaly, lymphadenopathy and CNS leukemia (Table 1).

Fifty patients were male; 22 patients among them were in good general condition which 18 of them had remission. The other 28 patients were in bad general condition and 23 of them had remission. Thirty-one patients were female, 9 were in good general condition with 7 of them had remission, while 22 patients remained in bad general condition, while 12 among them had remission. Figure 1

Sixty-seven of 81 patients (82.7%) experienced remission. In the good general condition group, 25 of 31 patients (80.6%) had remission and in the bad general condition group 42 of 50 patients (84%) also underwent remission. Statistical analysis showed that there was no significantly differences of remission rate in both groups. Table 2. The remission rate in the age group of less than 2 years and older than 10 years was 83% and was 82% for the 2-10 years age group. The difference of remission rates for both age groups was not significant (See Table 3).

Discussion

Eligible ALL patients in this study were given a combination of 3 cytostatic drugs, prednisone,

TABLE 1. PROGNOSTIC FACTORS OF ALL PATIENTS

Variable	Patient n=81
Age	
<2 years	9
> 10 years	15
Initial white blood cell count	
<100.000/ul	68
>100.000/ul	13
Sex	
Male	50
Female	31
FAB morphology	
L1	56
L2	24
L3	1
Hepatosplenomegaly	40
Lymphadenopathy	2
CNS leukemia	2

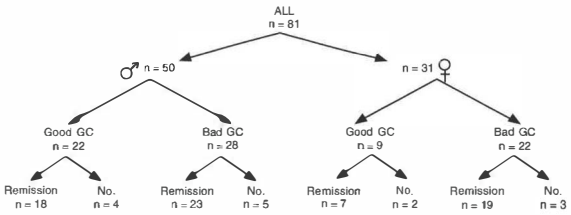

Figure 1. ALL patients who had remission

TABLE 2. COMPARISON OF REMISSION RATE BASED ON GENERAL CONDITION

General condition	Remission				Total
	+	%	-	%	
Good	25	80.6	6	19.4	31
Bad	42	84	8	16	50

p>0.05

TABLE 5. COMPARISON OF REMISSION RATES ACCORDING TO GENDER

Sex	Remission				Total
	+	%	-	%	
Male	41	82	9	18	50
Female	26	84	5	6	31

p>0.05

vincristine and L-asparaginase, during remission of induction phase. Remission rate was achieved as much as 82.7%. Remission rate of the group with good general condition was 80.6% while the group with bad general condition was 84%. This remission rate was lower than that found in previous studies. Administration of the combination of the 3 cytostatic drugs prednisolone, vincristine and L-asparaginase during remission induction phase resulted in a remission rate > of 95% in ALL patients.[3-6,9,13]

Abromowitch et al found 95% remission rate in ALL patients with standard risk.[14] Gaynon and his co-workers reported even a higher percentage of remission rate, i.e., 99& in high risk ALL patients on BFM regimen and 97% in those on the New York (NY) regimen.[15] Furthermore, Miller et al reported that administration of the combination of the 3 cytostatic drugs prednisolone, vincristine and L-asparaginase during remission of induction phase for ALL patients in lower risk, 95% remission rate was found without difference in ALL patients with higher risk; 95% remission rate was found without difference in ALL patients in higher risk, i.e., 93%.[16]

Initial white blood cell count, age at diagnosis and sex are known as prognostic factors in ALL patients.[7] The most important indicator is initial white blood cell count.[13] Male patients have a worse prognosis than females.[5,7,13] However, our data did not show

that the male gender was a significant risk factor. It is suggested that another prognostic factor related to gender may be present to aggravate the prognosis in males.[11]

In this study, there was no significant difference in remission rate in the age group of <2 years (82%). Leiper and Chessells J compared remission rate between the age group of <2 years and the age group of 2-14 years and found that the result was not difference (94% in age group of <2 years and 97% in age group of 2-14 years).[17] Although the differences of remission rate was not found in both age groups, the remission rate achieved in Leiper and Chessells' study was higher than this study.

In this study, remission rate among different genders was not significantly different. Remission rate of ALL patients whose initial white blood cell count was >100.000/µl (37%) was significantly lower than those with initial white blood cell count of <100.000/µl (90%) with $p<0.05$, in this study. Equiquren et al reported that remission rate achieved in ALL patients with hyperleukocytosis (>100.00/µl) was 94% using a combination of 7 cytostatic drugs during inuction phase for 8 weeks.[18] The remission rate reached in this study was much lower than study of Equiquren et al. It was due to our using of a combination of 3 cytostatic drugs for patients with hyperleucocytosis.

We did not find convulsion as an adverse effect of the administration of cytostatic drugs during induction phase. We found 2 children with convulsion due to CNS leukemia. Pikko HMD et al observed 9 children with reversible convulsion as the adverse effect where intra cerebral vascularization.[11] Johnston FL et al reported 4 cases with convulsion on the 5th and 6th day after vincristine sulfate injection. In their cases, there was no abnormality in lumbar puncture CT-scan or EEG.[12]

Priest JR and his co-workers reported that 13 of 18 children treated white vincristine, prednisone and L-asparaginase had deficiency of hemostatic plasma protein such as antithrombin, plasminogen and fibrinogen, which finally caused thrombus and intra cerebral hemorrhage.[19]

In conclusion, there was no significant difference of remission rate between ALL patients undergoing a combination 3 cytostatic drugs during the induction phase in good general condition and bad general condition. We did not find a significant difference mission rate based on age and gender, however, we found a significant difference of remission rates between the two groups based on initial white blood cell count. The obtained remission rate in our series was much lower than that in the literature or other studies. There was no convulsion observed as the adverse effect of treatment during induction phase in all of ALL patients.

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