Streszczenie w języku angielskim

Introduction

Acute lymphoblastic leukaemia (ALL) accounts for 80% of all leukaemia's among children. Although most patients achieve initial remission, approximately 19% of patients will relapse and survival among patients with early myeloid relapse decreases drastically. The absolute lymphocyte count (ALC) may be a hypothetical prognostic factor in the final stage of induction therapy. Investigated is its relationship with overall survival i.e., the time from diagnosis to death from any cause or until the date of the last follow-up meeting (OS - Overall Survival) and event-free survival i.e. death, recurrence, second cancer (EFS – Event-Free Survival).

Purpose

The main aim of the study was to assess hematopoietic recovery (expressed by ALC and other indices i.e., AMC - Absolute Monocyte Count, APC - Absolute Platelet Count) in children diagnosed with ALL, treated according to the ALL IC-BFM 2002 and 2009 program. The relationship between hematopoietic recovery and recognized ALL prognostic factors was also assessed: type of leukaemia, risk group, child's age at diagnosis, initial leukocytosis, status of central nervous system involvement, assessment of response to treatment, minimal residual disease (MRD), activity of lactate dehydrogenase (LDH) and clinical parameters (presence of hepatosplenomegaly). The impact of the above factors on OS and EFS in the study group was assessed.

Patients and Methods

The study group consisted of 151 patients (F : M - 71 : 80, mean age: 5.77 years, median age: 4.27) diagnosed with acute lymphoblastic leukaemia, treated at the Department of Paediatric Oncology and Haematology in Bialystok in the years 2002 - 2017. Blood count and biochemical parameters were assessed in all patients on the day of diagnosis, on days 8, 15 and 33 of induction therapy. The type of leukaemia, risk group, status of central nervous system involvement, response to treatment, MRD assessment, biochemical and clinical parameters were also analysed. Techniques of inferential statistics suitable for the characterization of the analyzed variables in statistical

modelling and hypothesis testing were used. The analysis of survival time for each of the analysed endpoints was carried out using non-parametric techniques (Kaplan-Meier estimator, Mantel-Cox method) and parametric techniques (AFT models). ALC was assessed as a continuous and categorized variable (patients qualified for the study were divided into 2 groups based on the ALC value on day 33, the ALC count of 750 cells/μL was used as a cut-off). Parameters such as AMC, APC, haemoglobin and WBC were similarly analysed.

Results

The mean follow-up period was 1791 days (4 years and 9 months). In the AFT model for survival, based on continuous predictors, a significant relationship was observed between the absolute number of lymphocytes on day 33 of ALL treatment and survival time ($P = 0.03$). In the AFT model for survival, based on continuous predictors, there was also a significant relationship between the absolute platelet count at day 33 of treatment and survival time ($P = 0.01$). Such a relationship was not observed in relation to the leukocyte count and haemoglobin (Hgb) concentration on day 33. In the case of multi-factor models built with simultaneous consideration of ALC and one of the collinear predictors (WBC, Hgb, APC), statistical significance was demonstrated for the relationship between time to death and ALC in each of the models. The value of this parameter in predicting time to death independently of other predictors has been confirmed. In the AFT model for survival, incorporating predictors in the form of categorized variables, it was shown that there is a positive, statistically significant relationship between ALC ($\geq 750/\mu L$, $P = 0.03$), WBC ($\geq 2.25x10^3/\mu L$, $P = 0.01$), APC ($\geq 190x10^3/\mu L$, $P = 0.03$) and survival time. Such relationship has not been proven for AMC and Hgb concentration. However, in the multivariate analysis which also utilised sex, risk group and response to prednisone as predictors, statistical significance was not obtained for any of the analysed variables.

The 3-years ESF and 3-years OS for the whole group were 81.54% and 86.05% and the 5-year ESF and OS were 69.90% and 79%, respectively. Overall survival and event-free survival at 3, 5, 7, and 10-years follow-up were assessed in both groups (grouping based

on ALC at day 33, cut-off 750 cells/μL). The number of deaths and adverse events was higher in the group with ALC < 750/μL regardless of the observation period.

Among the recognized risk factors, effects on survival (5-year OS) have been demonstrated for age, risk group and leukaemia subtype.

In addition, there were no statistically significant associations between ALC at day 33 and known risk factors. Central nervous system (CNS 3) involvement was more common in children with ALL with ALC >750 cells/μL on day 33.

Conclusions

A lower absolute number of lymphocytes at day 33 is associated with a worse prognosis and shorter survival time. The ALC and APC parameters after remission induction are positive predictors of survival time. This relationship holds when evaluating these values both as continuous and categorized variables and independent of the absolute leukocyte count, platelet count, and haemoglobin concentration. There were no statistically significant associations between ALC and known risk factors.

Key words: ALL - Acute Lymphoblastic Leukaemia, ALC - Absolute Lymphocyte Count, EFC – Event - Free Survival, OS – Overall Survival, lymphocytes, prognostic factor