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16. Early diagnosis of acute kidney injury in children with acute lymphoblastic leukemia during the induction phase of polychemotherapy

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Background and Objectives

Acute lymphoblastic leukemia (ALL) is the most common malignant disease in children, the treatment of which is based on intensive polychemotherapy (PCT). Despite high survival rates, therapy is associated with the risk of organ dysfunction, particularly kidney injury. Renal function in pediatric oncohematological patients is affected not only by the nephrotoxic effects of PCT but also by the intensity of the malignant process. In clinical practice, assessment of kidney function in children is based on the measurement of serum creatinine and/or Cystatin C, followed by estimation of the glomerular filtration rate (GFR). Dynamic monitoring of GFR is essential at different stages of ALL treatment for the timely detection of kidney injury.

Material and Method

The study included 18 children diagnosed with ALL, aged 1 to 17 years, including 11 boys and 7 girls. The study was conducted at the Hematology Department of City Clinical Children's Hospital №16 of Kharkiv City Council. All patients were treated according to ALL IC BFM 2009 protocol.

The patients were divided into two groups according to risk stratification. Group 1 included 11 patients with standard-risk ALL (standard risk, SR), while Group 2 consisted of 7 patients classified as high risk (high risk, HR).

Renal function parameters were assessed at two time points: before the initiation of PCT and at the end of the first phase of the induction protocol (approximately day 33 of treatment). In all patients, serum Cystatin C and creatinine levels were measured, and the GFR was calculated. GFR was estimated using the CKiD U25 creatinine-cystatin C equation.

Patients were additionally stratified according to the degree of GFR reduction based on the pRIFLE classification

Results

Serum creatinine levels prior to treatment initiation did not differ significantly between the SR and HR groups (67 (57; 74) vs 72 (64; 88) $\mu\text{mol/L}$, respectively; $p=0.204$).

On day 33 of induction PCT, creatinine levels also showed no significant intergroup differences (70 (63; 75) $\mu\text{mol/L}$ in the SR group vs 65 (61; 95) $\mu\text{mol/L}$ in the HR group; $p=0.891$). Over time, creatinine levels remained stable in both the SR group ($p=0.44$) and the HR group ($p=1.000$).

Serum Cystatin C levels before treatment did not differ significantly between groups (0.56 (0.45; 0.69) mg/L in the SR group vs 0.78 (0.67; 0.85) mg/L in the HR group; $p=0.051$).

By day 33 of treatment, cystatin C levels were higher in the HR group compared to the SR group (1.57 (1.32; 1.72) vs 0.74 (0.66; 0.84) mg/L; $p=0.0013$).

Over time, cystatin C levels increased in both groups: from 0.56 (0.45; 0.77) to 0.74 (0.66; 0.84) mg/L in the SR group ($p=0.0076$), and from 0.78 (0.67; 0.85) to 1.57 (1.32; 1.72) mg/L in the HR group ($p=0.018$).

Baseline GFR differed significantly between the SR and HR groups (96 (81; 119) vs 79 (72; 82) mL/min/1.73 m²; $p = 0.0416$). On day 33 of induction therapy, GFR was lower in the HR group compared to the SR group (54 (50; 62) vs 86 (70; 89) mL/min/1.73 m²; $p = 0.0032$).

GFR showed a significant decrease in both groups from baseline to day 33 (SR: $p=0.0026$; HR: $p = 0.0233$).

In 5 out of 7 children in the HR group, renal function corresponded to the Risk stage according to the pRIFLE classification ($\geq 25\%$ eGFR decrease), whereas in the SR group this was observed in 1 out of 10 patients.

A direct association was identified between HR group status and the probability of reaching the Risk stage: RR = 7.86 (95% CI 1.14–53.95).

Conclusions

1. Serum creatinine levels remained stable over time and showed no significant differences between the study groups, whereas cystatin C levels increased during treatment and were higher in the HR group on day 33 of therapy.
2. Glomerular filtration rate was significantly lower in the HR group both at baseline and during the first phase of induction PCT.
3. A $\geq 25\%$ reduction in GFR from baseline, corresponding to the “Risk” stage according to the pRIFLE classification, was observed 7.86 times more frequently in children with high-risk ALL compared to those with standard-risk disease.
4. The observed changes in renal function parameters may be associated not only with the effects of PCT but also with disease-related factors, including a higher degree of tumor activity at presentation.