Intracellular Neutrophil Myeloperoxidase Level in papediatric Oncological Patients During Chemotherapy: Possible New Tool for Leukopenia Management

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Introduction. Significant progress has been achieved in management of chemotherapy-induced complications. Still, leukopenia, particularly when associated with fever, remains life-threatening in paediatric patients, who, as a rule, undergo highly toxic regimens. Mortality during febrile leukopenia (FL) is about 5% in solid tumor treatment and as high as 11% in certain hematological tumors. At the same time, there are a few objective criteria for predicting severity and outcome of induced leukopenia.

Neutrophil myeloperoxidase (MPO) is a functionally active enzyme found in azurophylic granules of neutrophil leukocytes and in much smaller amount in monocytes. The synthesis starts at the earliest differentiation stages and continues through maturation. Finally, MPO is excreted during cell activation and phagocytosis, causing decrease of intracellular level. Hematological analyzer Advia 2120i (Siemens) routinely measures MPO in leukocytes to separate myeloid and non-myeloid cells, the measurement is calculated as a technical parameter – Myeloperoxidase Index (MPXi, standard range −10 to +10).

Aims. The aim of the study is to retrospectively analyze episodes of chemotherapy-induced leukopenia for dynamics of leucocyte count (WBC) and MPXi.

Material and Methods. Data from the Children's Clinical University Hospital Laboratory Information System (LIS) for the time period from 01.03.2011 till 31.01.2014 were selected. 336 episodes of leukopenia had been found; 294 representative "bowl-like" leukopenic cycles of 85 patients with total of 3824 blood tests were suitable for the assessment. MS Excel database was designed; statistical analysis was performed by using IBM SPSS v.21.

Results. In 283 cylces (96%) there was synchronous drop of WBC and increase of MPXi above + 10, followed by synchronous normalization. In another 5 circles (2%) the dynamics were the same, but MPXi did not reach the critical level of +10. The synchronous dynamics have not been found only in 6 cycles (2%), where irregular fluctuations of MPXi were seen. The curves of WBC and MPXi demonstrated excellent concurrence of critical points: MPXi increased above normal level simultaneously with WBC drop to critical counts, and both parameters reached their respective peaks simultaneously (median difference for both points – 0 days). MPXi reverted to normal earlier than WBC (median – 1 day, the difference statistically significant, Wilcoxon test $p < 0.001$).

Predictably, highly significant negative correlations between MPXi and WBC and neutropenia grade (Spearman $p < 0.001$ for both) were found. The duration of leukopenia significantly correlated with the time span of MPXi being > +10, with MPXi increase from initial till peak level and with maximal attained MPXi value (Spearman $p < 0.001$ for all three).

Conclusions. The results strongly support a biological relationship between destruction and restitution of neutrophil leukocytes during chemotherapy and their MPO content. In 98% of leukopenia cycles, cellular MPO grew synchronously with WBC decrease, and decreased along with WBC recovery. Cellular MPO measured by Advia 2120i could be used as a predictive factor in paediatric chemotherapy-induced leukopenia, as MPXi returned to normal before WBC, and duration of leukopenia significantly correlated with MPXi dynamics. MPXi is an excellent parameter for monitoring, since it is automatically measured during routine clinical blood tests and does not need any additional technical or financial extras. The results are completely original, no comparable published data have been found.