Two dose adjustment programs in high-dose methotrexate treatment for pediatric acute lymphoblastic leukemia

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Abstract

Background: Methotrexate is safely administered to most patients but can also cause severe toxicities. It is necessary to individualize methotrexate dose to maintain suf-ficient exposure while minimizing toxicities. Procedure: We enrolled 1174 cycles of high-dose methotrexate chemotherapy from 294 patients treated following the CCCG-ALL-2015 protocol and explored risk fac-tors of toxicities, methotrexate clearance delay and relapse. We compared those who received a fixed-dose reduction (Program 1) with those who were dose-adjusted by added methotrexate concentration test at 16h (Program 2) after methotrexate clear-ance delay existed the last cycle. Results: Female, IR/HR group, BSA<0.69m2 and C44h[?]1.0 μ mol/L were risk factors of toxicities(P<0.05). Significant covariates on methotrexate clearance delay were age >6years, male and IR/HR group (P<0.01). Male, IR/HR and C68h[?]0.2μmol/L group patients were at higher risk of relapse(P<0.05). No significant association was observed between methotrexate dose and relapse-free survival. 405 cycles from 168 patients were dose-adjusted by Program 1 and 118 cycles from 43 patients by Pro-gram 2. Patients who used Program 2 had a higher actual methotrexate infusion dose and infusion rate and was better in keeping C44h in our target value (P<0.001). Ab-normal serum potassium was more frequently in patients using Program2 (P<0.001), and prolonged myelosuppression was more commonly seen in IR/HR patients with Program2(P=0.003). Conclusions: No significant correlation between methotrexate dose or C44h and re-lapse-free survival time was found. Patients who were dose-adjusted by Program 2 received a higher therapeutic dose and better controlled the methotrexate concentra-tion to our target range.

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TABLE 1 Baseline patient demographics, treatment data and laboratory values based on risk group.pdf available at https://authorea.com/users/375977/articles/493148-two-dose-adjustment-programs-in-high-dose-methotrexate-treatment-for-pediatric-acute-lymphoblastic-leukemia

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TABLE 2 Risk factors of toxicity and methotrexate clearance delay at 44h.pdf available at https://authorea.com/users/375977/articles/493148-two-dose-adjustment-programs-in-high-dose-methotrexate-treatment-for-pediatric-acute-lymphoblastic-leukemia

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TABLE 4 Basic demographic information, treatment data and toxicity of two MTX dose adjustment programs.p
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