Conventional Compared with Individualized Chemotherapy for Childhood Acute Lymphoblastic Leukemia

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The rate at which children clear anti-leukemic agents is highly variable. Rapid clearance of anti-leukemic agents leads to lower levels of these medications in the patient's blood and worse outcome in the treatment of acute lymphoblastic leukemia.

Physicians at the St. Jude Children's Research Hospital in Memphis hypothesized that the outcome of treatment of childhood ALL would be improved if doses of anti-leukemic medications were individualized to a patient's metabolism to prevent low systemic exposure to chemotherapy drugs in patients with rapid metabolisms. One hundred and eighty-two children with newly diagnosed ALL were enrolled in this study. Study participants were randomly assigned to post-remission regimens that included high-dose methotrexate and teniposide. The doses of these drugs were different in the two treatment groups: In the conventional treatment group doses were based on body surface area which is the standard practice. In the individualized treatment group, doses were based on the rates of clearance of the three drugs in each patient. Patients with slow clearance received a lesser drug dosage than those with rapid clearance.

Patients in the individualized treatment group received significantly fewer courses of treatment with systemic exposure below the target range as compared to patients in the conventional treatment group. Outcome was significantly improved in patients with B-lineage leukemia who received the individualized treatment schedule. The mean rate of continuous complete remission at five years was 76% in the individualized patients vs. 66% in the conventionally treated patients.

Analysis of the medication schedules revealed that time-dependent exposure to methotrexate was significantly related to risk of early relapse in children with B-lineage ALL. This is the first major study to demonstrate that tailoring the dose of methotrexate to a child's rate of drug metabolism can improve outcome in childhood ALL.