Age and baseline creatinine as risk factors for methotrexate nephrotoxicity in children with acute lymphoblastic leukemia in resource-limited countries

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Abstract

Introduction. The search for risk factors for high-dose methotrexate (MTX)-induced nephrotoxicity in children with acute lymphoblastic leukemia (ALL) has been complex in the context of resource-limited countries where serum levels of MTX are not always available. Objective. To analyze the demographic, clinical, and biochemical factors associated with MTX-induced nephrotoxicity in children with ALL. Methodology. Case-control study in children with ALL from a General Hospital in Mexico over a four-year period (2016-2020). Kidney damage was defined with KDIGO criteria and the following variables were analyzed: sex, age, weight, height, creatinine, urea, transaminases, hematic cytometry, vomiting, mucositis, dermatitis, and number of MTX applications. Results: One hundred and eight children were studied, 22 females (38%) and 36 males (62%), ages 1 to14 years. The incidence of nephrotoxicity was 5.8% in 238 events of MTX administration. The children in the group with nephrotoxicity were older (average age 9.5 vs 5, p = 0.036), had higher baseline creatinine (0.5 mg/dL vs 0.4 mg/dL p = 0.006), and had lower baseline hemoglobin (10.1 g/dL vs 11.3 g/dL, p = 0.034). Mucositis was associated with nephrotoxicity with OR 13 95% CI 4-42, p <0.001. A cut-off value for creatinine of 0.44 mg/dL (AUC of 68%) and an age of 8 years (AUC of 64%) were identified for risk of nephrotoxicity. Conclusions: The incidence of MTX nephrotoxicity in children with ALL was 5.8%, with a high association with mucositis. The risk is greater for children older than 8 years and baseline creatinine higher than 0.44 mg/dL.

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TABLE 1 .docx available at https://authorea.com/users/437027/articles/538951-age-andbaseline-creatinine-as-risk-factors-for-methotrexate-nephrotoxicity-in-children-withacute-lymphoblastic-leukemia-in-resource-limited-countries

Graphic 1. Empirical ROC curve of acute kidney injury and basal creatinine



Area under the curve 68%. For an acute kidney injury incidence of 6%, the creatinine cut-off point of 0.44 mg / dl has a sensitivity of 71%, a specificity of 69% and a likelihood ratio of 2.2%.





Area under the curve 64%. For an acute kidney injury incidence of 6%, the age cutoff point of 8 years has a sensitivity of 64%, a specificity of 64% and a likelihood ratio of 1.8%.