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P-glycoprotein functional activity in healthy Caucasians and patients with non-Hodgkin's lymphoma

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Abstract

P-glycoprotein (P-gp) functions as a trans-membrane ATP-dependent pump, decreasing the intracellular concentration of different toxic substances, including antineoplastic agents. P-gp activity may influence the distribution and bioavailability of P-gp substrates, thereby changing the response to chemotherapy.

The aim of the investigation was to estimate the P-gp activity in a control group of healthy persons and patients with non-Hodgkin's lymphoma (NHL), and analyze the relationship of P-gp function with tumor malignancy grade, chemotherapy protocols, and the response to chemotherapy.

Methods: P-gp activity was assessed using flow cytometric assay based on fluorescent

P-gp substrate rhodamine 123 (Rh123) efflux inhibition by P-gp inhibitor verapamil in lymphocytes in a control group of healthy persons (n=49) and patients with NHL (n=76).

Results: P-glycoprotein function in treated NHL patients was significantly (p=0.02) higher than in untreated patients. The study of P-gp function in NHL patients showed that P-gp activity was associated with a different tumor malignancy grade (p=0.01): P-gp activity in the patients with high-grade NHL was significantly (p=0.009) higher in comparison to patients with low-grade NHL. Although P-gp function in treated NHL patients tended to be higher in patients who received more aggressive chemotherapy, this difference wasn't statistically significant. P-glycoprotein function was higher in chemoresistant patients (disease progression) than in those who were sensitive to chemotherapy (complete or partial remission, stable disease), but the difference did not reach a statistical significance.

In conclusion, P-gp activity was higher in patients with NHL than in the control group of healthy persons, and associated with tumor malignancy grade.

Keywords: P-glycoprotein activity, non-Hodgkin's lymphoma, chemotherapy resistance

<-- Previous abstract Contents Next abstract -->

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Top