Glycogen phosphorylase BB as a marker of cardiac toxicity during high-dose chemotherapy followed by hematopoietic cell transplantation

Cardiotoxicity is a potentially serious complication of oncology treatment. Myeloablative preparative regimen (PR) followed by hematopoietic cell transplantation (HCT) represents high risk for the development of cardiotoxicity [1]. Various methods have been recommended for monitoring cardiotoxicity in oncology. Recently, the applicability of cardiac troponins (cTnT, cTnI) has been investigated in this context and the results are inconsistent [2, 3]. Therefore, we evaluated the possible role of new perspective biomarkers of cardiac injury—heart fatty acid-binding protein (H-FABP) and glycogen phosphorylase BB (GPBB) [4, 5]. According to the available literature, there are no data on using these biomarkers in this context.

The aim of our pilot study was to assess cardiotoxicity during PR and HCT with biomarkers of myocardial injury—myoglobin, creatine kinase MB (CK-MB) mass, cTnT (Roche), cTnI, H-FABP and GPBB (Randox).

Nineteen patients (mean age 42.8 ± 10.0 years, 13 males) pretreated with anthracycline-based chemotherapy for acute leukemia were studied. PR consisted of high-dose cyclophosphamide 120 mg/kg in combination with busulphan or total body irradiation, followed by HCT. All patients had normal liver and renal functions during the study. Biomarkers of cardiac injury were measured on Elecsys Roche and Evidence Randox analyzers the day before PR (baseline), the day after PR, the day after HCT and 14 days after HCT. Concentrations of cardiac biomarkers diagnostic for cardiotoxicity of oncology treatment have not been established yet. In our study, values above the reference range recommended by the manufacturer were considered elevated. The cut-off values were as follows: 76.0 μg/l for myoglobin, 4.80 μg/l for CK-MB mass, 0.01 μg/l for cTnT, 0.40 μg/l for cTnI, 4.50 μg/l for H-FABP and 7.30 μg/l for GPBB.

Before PR, all biomarkers were below the cut-off values in all patients. GPBB became elevated (>7.30 μg/l) in five (26.3%) patients the day after PR, remained elevated in five (26.3%) the day after HCT and in one (5.3%) 14 days after HCT. The changes in GPBB were significant in comparison with the baseline values (P < 0.01). Other biomarkers (myoglobin, CK-MB mass, cTnT, cTnI and H-FABP) remained within the reference range in all the patients.

Our results show that administration of PR containing high-dose cyclophosphamide followed by HCT may be associated with myocardial injury manifested by increased release of GPBB from cardiomyocytes in our cohort in five (26.3%) patients early after PR and HCT. These findings could be considered a sign of acute subclinical cardiotoxicity of this treatment. Whether these acute changes will predict treatment-related cardiomyopathy in the future is unclear and must be evaluated during a prospective follow-up. Persistent GPBB elevation in one (5.3%) patient 14 days after HCT could be a sign of subacute cardiac toxicity related to undergone oncology treatment (prior anthracycline-based chemotherapy and recent administration of PR). According to our results, other sensitive markers of myocardial injury (cTnT, cTnI, H-FABP, CK-MB mass and myoglobin) do not seem to be of value in the detection of cardiotoxicity during PR and HCT in acute leukemia. Further studies will be necessary to confirm our preliminary results and define the potential role of new biomarkers in this context.

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