AC-Mode of Chemotherapy Driven Hyperhomocysteinemia

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Nowadays, mortality from cardiovascular (CVD) and oncological diseases have become the leading cause of death in countries with high and average GDP and HDI. In the context of the above, the issue of chemotherapy-induced cardiotoxicity seems fundamentally relevant. Despite the dynamic progress of therapeutic oncology, anthracycline drugs which have been considered as highly effective but cardiotoxic ones since the 70s of the 20th century, without losing their demand, still remain irreplaceable components of different chemotherapy modes such as AC, FAC, etc. AC-mode of chemotherapy is: Doxorubicin (adriamycin) + cyclophosphamide; FAC-mode of chemotherapy is: Fluorouracil, Doxorubicin (adriamycin) and Cytoxan.
Despite a comprehensive and versatile assessment of this issue, the question of anthracyclin's-induced iatrogenic cardiotoxicity, particularly doxorubicin (DOX)-related impairment of cardiovascular homeostasis, remains obscure. Doxorubicin is found to be an orchestrator of various pathophysiological mechanisms and pathobiochemical aspects underlying cardiovascular morpho-functional homeostasis's disequilibrium. In this regard, we decided to investigate the possible relationship between the AC mode of chemotherapy components and homocysteine level.
For this experimental work, 20 inbrand Wistar rats were used. Trimetazidine (TMZ) was used as a stabilizer of morphofunctional homeostasis of the cardiovascular system. The course dose of DOX was 15 mg/kg, cyclophosphamide (CY) 150 mg/kg, and the course dose of TMZ was 42 mg/kg. The experiment lasted 14 days. Homocysteine determination was carried out by a quantitative, enzyme-linked immunosorbent assay using the Rat Homocysteine ELISA Kit (CSB-E13376r, Cusabio Biotech Co Ltd., China). The test system's measuring range was 0.78-50 nmol/ml, while the sensitivity threshold was 0.195 nmol/ml.
The study's results were as follows: group #1 (administration of sodium chloride solution) 150.60 nmol/ml; group #2 (administration of DOX and CY) 478.62 nmol/ml; group #3 (administration of DOX and CY with TMZ) 276.59 nmol/ml; group #4 (TMZ administration) 147.69 nmol/ml. Statistical characteristic was $F=15450.63$, $P<0.0001$.
After analyzing the above data, it should be noted that the administration of AC mode of chemotherapy is to be considered as a potential trigger of hyperhomocysteinemia development, a generally accepted risk factor for CVD development and progression, whereas trimetazidine by demonstrating its CVD-preventive effect had a modifying effect on the homocysteine level.

Key Words: Cardiotoxicity, chemotherapy, doxorubicin, homocysteine.

Abbreviations:
CVD – Cardiovascular Disease,
GDP – Gross Domestic Product,
HDI – Human Development Index,
DOX – Doxorubicin,
CY – Cyclophosphamide,
TMZ – Trimetazidine.