

INVESTIGACIÓN - MEDICINA

EFFECT OF PRECONDITIONING WITH PHOTOBIMODULATION ON THE EXPRESSION OF MICRORNAS RELATED TO CARDIAC HYPERTROPHY IN HUMAN VENTRICULAR CARDIOMYOCYTES DERIVED FROM PLURIPOTENT STEM CELLS SUBJECTED TO DOXORUBICIN.

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INTRODUCTION: Cardiotoxicity is a well-recognized adverse effect associated with cancer therapy, with long-term consequences. Doxorubicin, a chemotherapeutic agent in the treatment of malignant neoplasms, presents as major side effects the cardiac toxicity, raising significant concerns about its clinical use. Photobiomodulation triggers a cascade of molecular events with therapeutic potential in cardiovascular diseases, and the use of light irradiation has been explored as a treatment source to promote beneficial effects in biological tissues. **OBJECTIVE:** The aim of this study was to analyze the microRNA (miRNA) expression profile in ventricular cardiomyocytes derived

from human induced pluripotent stem cells (HiPSC-vCMs) subjected to photobiomodulation preconditioning and exposed to doxorubicin.

METHODS: The in vitro experimental study was conducted using HiPSC-vCMs preconditioned with photobiomodulation and exposed to doxorubicin. The HiPSC-vCMs were allocated into three groups: 1 - Control (not exposed to DOX or PBM; irradiated with standard lamp; addition of saline); 2 - DOX group (addition of 2 μ M DOX for 24 hours); and 3 - DOX + PBM group (preconditioning with PBM; addition of 2 μ M DOX). Dosimetric parameters of the LED device were wavelength of 660 nm $\pm$ 10 nm, irradiance of 10 mW/cm², for 500 seconds, resulting in a dose of 5 J/cm². Cytotoxicity analysis was assessed by MTT assay. The expression of microRNAs associated with cardiac hypertrophy was assessed by quantitative real-time polymerase chain reaction (qPCR). **RESULTS:** Doxorubicin treatment reduced the expressions of miR-1 and miR-208, while increased miR-21 expression. In the DOX+PBM group, the expression levels of these miRNAs were reverted to values similar to the control group.

CONCLUSION: Photobiomodulation preconditioning significantly restored the expression of deleterious miRNAs related to cardiac hypertrophy in cardiomyocytes in vitro.

Palavras-chave: photobiomodulation; ventricular cardiomyocytes; pluripotent stem cells; mirnas; cardiotoxicity.