OMEGA-3 FATTY ACID SUPPLEMENTATION ATTENUATES DOXORRUBICIN-INDUCED CARDIOTOXICITY IN RATS, BUT NOT BY SPHINGOMYELINASE/CERAMIDE PATHWAY

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INTRODUCTION

Cardiotoxicity is the most serious side effect of treatment with the chemotherapy drug doxorubicin (DOX)[1]. Pathophysiological mechanism of DOX-induced cardiotoxicity is not well established. Ceramide is formed from the breakdown of sphingomyelin present in the plasma membrane carried out by neutral sphingomyelinase enzymes (nSMase) and acts as a cellular mediator of oxidative stress[2,3,4]. Omega-3 fatty acid (w3) supplementation could act in the ceramide/sphingomyelinase pathway.

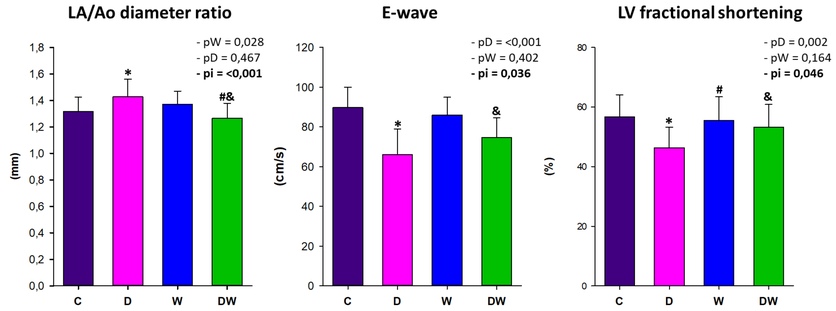
AIM

Evaluate the involvement of the sphingomyelin/ceramide pathway in the pathophysiology of DOX-induced cardiotoxicity and the possible protective effect w3.

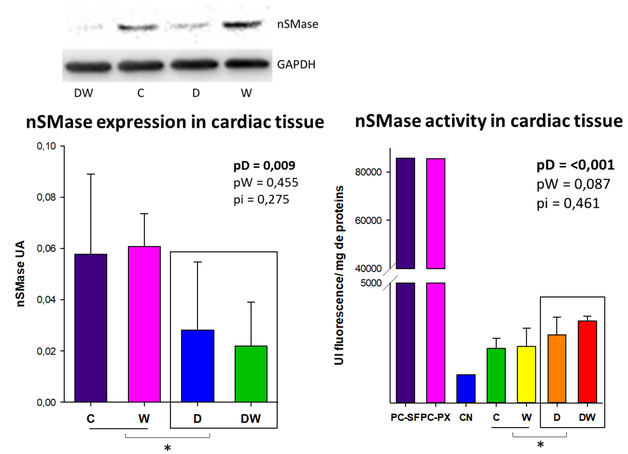
RESULTS

The D group exhibited increased left atrium/aorta diameter ratio and decreased in the E wave, characterizing diastolic dysfunction, and decreased left ventricular fractional shortening when compared to group C, characterizing systolic dysfunction.

The DW group showed improvement in these variables. Both myocardial nSMase expression and nSMase activity in cardiac tissue were lower in rats treated with DOX when compared to animals that did not receive the chemotherapy. The w3 supplementation did not interfere with these variables.

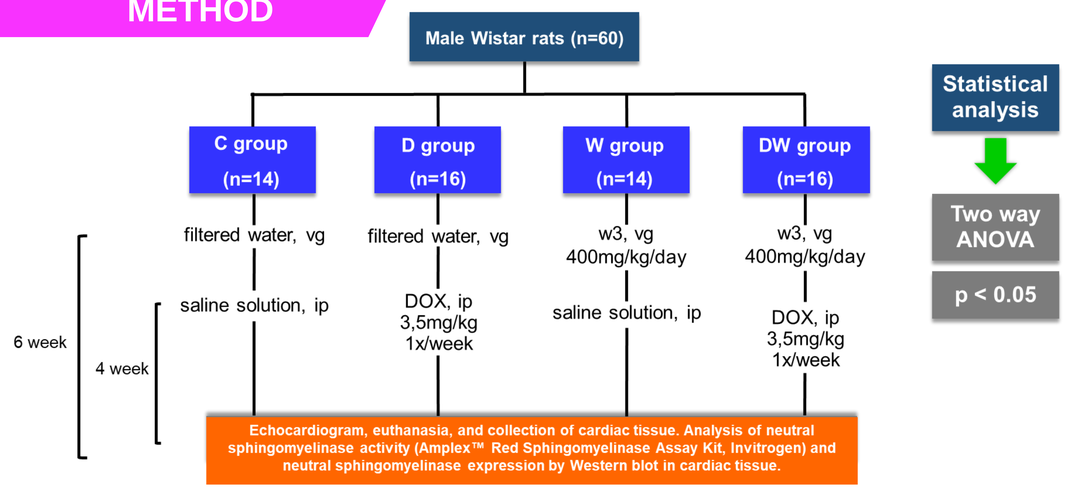


LA: left atrium; Ao: aorta; LV: left ventricle; C: control group; D: doxorubicin group; W: omega 3 fatty acid group; DW: doxorubicin + omega 3 fatty acids. Data expressed as mean ± standard deviation. p-value: two-way ANOVA, where pD: p-value for the DOX effect; pW: p value for the w3 effect; pi: p value for the interaction between the factors.*: p <0.05 when compared to group C. #: p <0.05 when compared to group D. &. p < 0.05 when compared to the W group.



nSMase: neutral sphyngomielynase; C: control group; D: doxorubicin group; W: omega 3 fatty acid group; DW: doxorubicin + omega 3 fatty acids. Data expressed as mean ± standard deviation. p-value: two-way ANOVA, where pD: p-value for the DOX effect; pW: p value for the w3 effect; pi: p value for the interaction between the factors.*: p<0.05 when comparing all animals that received DOX with animals that did not receive DOX

METHOD



Statistical analysis

Two way ANOVA

p < 0.05

CONCLUSIONS

Administration of w3 attenuated cardiac dysfunction induced by doxorubicin in rats. The sphingomyelinase/ceramide pathway is possibly involved in the pathophysiology of cardiotoxicity; however, this is not the mechanism by which w3 attenuated cardiac dysfunction.

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