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Reply to Letter to the Editor: "Can ARNI Prevent Doxorubicin-Induced Cardiotoxicity?"

LETTER TO THE EDITOR REPLY

To the Editor,

We thank the authors for reading with great interest. In our study, as in previous studies, semi-quantitative histological analysis was performed.[1]

It was stated that the limitations of our study were that imaging methods, especially invasive methods and hemodynamic measurements, were not used. Doxorubicin (DOX)-induced cardiotoxicity can occur in acute and chronic periods. It is known in the literature that left ventricular systolic dysfunction accompanies DOX-induced ventricular-related acute arrhythmogenic events.[2,3] In a recent study, it was found that natriuretic peptide levels predicted late-stage cardiotoxicity due to DOX.[4] In our study, the ability of electrocardiography and natriuretic peptide data to predict both acute and chronic cardiotoxicities due to DOX has been already proven in clinical studies in the literature.

The data in the study cannot explain the mechanism of action of anthracycline associated with topoisomerase 2β (TOPO2β) inhibition and downregulation of peroxisome proliferator-activated receptor-gamma coactivator1-alpha. However, recent studies have suggested that DNA topoisomerase-related cytotoxic mechanisms affect highly proliferating cells such as cancer cells and that another mechanism is responsible for the cardiotoxicity of DOX.[5] In addition, it has been suggested that TNF-related apoptosis-inducing ligand, a member of the cytokine superfamily, binds to death receptors and causes cardiotoxicity through caspase activity.[5] However, the cardiotoxic effect of DOX, which has not been eliminated for years, is not due to a single mechanism, and basing it on a single mechanism may result in the blocking of new treatment modalities. Also, no blocker or chelator utility was claimed in study that would require the explanation of the effect of sacubitril-valsartan (SAC/VAL) on the direct DNA topoisomerase. The authors are quite right that the DOX-induced cardiotoxicity of reactive oxygen derivatives is a consequence. That is why, in our study, the therapeutic protective effect of SAC/VAL was investigated with the parameters of the existing pathways that may show response to treatment.

It will certainly evaluate the protective effect of SAC/VAL in DOX-induced cardiotoxicity, and our results need to be validated in the future, particularly with clinical studies.

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