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Doxorubicin-induced cardiotoxicity – Are plants the answer?

Cardiotoxicidade induzida pela doxorubicina – Serão as plantas a resposta?

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One of the backbones of cancer treatment is the anthracycline doxorubicin. Its use has been shown to significantly slow disease progression in several types of cancer and is regarded as one of the most potent chemotherapeutic drugs(1). While effective, its use is limited by its toxic effects in most organs, including the liver, kidneys, reproductive organs and brain, but more importantly on the heart(2). Depending on the dose, up to 9% of patients receiving doxorubicin develop cardiac dysfunction associated with its use(3), and while known for decades, its pathophysiology is still unclear and worrisome creating the need for the establishment of transdisciplinary cardio-oncology teams(4).

Strategies to reduce cardiotoxicity induced by doxorubicin include analogous compounds, specific drug formulations such as lipid-based carriers or co-treatment with cardioprotective medication(2). More recently, sodium-glucose transport protein 2 (SGLT2) inhibitors have been shown to attenuate cardiac dysfunction associated with anthracycline use(3), and while clinical trials are ongoing (NCT05271162), more research is needed to elucidate its impact when comorbidities (such as diabetes are absent) as well as anticancer effects(5).

In the current issue, Khairnar SI (6), et al, tackle doxorubicin-induced cardiotoxicity by using a naturally occurring, plant-derived compound, chelidonic acid (CA). When administered orally with CA for 4 weeks, rats showed a significant improvement in doxorubicin-associated cardiac dysfunction, and in some parameters even showed superiority over the dexrazoxane. As the authors mention, CA possesses analgesic and sedative effects, which could pose a limitation in its clinical application, however the fact that the lower dose tested shows similar effects to all others might permit a dosing regimen that has cardioprotective benefits without central nervous system side effects.

Of note, oxidative stress, one of the main mechanisms of doxorubicin-induced cardiotoxicity, was attenuated with CA treatment at the cardiac tissue level. The same was true for tissular inflammation and circulatory markers of myocardial injury, including cardiac troponin-T.

A comprehensive hemodynamic evaluation is essential to determine the true potential of any cardiac-targeted therapy, and the same is true for CA. While the authors show a beneficial effect in terms of resolving hypotension, a lack of volumetric parameters compromises a full

interpretation of the results, warranting further research. Parallel to this, a more detailed histopathological analysis would greatly benefit this data, which still shows, albeit in simple terms, an improvement of cardiomyocyte structure and fibrosis deposition when CA was administered.

Modest in its nature, the work by Khairnar SI, et al opens the way for a new treatment approach for cardiotoxicity associated with cancer treatment, which should incite the authors and the scientific community to take this knowledge further in a much-needed area of research.

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