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EDITORIAL COMMENT

Doxorubicin-induced cardiotoxicity – Are plants the answer?

Cardiotoxicidade induzida pela doxorrubicina – 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 chemotherapy drugs.[1] While effective, its use is limited by its toxic effects on 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, thus creating the need for the establishment of transdisciplinary cardio-oncology teams.[4]

Strategies to reduce doxorubicin-induced cardiotoxicity 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 et al.,[6] 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 to 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 tissue 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

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more detailed histopathological analysis would greatly benefit these data, which still reveal, albeit in simple terms, an improvement in cardiomyocyte structure and fibrosis deposition when CA was administered.

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

Conflicts of interest

The authors have no conflicts of interest to declare.

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