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Hypertension Comorbidity Exacerbates Cardiotoxicity of Anti-Cancer Drugs: Evidences and Promising Novel Therapeutic Strategies

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Background

Anthracyclines are one of the most widely studied drugs in terms of cardiotoxicity, and are a mainstay component of anti-cancer regimens. Not only do one-third of those with cancer have hypertension, but it is also the most commonly reported comorbidity in cancer registries. In order to provide optimal treatment for the health of the growing population of cancer patients with hypertension comorbidity, it is necessary to understand the potential effects, if any, their hypertension and anthracycline treatment will have on short- and long-term cardiac function.

Objectives

- To assess whether anthracycline chemotherapy exacerbates cardiotoxicity in patients with hypertension comorbidity.
- To describe its molecular and pathophysiologic mechanisms
- To identify novel therapeutic modalities to combat potential exacerbation

Methods

We performed a literature search using the Medline database on Pubmed on all articles addressing the relationship of anthracycline cardiotoxicity and hypertension.

Results

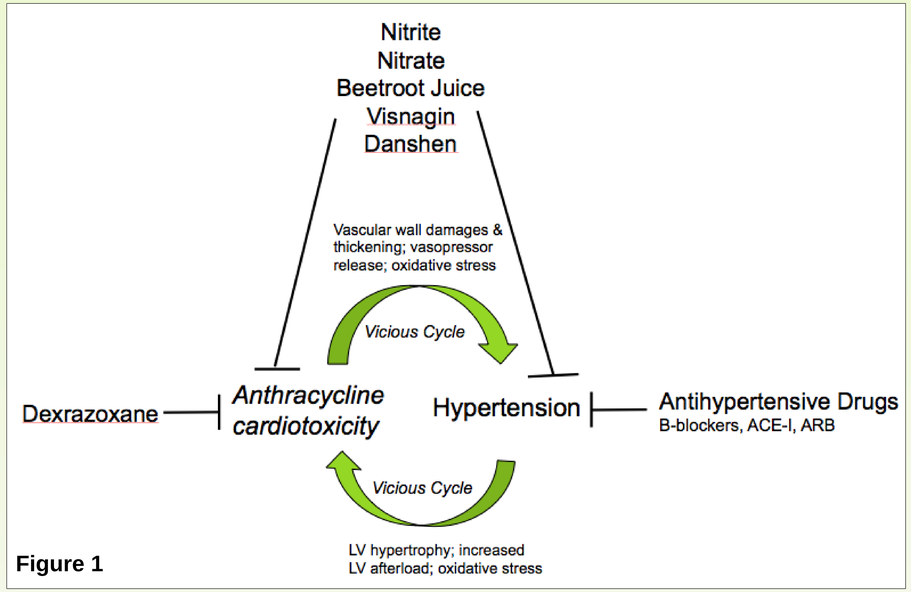

Figure 1: Diagrammatic summary of the vicious cycle for cardiovascular pathology under the comorbidity of anthracycline cardiotoxicity and hypertension. The current and potentially promising novel therapeutic strategies are also indicated. *Abbreviations*: LV – left ventricular; ACEI – angiotensin converting enzyme inhibitor; ARB – angiotensin receptor blocker.

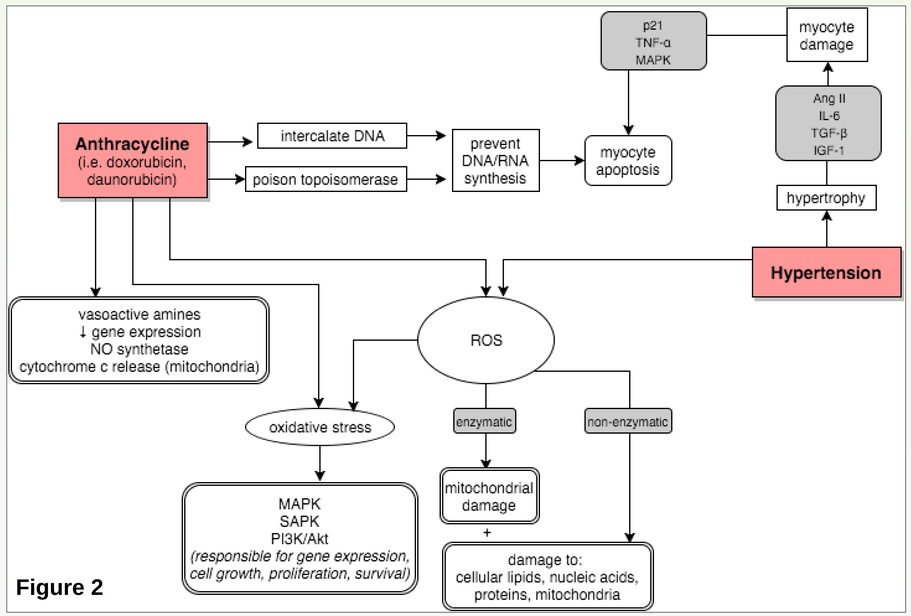

Figure 2: Summary of mechanistic overlap of anthrayclines and hypertension.

- Von Hoff et al. reported the earliest link between hypertension and doxorubicin cardiotoxicity through a retrospective analysis of 4018 patients in cooperative group trials (Von Hoff *et al.*, 1979).
- The results of a study by Herman et al. demonstrate that hypertensive rats were more prone to cardiac damage by doxorubicin than the normotensive rats (Herman *et al.*, 1985).
- Even when compared to hypertension comorbidity, total cumulative dose still remains the most significant and major risk factor for anthracycline-related CHF.
- As demonstrated in Figure 1 and Figure 2, a pathophysiologic overlap exists between hypertension and anthracycline in terms of cardiotoxicity.

Conclusion

- We summarize evidence from the literature as well as animal models that support the claim that hypertension does indeed worsen the cardiotoxic effects of anti-cancer chemotherapeutic drugs.
- Management should rest upon a careful balance of risks and benefits. Meticulous attention should be paid on pretreatment screening for risk factors, robust monitoring of cardiac function, and early intervention for preexisting comorbidities.
- In nearly all cases, it is recommended to first manage the patient's hypertension before administering anthracycline treatment.
- Cardioprotectants (i.e. dexrazoxane) should be explored as a viable solution on a case-by-case basis.

Future

- As the mean age of the population increases, and concurrently the risk of hypertension and cancer, cardio-oncologists are needed to effectively satisfy the management of a growing subgroup of patients.
- Further research is needed to aid in the clinical management of these patients. For example, little information is available on dosing adjustments and follow-up scheduling. Additionally, combinations of anticancer drugs are increasingly being used to aggressively treat various forms of cancer. While these drugs have various cardiac implications, it is important to investigate the potential additive or interactive effects of these drugs.