Mini Review
Volume 7:3, 2022

Journal of Oncology Medicine & Practice

ISSN: 2157-7145 Open Access

A Brief Analysis of Drug Combinations and Mechanisms

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Abstract

Cancer patients now have hope thanks to chemotherapy, radiation, targeted therapy, and immunotherapy. Cancer-therapy-induced cardiovascular damage has garnered interest as cancer patient survival times have increased and clinical experience has grown. Deeper understanding of the molecular biology underlying the disease is necessary to develop appropriate preventative and treatment strategies for the side effects of cancer therapy that can be fatal or cause long-term morbidity. Traditional Chinese medicine formulations are effective in addition to the common cardio-protection medications and can be expected to achieve "tailored treatment" from a variety of angles. Furthermore, "reverse cardio-oncology" has emerged as a result of the rising incidence of cancer in people with cardiovascular disease, underscoring the urgent need for collaboration between cardiologists and oncologists.

Keywords: Cardiovascular disease • Radiation therapy • Antioxidants • Cardio toxicity • Cardiomyocytes

Introduction

The proportion of cancer patients who also have heart disease rises as cancer mortality drops and the population still alive ages. Cardiovascular disease is more likely to develop in cancer survivors than tumour recurrence, and the increased risk of cardiovascular disease is related to cancer treatment. Anti-cancer medication-related cardiovascular problems, such as heart failure and arrhythmia, are rather frequent. The chance of dying from heart disease is higher among older breast cancer survivors than it is from the disease itself. Additionally, a cohort analysis of pediatric cancer survivors revealed that cardio toxicity has overtaken the tumour itself as the second-leading cause of long-term mortality. Cardio toxicity in juvenile patients receiving DOX was first documented in 1976. Since then, other initiatives have been launched to further minimize toxicity while also separating the cardio toxic and anticancer effects of ANTs. The cardio toxicity of ANT has also received increased attention concurrently. Studies have shown that the cumulative dose, schedule of administration, and age all had an impact on its hazardous consequences.

Monoclonal antibodies, inhibitors, immunotherapy, and other medicines been developed as a result of a thorough understanding of the mechanism behind the cancer development. Although these medications effectively treat cancer, a major issue influencing patient survival, prognosis, and quality of life is the cardio toxicity they produce. So, "cardio-oncology" has become a more advanced field. Because myocardial cells are directly damaged, decreased heart function after cancer therapy may be caused by primary cardiomyopathy. Changes in the hormonal system or in the innervation lead to secondary cardiomyopathy. As an alternative, inflammatory cells infiltrate the myocardium to create myocarditis. The foundation of cardio-oncology is the evaluation and treatment of cardio toxicity brought on by anticancer medication or the malignant process it. In order to prolong meaningful lives and provide individuals with supportive cardiovascular care while pursuing optimal cancer care, it is important to strike a balance between antitumor efficacy and cardiac events connected to cancer therapy.

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Date of Submission: 02 June, 2022, Manuscript No. jomp-22-74700; **Editor Assigned:** 07 June, 2022, PreQC No. P-74700; **Reviewed:** 18 June, 2022, QC No. Q-74700; **Revised:** 23 June, 2022, Manuscript No. R-74700; **Published:** 28 June, 2022, DOI: 10.37421/2157-7145.2022.7.160

In order to achieve this goal, researchers have concentrated on preventing and reducing the cardio toxicity related to cancer treatment. The development of "tumour cardiology" has involved efforts to combine cardiovascular and anti-cancer medications without altering the anti-cancer efficacy while attaining cardiac cleansing. The risk of cardiovascular disease in cancer patients is the main focus of traditional cardio-oncology. Reverse cardio-oncology is based on the likelihood that people with cardiovascular disease will get cancer in the future. These two avenues of development point to a complex interaction between the two disorders. The collaboration between cancer and cardiology as well as the prevention and treatment of linked disorders can all benefit from an understanding of this bidirectional interaction. In this article, we examine the processes of cardio toxicity brought on by cancer treatment, combination therapy, and some recent advances in reversing cardio-oncology.

Literature Review

Chemotherapy, radiation, targeted therapy, and immunotherapy are the main types of treatments for advanced cancer; all of them have a detrimental effect on the cardiovascular system and have been widely documented. Cardio toxicities brought on by chemotherapy and radiation therapy in particular are the main cause of morbidity and mortality in cancer survivors [1]. There is established cardio toxicity linked to ANT usage in chemotherapy. Contrarily, there are few reports of cardio toxicity linked to relatively new medicines like target therapy and immunomodulation. ANTs' anticancer method involves causing DNA damage. They primarily affect cells in the S and G2 stages of proliferation [2]. Through non-specific insertion, the parent nucleus of the anthracene ring is parallel to the DNA base pair and creates a relatively stable complex. Since DNA is negatively charged, the parent nucleus' positive charge has a strong affinity for it. The molecule's quinone structure can easily take part in electron transfer processes that result in oxygen free radicals. On the one hand, ANTs are DNA-embedded and obstruct DNA transcription and replication. However, using ANTs causes double-strand breaks in DNA and oxidative damage to nucleic acids by boosting the generation of reactive oxygen species [3].

Additionally, topoisomerase type 2, DNA unwinding, helicase activity, and consequent strand separation of DNA are all directly affected by ANTs. According to the period of onset, acute and chronic cardio toxicity can be separated. Rare cases of acute cardio toxicity brought on by ANT therapy include myocardial damage, interstitial edoema, and infiltration of inflammatory cells [4]. This condition is pathologically comparable to abrupt toxic myocarditis. Contrarily, dilated cardiomyopathy in laboratory models and human hearts is a more frequent symptom of chronic cardio toxicity brought on by ANTs. Increased heart weight and dilated heart chambers are the hallmarks of the pathology. In human tissue and animal models, vacuolar degeneration

with sarcoplasmic reticulum swelling and consolidation represent the most prevalent patterns, respectively [5].

Discussion

Chronic cardio toxicity is classified into early and late forms based on when it first manifests. Early-onset chronic cardio toxicity usually presents as a dilated and hypokinetic cardiomyopathy and results in HF. It usually arises within a year after therapy termination. After chemotherapy has ended, years or even decades, late-onset persistent cardio toxicity may appear. The latter produces H2O2, which has the ability to be changed into a number of ROS-related compounds that ultimately result in DNA damage response and the death of many cardiomyocytes. According to numerous researches, the cardio toxicity of ANTs can be decreased by using antioxidants including N-acetyl cysteine, vitamin E, and coenzyme. However, persistent antioxidant use did not produce the anticipated outcome in several animal tests. As a result, it is unclear how much of an impact oxidative stress and the generation of primitive ROS have on the cardio toxicity caused by ANT. The fact that ANTs exhibit a specific preference for the mitochondria in cardiomyocytes is another intriguing element of ANT-induced cardiotoxicity. Studies have demonstrated a connection between mitochondrial malfunction and ROS generation. The abundant phospholipid cardiolipins on the inner mitochondrial membrane can directly bind to DOX, which can then block complexes I and II, obstruct the electron transport chain, and generate ROS. Then, ROS act on mitochondria, causing mitochondria to enlarge, causing the mitochondrial permeability transition pore to open, and causing the mitochondrial membrane potential to dissipate. In neonatal rat cardiomyocytes exposed to DOX, aberrant mitochondrial structure and mitochondrial damage have indeed been observed.

Through preventing Sestrin2 (SESN2) from interacting with Parkin and p62, DOX interferes with mitophagy. Additionally, cytoplasmic p53, which binds to Parkin and prevents it from trans locating to mitochondria to inhibit phagocytosis, may be associated to the DOX-induced regulation of mitochondrial autophagy. On the other hand, other investigations have suggested that excessive autophagy induced by DOX is the cause of cardiotoxicity and activation of the PINK1/Parkin pathway-which encourages PINK1/Parkin translocation to mitochondria-are its outward signs. In addition, mitophagy reduction reduces mitochondrial dysfunction and guards against cell death in cardiomyocytes. Later, "macroautophagic," a process by which DOX causes cardiotoxicity by influencing autophagy, is explored in addition to mitophagy. Antitumor therapy-induced cardiotoxicity has raised questions about the involvement of autophagy in this. Maintaining cellular homeostasis requires the lysosome-dependent bulk breakdown pathway known as autophagy. Beginning with the inhibition of the mammalian target of rapamycin signalling pathway and activation of the adenosine 5'-monophosphate-activated protein kinase pathway, autophagy occurs. Other research, however, have focused on ANT-induced cardiotoxicity brought on by autophagy suppression. that DOX stimulates the Toll-like receptor-9 downstream signalling pathway, phosphoinositide 3-kinase gamma/protein kinase B, activating mTOR, which in turn suppresses Ulk-1 and prevents the start of autophagy. Discovered that receiving DOX therapy did not sufficiently activate cardiac autophagy.

It is challenging to pinpoint the specific involvement of autophagy in DOX-induced cardiotoxicity, and those investigations lacked a thorough evaluation of autophagic flux. Increased LC3-II levels might indicate a problem with autophagosome fusion or improved autophagosome formation. There are some distinctions between the clinical symptoms of acute cardiotoxicity and chronic cardiotoxicity brought on by DOX, and the cardiotoxicity of DOX is amount of the drug. Controversial findings could potentially be a result of research on dosage and modelling duration being lacking. However, regardless of whether DOX causes cardio toxicity by activating or suppressing autophagy, it is highly intriguing that reversing autophagy at that moment can reduce cell death.

Conclusion

The processes by which cancer therapy causes cardiovascular toxicity are outlined in this study, along with the use of antineoplastic and cardio protective medications in combination and new developments in reverse cardio-oncology. The main modalities utilised in cancer treatment include surgery, radiotherapy, and chemotherapy. Breast, thyroid, prostate, head and neck cancers can all be effectively treated with radiotherapy. The primary ways that radiotherapy damages DNA are through ionising molecules in radioactively-damaged tissue, preventing DNA replication, and eliminating tumour cells.

Conflicts of Interest

None.

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How to cite this article: Lee, Sophia. "A Brief Analysis of Drug Combinations and Mechanisms." J Oncol Med & Pract 7 (2022): 160.