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Use of Beta-antagonists or HMG-CoA Reductase Inhibitors for Cardioprotection During Chemotherapy in Oncology Patients

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Abstract

Over the years, oncologists are better able to fight cancer and have increased cancer survival, but we are also finding out that these lifesaving treatments can affect the heart and other parts of the body in a negative way. Chemotherapy is excellent at destroying cancer cells, but it also causes collateral damage. There are certain chemotherapeutic agents that are known to cause cardiotoxicity. Currently, we are monitoring the heart function of the patients who are receiving these cardiotoxic chemotherapy agents and understanding the risk of developing heart failure during and after treatment. However, there are currently no studies in which cardioprotective agents are being used to prevent chemotherapy-induced cardiotoxicity. The intention of this scholarly review is to look into the benefits and compelling results in adrenergic beta-antagonists and HMG-CoA reductase inhibitors to prevent the risk of developing chemotherapy in oncology patients. The goal of this paper is to look at the research and hopefully conclude that either beta-antagonists or HMG-CoA reductase are a reliable option to prevent chemotherapy-induced cardiotoxicity. An extensive literature review was performed and at this time, there are no concrete benefits of using either a beta-blocker or a statin to reduce chemotherapy-induced cardiotoxicity. In the research that has been done, there is some evidence of using these agents to protect the heart. More long-term studies need to be conducted as well as more precise inclusion terms need to be used, such as the exact chemotherapy regimen or the particular cardioprotective medication that is used in the study. At this time, recommendations to prevent chemotherapy-induced cardiotoxicity remains inconclusive.

Introduction

• Over the years, oncologists are better able to fight cancer and have increased cancer survival, but we are also finding out that these lifesaving treatments can affect the heart and other parts of the body in a negative way. Since chemotherapy is not able to target just the tumor, there is collateral damage to other cells throughout the body. This, oftentimes, destroys the heart. It can lead to the expansion of the heart and this is known as an enlargement of the heart. The enlargement of the heart leads to a decrease in pump function and heart failure. The heart strain is the most common side effect of chemotherapy but it can also cause heart blockage, arrhythmias, and even death. There is also silent internal damage being done to the heart muscle and it is thought that these changes will appear immediately after receiving chemotherapy or at times the damage may not surface for years after treatment. There are not a lot of research studies available to look at what options can be done to protect the healthy cells from the effects of the chemotherapy. This is important to consider because the costs to date have been astronomical and the chemotherapy has caused cardiotoxicity, attributing mostly to the creation of oxygen free radicals causing oxidative stress. More recent research has revealed that there is a maximum cumulative dose and the cardiotoxicity is due to DNA damage from chemotherapy. There are other chemotherapeutic agents associated with cardiotoxic side effects, which include, taxanes, alkylating agents, and topoisomerase inhibitors, which cause damage to the heart cells. 

• One of the most well known and most studied chemotherapeutic agents that is associated with adverse cardiac events are anthracyclines, such as doxorubicin. Anthracyclines are often used to treat adult malignancies such as breast cancer, sarcoma, lymphoma, or gynecological cancer. Anthracyclines have been shown in many studies to have a positive correlation with heart failure. Chemotherapy has caused cardiotoxicity, attributing mostly to the creation of oxygen free radicals causing oxidative stress. More recent research has revealed that there is a maximum cumulative dose and the cardiotoxicity is due to DNA damage from chemotherapy. There are other chemotherapeutic agents associated with cardiotoxic side effects, which include, taxanes, alkylating agents, and topoisomerase inhibitors, which cause damage to the heart cells. 

• The intention of this scholarly review is to look into the benefits and compelling results of adrenergic beta-antagonists in reducing the risk of cardiotoxicity and to help oncologists when deciding which chemotherapy regimen to give to their patients. The review is meant to be used to look at the research and hopefully conclude that beta-antagonists are a reliable option for heart protection during anthracytide treatment. 

Statement of the Problem

It is known that certain chemotherapeutic agents have the potential to lead to heart damage, but there is no known method to protect the heart cells from the cytotoxic drugs. Anthracyclines are the most common chemotherapeutic treatment, during the course of treatment, and following the completion of treatment is already being done for patients that are receiving chemotherapy. The chemotherapeutic agents known to cause cardiotoxicity are investigated. Methods to prevent this myocardial damage are still being researched. In particular, anthracycline- and anthraquinone-based chemotherapy can cause cardiac injury. HMG-CoA reductase to prevent chemotherapy-induced cardiotoxicity. Adrenergic beta-antagonists and HMG-CoA reductase inhibitors may be the most promising cardioprotective agents for patients who are receiving chemotherapy.

Research Question

In adult oncology patients, do either adrenergic beta-antagonists or HMG-CoA reductase inhibitors reduce the risk of cardiotoxicity in patients receiving chemotherapy?

Literature Review

Etiology, prevalence, and outcomes of cardiotoxicity in adult patients receiving chemotherapy.

• Cardiac toxicity has been related to many cytotoxic agents including, anthracyclines, anthraquinones, antimitobolites, antimicrotubulins, vincristine, and tyrosine kinase inhibitors, Babek et al. (2018). There is no consistent evidence that either heart failure or cardiotoxicity is defined and there was varying degrees of heart function prior to starting therapy.

• Cardiotoxicity related to chemotherapy is unusual in adults. The cumulative doxorubicin doses less than 300 mg/m² and the rate of heart failure is approximately 7.2% at 550 mg/m² and at a rate of 18-48%, if cumulative. Due to the cumulative nature of cardiac failure, there is a maximum lifetime cumulative dose of anthracycline cardiotoxicity. The recommendation is to use the cumulative lifetime dose is 400-550 mg/m² adults.

• Asymptomatic systolic or diastolic heart failure are the most common signs of chronic cardiotoxicity. Foudraine et al. (2018). This makes close monitoring an essential step not only just during treatment but also at follow up. The maximum cumulative doxorubicin dose seems to be the best predictor of heart failure with a median dose of 90 mg/m² in the patients who developed heart failure and 80 mg/m² in those patients who did not develop heart failure. In patients who received greater than 400 mg/m², the incidence of congestive heart failure was 3%, in those that received 400-550 mg/m², and 18% in patients who received doses greater than 550 mg/m², Nathan et al. (2016) received doses greater than 550 mg/m², Nathan et al. (2016). 

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• Volkova et al. (2011) reported that heart failure prevalence seems to be high at a cumulative doxorubicin therapy. Research is limited due to patients having different medical histories, varying cancer diagnoses, and different treatments. Table used to compare cumulative doxorubicin dose and percentage of patients with CHF.

Prevention of chemotherapy-induced cardiotoxicity with the use of HMG-CoA reductase inhibitors.

• Patients (n = 40) undergoing anthracycline-based chemotherapy with mean EF for the study group was unchanged before and after chemotherapy (61 ± 8% vs. 61 ± 10%, p < 0.0001). Sharalaya et al. (2018). Low EF overall was lower in the control group (60.7% vs 55.8% 16.1%, p = 0.001). Sharalaya et al. (2018). The authors concluded the control group had a lower incidence of heart failure, Sharalaya et al. (2018). Volkova et al. (2011) also reported that heart failure prevalence seems to be high at a cumulative doxorubicin therapy. Research is limited due to patients having different medical histories, varying cancer diagnoses, and different treatments. Table used to compare cumulative doxorubicin dose and percentage of patients with CHF.

• Upshaw (2018) compared several medications to reduce chemotherapy-induced cardiotoxicity. Most showed promise, including beta-antagonists and HMG-CoA reductase inhibitors. However, this study was limited by using various medications in one specific class.

• Riad et al. (2009) looked if fuvastatin pretreatment can attenuate doxorubicin-induced cardiotoxicity. The study was done in mice, not humans.

Discussion

Chemotherapy agents can cause cardiotoxicity that can be seen as an adverse effect of chemotherapy. These effects can be seen throughout the course of chemotherapy or they can be seen months or even years following the completion of chemotherapy.

• Clinical trials have revealed that anthracycline cardiotoxicity with the use of HMG-CoA reductase inhibitors.

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• Adrenergic beta-antagonists

• Effect on heart function in patients receiving doxorubicin chemotherapy. Riad et al. (2009). The study of beta-antagonists and HMG-CoA reductase inhibitors to prevent chemotherapy-induced cardiotoxicity is promising. The use of any pharmacological therapy to reduce chemotherapy-induced cardiotoxicity cannot yet be recommended. There is evidence that both HMG-CoA reductase inhibitors and adrenergic beta-antagonists to be beneficial in reducing chemotherapy-induced cardiotoxicity and long-term studies looking at heart function, no specific recommendations may be made to prevent chemotherapy-induced cardiotoxicity.