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CARDIOTOXICITY OF CHEMOTHERAPY AND ITS EARLY DETECTION

Summary. Oncopathology is a serious public health problem both in our country and in other countries of the world. So, if you look at the statistics, we will see an increase in the incidence of malignant neoplasms. Chemotherapy is one of the components of treatment that can reduce the mortality of patients, which, in turn, causes a number of complications. Most of the toxicities associated with cytostatics are associated with rapidly proliferating cell systems, but cells with limited regenerative capacity (cardiomyocytes) may be susceptible to the transient effects of chemotherapeutic agents.

Key words: cardiotoxicity, cancer patients, anthracyclines, arterial hypertension.

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КАРДИОТОКСИЧНОСТЬ ХИМИОТЕРАПИИ И РАННЕЕ ЕЁ ВЫЯВЛЕНИЕ

Резюме. Онкопатология является серьезной проблемой здравоохранения как в нашей стране, так и в других странах мира. Так, если посмотреть данные статистики мы увидим увеличение заболеваемости злокачественными новообразованиями. Одним из компонентов лечения, позволяющим снизить смертность больных, является химиотерапия, которая, в свою очередь, вызывает ряд осложнений. Большинство ассоциированных с цитостатиками видов токсичности связано с быстро пролиферирующими клеточными системами, но и клетки с ограниченной регенеративной способностью (кардиомиоциты) могут быть восприимчивыми к преходящему воздействию химиотерапевтических агентов .

Ключевые слова: кардиотоксичность, онкологических больных, антрациклины, артериальная гипертензия.

Introduction: The increasing number of patients with long-term survival, as well as the use of new anticancer drugs, make the problem of cardiotoxicity more and more urgent.

Cardiotoxicity is a term that includes various adverse events associated with the cardiovascular system, against the background of drug therapy for cancer patients.

Patients with malignant neoplasms are hypercoagulable, and chemotherapy may increase the risk of venous or arterial thromboembolism. For example, the use of cisplatin was the cause of venous thromboembolism in 18% of patients; most likely, the direct endothelium toxic effect and changes in the blood coagulation system are "responsible" for this side effect. A similar risk of arterial thromboembolism was observed with sunitinib, sorafenib, and tamoxifen. Anticoagulant prophylaxis is recommended only for high-risk patients (hospitalized, postoperative, with multiple myeloma). Currently, studies are

underway on low molecular weight heparins for the prevention of thromboembolism in cancer patients.

Target. Suter and Ewer proposed to classify all cytostatics and targeted drugs according to the type of damaging effect on the cardiovascular system.

Materials and methods. Type I - irreversible myocardial dysfunction due to the death of cardiomyocytes, an example of such an effect is anthracyclines. The degree of myocardial damage in this case depends on the cumulative dose.

Type II - reversible myocardiocyte dysfunction, due to mitochondrial and protein damage. Most typical for trastuzumab and does not depend on the cumulative dose.

However, this classification is relative, since does not take into account all the factors contributing to the development of cardiotoxicity. For example, trastuzumab belongs to type II, but in patients with concomitant cardiac pathology or cardiotoxicity from anthracyclines, it can contribute to the development of the damaging effect of type I. The reversibility of cardiovascular complications such as angiotensin-inhibitor-induced hypertension and nephrotoxicity has not yet been studied.

Research results. As a result of the action of chemotherapy drugs, various types of cardiovascular complications can develop.

The most significant are cardiac dysfunction and heart failure. For example, commonly used chemotherapy drugs such as anthracyclines, antimetabolites and cyclophosphamide can cause permanent myocardial damage and cardiac remodeling; inhibitors of human epidermal growth factor 2 (HER2 / erbB2) receptors and angiogenesis predominantly affect cardiac metabolism and contractile proteins, resulting in transient contractile dysfunction.

Chemotherapy-induced arterial hypertension is now recognized as associated with the use of angiogenesis inhibitors. These drugs can worsen or lead to existing hypertension. It is difficult to determine the true incidence of induced hypertension, as the studies used different methods for determining hypertension and measuring blood pressure. A recent meta-analysis of studies with bevacizumab

reported an incidence of hypertension of more than 23%. The incidence of hypertension associated with sunitinib and sorafenib is approximately the same; patients with pre-existing hypertension or kidney cancer are at higher risk. Hypertension can develop at any stage of treatment: complications include heart failure, proteinuria with renal thrombotic microangiopathy, intracerebral hemorrhage (often reversible posterior leukoencephalopathy). Most patients improve when treatment with an angiogenesis inhibitor ends, but in some cases, severe hypertension persists.

The next one of the most serious complications is vasospastic and thromboembolic ischemia associated with chemotherapy. The most common agents associated with coronary artery spasm are pyrimidine analogs of 5-fluorouracil (5-FU) and oral analogs of capecitabine. Vasospastic angina has developed both in patients with prior coronary artery disease and in patients with normal coronary arteries, and has been associated with spasms of the coronary arteries during treatment with these drugs. Ischemia most often occurs after the second or third administration of these antimetabolites, for the treatment and prevention of which nitroglycerin and calcium channel blockers have been successfully used. In rare cases, myocardial infarction has developed.

Arrhythmias associated with anticancer therapy are usually transient and not particularly troubling to patients. They are usually caused by metabolic changes and resolve after restoration of electrolyte homeostasis. The use of anthracyclines, for example, is associated with supraventricular arrhythmias and ventricular premature beats during or immediately after administration. Taxanes can cause sinus bradycardia during treatment, but it is not serious and usually is not treated. Prolongation of the QT interval is associated with the use of a number of anticancer drugs and can be a serious problem. A prime example is arsenic trioxide, which is used to treat leukemia, can prolong the QT interval in 40% of patients and increase the risk of torsades de pontes. The presence of concomitant diseases, including electrolyte disturbances caused by diarrhea, vomiting, taking

other medications (psychotropic and antiemetic drugs) can additionally lead to a prolongation of the QT interval.

The importance of early detection of cardiotoxicity has been noted by many authors, for example, according to Rickard J et al., Anthracyclines-induced cardiomyopathy has a worse prognosis than other causes and has less than 50% survival within 2 years. Basically, after the onset of HF symptoms, it is very difficult to achieve a positive treatment result, and the patient's prognosis worsens [23]. Early detection of chemotherapy-induced cardiotoxicity makes it possible to change the dosage and / or rate of drug administration, use drugs comparable in the effectiveness of antitumor treatment, but less cardiotoxic, and use new drug combinations. Due to the difficulties of early diagnosis of cardiotoxicity, various methods for assessing cardiac function are being used and studied.

Conclusions. Since cardiotoxicity can manifest itself in different forms, the simplest common methods can also be used to detect it: taking anamnesis and complaints, general examination, measuring blood pressure, ECG. But the effect of chemotherapy on the heart can begin imperceptibly, and at the same time it is impossible to detect changes with available research methods. Endomyocardial biopsy was considered the most accurate method for establishing cardiotoxicity, since it provides accurate information about microscopic changes in the heart muscle. But a number of factors limited its availability: the invasive method of material sampling, a small number of specially trained specialists, the quality of the material taken, the heterogeneity of myocardial damage. And endomyocardial biopsy has not become widely used as a method for early diagnosis of the cardiotoxicity of chemotherapy.

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