Asian journal of Pharmaceutical and biological research 2231-2218
http://www.ajpbr.org/
Volume 10 Issue 2
MAY-AUG 2021
10.5281/zenodo.5379517

TREATMENT AND PREVENTION OF ARRHYTHMIAS ASSOCIATED WITH ANTICANCER THERAPY

Ergashov Bobir Bahodirovich

Bukhara state medical institute, Bukhara, Uzbekistan

ABSTRACT. The given review is devoted to the problem of the cardiotoxicity of chemotherapeutic agents. Many of chemotherapeutic agents can cause cardiovascular complications such as left ventricular dysfunction and heart failure development, myocardial ischemia, arterial hypertension, thromboembolism, QT prolongation and arrhythmias. The toxic influence of the most often used chemotherapeutic agents on heart (such as antimetabolites, alkylating agents, platinum compounds, taxanes, vinca alkaloids, monoclonal antibodies, anthracycline antibiotics, topoisomerase and protein kinase inhibitors, immunomodulatory agents and cytokines) has been described. The results of recent studies on etiology, pathogenesis and clinical features of chemotherapy-induced cardiotoxicity were present in the first part of review. The clinical features, diagnosis, treatment and prevention of the cardiotoxicity of chemotherapeutic agents, are described in the second part of the review

Keywords: chemotherapy; cardiotoxicity; pathogenesis; drug-induced cardiomyopathy.

INTRODUCTION.

The manifestations of cardiotoxicity (CT) are very variable and can be observed both on the first day of taking the drug and decades after the start of treatment. In patients receiving therapy with antimetabolites, taxanes, monoclonal antibodies and protease inhibitors, CT can manifest as acute coronary syndrome (ACS) (intense chest pain of a pressing, compressing or burning character, often radiating to the left arm, lower jaw, severe weakness and pallor , difficulty breathing, sweating, etc.) [1–4]. A number of patients on the background of chemotherapy (CT)

Asian journal of Pharmaceutical and biological research 2231-2218
http://www.ajpbr.org/
Volume 10 Issue 2
MAY-AUG 2021
10.5281/zenodo.5379517
develop various rhythm and conduction disturbances, including life-threatening variants [1].

Tyrosine kinase inhibitors and anthracyclines are capable of prolonging the Q-T interval. The duration of the Q-T interval and the risk factors contributing to its lengthening should be monitored before, during and after the course of treatment, since prolongation of the Q-T interval is associated with the risk of life-threatening tachyarrhythmias and sudden cardiac death [4]. The risk of lengthening the Q-T interval varies for different drugs, this is especially true in the case of using arsenic trioxide (when using it, Q-T interval lengthening is observed in 26–93% of cases) [1, 5].

Against the background of therapy with sorafenib and immunomodulatory agents, venous thromboembolic complications (VTO) may develop with an appropriate clinical picture depending on the localization of the process.

The use of anthracycline antibiotics very often leads to the development of left ventricular (LV) dysfunction and / or severe heart failure (HF) with a corresponding clinical picture [5, 6].

Treatment

Heart failure

Patients receiving anthracyclines therapy and having signs of heart failure, as well as patients with asymptomatic LV dysfunction, are shown to be prescribed angiotensin-converting enzyme inhibitors (ACE inhibitors) or angiotensin II receptor blockers (ARBs) in combination with β-blockers [1]. However, this kind of treatment can be effective only if it is carried out in the early stages of the onset of changes in the heart. For patients with end-stage HF who are resistant to drug therapy, synchronized ventricular pacing, implantable cardiac devices, or heart transplantation should be considered if necessary. If clinically significant heart failure occurs in patients receiving trastuzumab, it is recommended that the drug be discontinued. If the drug is discontinued, as a rule, regression of symptoms in patients occurs after 1–

Asian journal of Pharmaceutical and biological research 2231-2218
http://www.ajpbr.org/
Volume 10 Issue 2
MAY-AUG 2021
10.5281/zenodo.5379517
1.5 months. Patients who have made significant progress in the treatment of neoplastic pathology with the use of trastuzumab, after the disappearance of the symptoms of HF, may be reappointed, provided that they take cardioprotective drugs and careful monitoring of heart function [1, 8].

Myocardial ischemia

Patients with suspected ACS should be monitored and treated according to current guidelines [1, 12]. Currently, percutaneous coronary interventions, antiplatelet and anticoagulant therapy remain the cornerstone in the treatment of ACS in cancer patients. Patients who, as a result of chemotherapy, develop ACS or symptoms of coronary artery disease concurrently with thrombocytopenia, present a special problem and require multidisciplinary observation in each case. There are few options for drug and interventional treatments, as the use of antiplatelet and anticoagulants is limited due to the hematological toxicity of anticancer drugs. In patients undergoing percutaneous coronary intervention and subsequently diagnosed with a tumor, dual antiplatelet therapy should be continued as long as possible without increasing the risk of bleeding [3].

Arterial hypertension (AH)

Hypertension is a complication of anti-angiogenic drug therapy (bevacizumab, sorafenib, sunitinib). The main goal of the treatment of hypertension in cancer patients is to reduce the risk of damage to target organs (cardiovascular, cerebrovascular complications, renal failure). Therapy should be carried out in accordance with the current recommendations of the European Society of Cardiology [1, 12]. Treatment of hypertension in the presence of chemotherapy, as a rule, requires the appointment of more than one antihypertensive drug and careful monitoring of blood pressure. The need to discontinue antiangiogenic therapy due to hypertension is still controversial [3, 5]. Sorafenib should not be used concomitantly with calcium channel blockers of the dihydropyridine series, since both of these drugs are inhibitors of the CYP3A4 enzyme (cytochrome P-450 system), and their

Asian journal of Pharmaceutical and biological research 2231-2218
http://www.ajpbr.org/
Volume 10 Issue 2
MAY-AUG 2021
10.5281/zenodo.5379517
simultaneous administration entails a significant increase in the level of sorafenib in the blood [6]. There are currently no specific recommendations for the appointment of a particular antihypertensive drug for patients with hypertension associated with chemotherapy. It should also be noted that glucocorticoids, which are included in many chemotherapy regimens, also lead to the development of hypertension.

Thromboembolic complications

Thromboembolic complications are a common side effect of therapy with sorafenib and immunomodulatory agents. In patients with diagnosed venous thrombosis, further therapeutic measures should be aimed at relieving symptoms and preventing embolic complications. When deciding on the appointment of anticoagulants for the prevention of venous thromboembolic complications (VTC) in cancer patients, the risk of bleeding and the patient's life expectancy should always be taken into account; they can change over time, which requires periodic reassessment. Treatment of confirmed acute VTC in hemodynamically stable patients includes low molecular weight heparins (LMWH) administered for 3–6 months. In clinical trials, this method is more effective than treatment with vitamin K antagonists (VKA) in reducing the incidence of thromboembolic events without difference in mortality or bleeding. Given the fact that malignant tumors are a risk factor for recurrent VTC, the prescription of anticoagulants on an ongoing basis after treatment of acute thrombosis should be considered until the malignant tumor is considered cured. When choosing a further strategy (discontinuation of anticoagulants, maintenance therapy with LMWH, or switching to VKA), factors such as the effectiveness of anticancer treatment, the risk of relapse and bleeding, and the patient's desire should be taken into account [7, 8, 9]. If there are contraindications to anticoagulants or ineffectiveness of therapy, they can be implanted with a permanent or temporary cava filter. However, one should not forget about the risk of thrombosis and filter occlusion in post-thrombophlebitic syndrome leading to distal thrombosis. In the

Asian journal of Pharmaceutical and biological research 2231-2218
http://www.ajpbr.org/
Volume 10 Issue 2
MAY-AUG 2021
10.5281/zenodo.5379517
studies carried out, the installation of a cavailter in addition to anticoagulant therapy with fondaparinux has not shown any clinical benefits [1, 7, 10].

Bradycardia

In case of bradycardia with progressive atrioventricular block and / or clinically significant hemodynamic disorders (which can develop while taking paclitaxel), it is shown that the chemotherapy infusion is stopped and the issue of prescribing appropriate drug therapy and / or cardiac stimulation (temporary or permanent) is indicated [1, 12].

Prolongation of the Q-T interval

In addition to the listed cardiovascular side effects, anticancer drugs can disrupt the repolarization processes in the myocardium with prolongation of the Q-T interval, which in turn threatens hicardia (torsades de pointes). If a patient develops arrhythmias of the torsades de pointes type, 2 g of magnesium sulfate is recommended as a first-line therapy, regardless of the serum magnesium level and, if indicated, intravenous stimulation in the mode of forced acceleration of the rhythm (overdrive pacing) or administration of isoprenaline to the heart rate contractions of more than 90 beats / min in order to prevent new episodes of rhythm disturbances [3, 4]. Unsynchronized defibrillation is indicated in cases of ongoing hemodynamically unstable polymorphic ventricular tachycardia or the development of ventricular fibrillation [7].

Prophylaxis

The timing and method of cardiovascular protection depends on different clinical conditions. If the initial risk of developing CT is high due to existing cardiovascular diseases preceding chemotherapy with anthracyclines, or poorly controlled risk factors, then a strict correction of risk factors and prophylactic prescription of cardioprotective drugs are necessary [1, 5–7].

There are currently no clear data on the effectiveness of prophylactic administration of ACE inhibitors, ARBs, or β-blockers in patients receiving

anthracyclines with an initially low risk of CT. Currently, there is some evidence that the correction of cardiovascular risk factors before starting chemotherapy reduces the incidence of corresponding complications of anticancer therapy in patients with hypertension, diabetes mellitus, and heart failure. Cancer patients with initially clinically expressed heart failure or significant LV dysfunction require a specialized cardiac examination, preferably in a specialized clinic [1, 6, 8]. Before treatment, the risk / benefit ratio should also be assessed when choosing a chemotherapeutic drug (regimen) [7]. Options include choosing an alternative non-cardiotoxic CT, prescribing anthracyclines to people with low CT levels (eg, liposomal doxorubicin), low-dose CT regimens, and / or using additional cardioprotective drugs (ACE inhibitors, β-blockers, aldosterone antagonists, or dexrazoxane).

It is necessary to identify criteria for early CT, which would be confirmed by data on late morbidity and mortality of patients. For early detection of myocardial dysfunction, periodic determination of LVEF is not enough. The combined approach with the definition of biomarkers and data from imaging techniques also has many disadvantages. Several circulating biomarkers (troponin I, NP-B, N-terminal fragment of natriuretic peptide B-type) are considered sensitive for the early detection of myocardial dysfunction and overt heart failure associated with the treatment of oncopathology. Nevertheless, reliable data are needed on their predictive value for clinically significant long-term effects of anticancer therapy. Currently, there are numerous experimental and clinical studies aimed at finding various drugs as agents with cardioprotective properties in both types of CT [1, 7, 9, 10].

CONCLUSION

Thus, CT is an important problem affecting many aspects of oncology, hematology and cardiology. And, despite certain achievements, today there are many unresolved issues related to its diagnosis, prevention and treatment. It is hoped that future studies on CT chemotherapy can not only expand the body's tolerance to

special treatments, but also increase their effectiveness without developing serious side effects.

REFERENCES

1. Ergashov B.B. **A** causal relationship of anticancer drugs with specific arrhythmias Asian journal of Pharmaceutical and biological research. Volume 10 Issue 2 may-aug 2021. P. 47-50.

2. Akhmedova N.Sh., Ergashov B.B., Nuralieva H.O., Safarova G.A. Influence of collected modified risk factors on the development and progression of chronic kidney disease // International Journal of Current Research and Review Vol 13 • Issue 02 • January 2021 P. 13-17

3. Zamorano J.L., Lancellotti P., Muñoz D.R. et al. ESC Position Paper on cancer treatments and cardiovascular toxicity developed under the auspices of the ESC Committee for Practice Guidelines. Eur. Heart J. 2016; 37(36): 2768-801. doi:10.1093/eurheartj/ehw211

4. Manrique C.R., Park M., Tiwari N., Plana J.C., Garcia MJ. Diagnostic strategies for early recognition of cancer therapeutics-related cardiac dysfunction. Clin. Med. Insights. Cardiol. 2017; 11: 1–12. Doi: 10.1177/1179546817697

5. Makhmudova L.I., Akhmedova N.Sh., Ergashov B.B. Clinical manifestation of irritable bowel syndrome Art of Medicine Volume-1 International Medical Scientific Journal Issue-2 P. 24-33.

6. Abdullaeva U.K. Predicting the risk of atrophic transformation in chronic gastritis using serum pepsinogen // World journal of pharmaceutical research, Faculty of Pharmacy Medical University, Bulgaria, Vol. 8, Iss. 13, 2019, P. 219-228.

7. Abdullaeva U.K., Sobirova G.N., Karimov M.M., Aslonova I.J. The prevalence and possibilities of prevention of noncardial gastric cancer in the Bukhara region // American journal of medicine and medical sciences, 2020, 10(9), P. 679-681.

8. Sobirova G.N., Abdullaeva U.K., Nosirova M.S., Aslonova I.J. Evaluation of the gastrointestinal mucosa by the OLGA system in chronic atrophic gastritis // Journal of critical reviews, Kuala Lumpur, Malaysia, Vol. 7, Iss. 2, 2020, P. 409-413.

9. Karimov M.M., Sobirova G.N., Abdullaeva U.K., Aslonova I.Zh., Tulyaganova F.M. Possibilities of serological diagnosis of atrophic processes of the gastric mucosa // European Journal of Molecular & Clinical Medicine Vol. 7, Iss. 11, 2020, P. 2955-2960.

10. Makhmudova L.I., Shazhanova N.S., Akhmedova N.Sh., (2021). Clinical Features Of Irritable Intestinal Syndrome. The American Journal of Medical Sciences and Pharmaceutical Research, 3(04), 154-159.

11. Makhmudova L.I, Akhmedova N.Sh. Irritable bowel syndrome: a new look at the problem // Academicia. 10.5958/2249-7137.2020.00983.0. 433-38

12. Abdullayev R. B., Makhmudova L.I. Features of Chemical Elements in Various Forms of Irritable Bowel Syndrome // Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 2, 2021, Pages. 2993 – 3000