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COMBINED ANTIHYPERTENSIVE THERAPY FOR BEVACIZUMAB-INDUCED HYPERTENSION

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Relevance. Arterial hypertension (AH) is a common cardiotoxicity of anti-VEGF agents that occurs in 35% of patients receiving bevacizumab, a humanized IgG1 monoclonal antibody to vascular endothelial growth factor (VEGF).

Aim: To identify the relationship between changes in blood pressure (BP) and initial antihypertensive treatment in patients who developed arterial hypertension induced by bevacizumab.

Materials and methods. A retrospective study included 110 patients treated with bevacizumab (15 mg/kg/3 weeks, maximum dose) who were treated at the Kursk Cancer Research Clinical Center. G.E. Ostroverkhov from January to December 2020 with metastatic colorectal cancer and with metastatic breast cancer. The mean age of the patients was 66±4.2 years. All patients had morphological (histological) verification of the diagnosis according to the 8th edition of the TNM classification (UICC, 2017). The study group received bevacizumab in addition to combination chemotherapy. The choice of antihypertensive drugs was as follows: group 1 of 35 patients was assigned to dual antihypertensive therapy - angiotensin-converting factor inhibitor (ACE) + calcium channel blocker (CCB), group 2 of 35 patients - angiotensin II receptor blocker (ARB) + CCB, and group 3 out of 40 patients - ACE inhibitor + diuretic. The hemodynamic parameters of the activity of the cardiovascular system were assessed: systolic and diastolic pressure (SBP and DBP) by the method of N.I. Korotkov. The studied parameters were described with the calculation of the mean (M) and standard deviation (SD). Quantitative indicators were evaluated by Student's t-test for dependent variables. Statistically significant differences were considered between the indicators at $p<0.05$.

Results and their discussion. Median BP before bevacizumab therapy was 134/86 mmHg. The median time to onset of bevacizumab-induced hypertension was 2.8 months. The indices of hypertensive effect in the group of AH of degree III (CTCAE v5.0 scale) (n=50) and in the group of AH of degree II (n=60) were: SBP - 166±4.3; DBP - 107±5.4 mmHg and SBP - 153±3.7; DBP - 96±2.9 mmHg ($p<0.05$), respectively. Combined antihypertensive therapy taken by patients had the following effect. Median BP after antihypertensive therapy (12 weeks) significantly improved and amounted to 142/95 mmHg ($p<0.05$). The dynamics of changes in blood pressure in the group taking ACE inhibitors + CCB: SBP decreased by 11.18%, DBP - by 9.43%; in the ARB + CCB group: SBP decreased by 12.88%, DBP - by 8.33%; in the group taking ACE inhibitor + diuretic: SBP decreased by 10.98%, DBP - by 5.83% ($p<0.05$).

Conclusion: thus, the use of combined antihypertensive therapy made it possible to reliably record a decrease in blood pressure. However, it should be noted that the median BP after antihypertensive treatment was higher than the median before chemotherapy in combination with bevacizumab. The combination of ARBs + CCBs had the most significant hypotensive effect on SBP, while the combination of ACE inhibitors + CCBs had the most significant effect on DBP.