

Detection of Side Effect of Antiangiogenetic Agents

Abdullayeva Nargiza Erkinovna

Urgench branch of Tashkent Medical Academy

Abstract: The formation of new blood vessels that transport oxygen and nutrients is the basis of most physiological and pathological processes. However, microangiogenesis is one of the stages of tumor growth and subsequent tumor spread, progression and metastasis. Various proangiogenic and antiangiogenic factors play a role in the regulation of neoangiogenesis.

Methods and materials. Effect of therapy is assessed with ultrasound examination, CT, tonometry, ECG, ExoKG and MRI. 50 patients have operated and effect is assessed with hystological examination as well.

Summary. We believe that as the usage of VSP inhibitors increases, treatment-induced hypertension resulting from earlier tumor diagnosis and longer medication duration will become more common. During a patient's follow-up, we advise oncologists to be aware of this possibility and make sure that blood pressure is closely checked..

Keywords: hydronefrosis, excretor urography, hypertension, tonometry.

Urgency: The formation of new blood vessels that transport oxygen and nutrients is the basis of most physiological and pathological processes. However, microangiogenesis is one of the stages of tumor growth and subsequent tumor spread, progression and metastasis. Various proangiogenic and antiangiogenic factors play a role in the regulation of neoangiogenesis. Vascular endothelial growth factor (VEGF) is of greatest importance in the regulation of this process. The formation of new blood vessels (microangiogenesis) is a prerequisite for tumor growth and metastasis, while the processes of neoangiogenesis are characteristic of the earliest stages of tumor progression. Microangiogenesis during tumor progression stimulates “itself” due to the fact that with the rapid growth of tumor tissue, cells experience hypoxia, which increases the level of hypoxia-inducible factor-1 α (HIF-1 α), which, in turn, activates VEGF, and also its interaction with VEGFR – processes that cause activation of endothelial cells, their proliferation and migration, leading to neoangiogenesis [3, 4]. The use of antiangiogenic drugs that block tumor vascularization leads to inhibition of microangiogenesis and a decrease in the number of vessels [3]. Antiangiogenic drugs are widely used in the treatment of tumors of various locations: colorectal cancer, ovarian cancer, gastric cancer, non-small cell lung cancer, and breast cancer. Basically, drugs that block neoangiogenesis are used in the treatment of common forms of the disease in the presence of metastatic disease, which implies long-term treatment (until toxicity or signs of progression). Bevacizumab is only antiangiogenic drug which is registered in the Uzbekistan at present. It blocks VEGF-A in blood plasma and inhibits the VEGFR1 and VEGFR2 receptor signaling pathways. This leads to normalization of the structure of altered tumor vessels, a decrease in the density of the microvascular bed and inhibition of neovascularization mechanisms, which facilitates the availability of tumor cells for the delivery of chemotherapy drugs(5). The effectiveness of adding bevacizumab to various chemotherapy regimens for various types of tumors (for example, colorectal cancer, ovarian cancer, gastric

cancer) has been demonstrated in a large number of international clinical trials: for example, in the ECOG E3200 study, the addition of bevacizumab to the FOLFOX regimen (oxaliplatin 85 mg/m², calcium folinate 400 mg/m², 5-fluorouracil 400 mg/m² intravenously - IV bolus, 5-fluorouracil 2400 mg/m² IV) in the 2nd line of chemotherapy for metastatic colorectal cancer led to a significant increase in overall survival [6].

Arterial hypertension The use of antiangiogenic drugs is accompanied by the development of endothelial dysfunction and damage to glomerular epithelial cells (podocytes). Moreover, the most common clinical manifestations of nephrotoxicity of these drugs are arterial hypertension (AH) and proteinuria [9]. Hypertension usually develops after the first cycle of treatment with anti-VEGF drugs [10].

Aim of investigation. Assessment of side effects of antiangiogenic agents likewise, nephrotoxic and arterial hypertension in the patient who has cancer disease.

Materials and method of investigation. We have investigated 146 patients have received antiangiogenic agents with different cancers from 2018 to 2023 years. 79 of them with colorectal cancer, 22 of them stomach cancer, 24 of them ovarian cancer, 18 of them kidney cancer as well as 3 of them brain cancer.

5 kinds of agents are used, likewise sunitinib, sorafenib, lenvatinib, regorafenib and bevacizumab (table 2).

According to gender, 100 of them male, 46 of females. The age of the patients from 45 to 72, average 58.5 years old. All patients are treated in Khorezm branch of Republican Scientific-practical cancer centre and 79 of them with colorectal cancer, 22 of them stomach cancer, 24 of them ovarian cancer, 18 of them kidney cancer as well as 3 of them brain cancer (Table 1). It is examined renal function, hypertension and urine tests after every chemotherapy.

Table 1

№	Diseases	Amount	Average number of ChT
1	colorectal cancer	79	21
2	stomach cancer	22	8
3	ovarian cancer	24	8
4	kidney cancer	18	4
5	brain cancer	3	4

Effect of therapy is assessed with ultrasound examination, CT, tonometry, ECG, ExoKG and MRI. 50 patients have operated and effect is assessed with histological examination as well.

Table 2.

№	Diseases	lenvatinib	sunitinib	sorafenib	regorafenib	bevacizumab
1	colorectal cancer	-	-	-	+	+
2	stomach cancer	-	-	-	+	+
3	ovarian cancer	-	-	-	-	+
4	kidney cancer	+	+	+	-	+
5	brain cancer	-	-	-	-	+

Results. The frequency of hypertension was 21.8% (n=31), in 5 patients detected 1st stage, 17 patients 2nd stage, 9 of them 3rd . 9% (n=3) of these patients who have hypertension detected proteinemia during treatment with bevacizumab.

33 % (n=48) have found out proteinemia during treatment and it is eliminated after finishing therapy independently. 19.2% patients are diagnosed proteinuria.

In term of renal tests, 53% (n=78) patients have determined high level of serum creatinin, 15%(n=12) of them detected renal insufficiency, 29%(n=23) of them due to hydronefrosis, 71%(n=55) without. 2% patients are found unfunctioned kidney in excretor urography.

12% of the patients who has colorectal cancer have been detected fully remission, 45% of them parcially remission,

Summary. Treatment-induced hypertension brought on by VSP inhibition medication is a frequent side effect that almost never necessitates stopping cancer treatment. It may be difficult to measure observed rates of hypertension for certain medications due in part to modifications in recommended courses of care.

There remain unsolved concerns regarding the nature of the link between the VSP inhibition and the development of hypertension, which may further illustrate why some drugs are more prone to this effect than others. Moreover, the reason why some tumors, like RCC, are more prone than others to treatment-induced hypertension is still unknown.

We believe that as the usage of VSP inhibitors increases, treatment-induced hypertension resulting from earlier tumor diagnosis and longer medication duration will become more common. During a patient's follow-up, we advise doctors to be aware of this possibility and make sure that blood pressure is closely checked.

Literacy.

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