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RAS blockers and AT1R receptor density in patients with multifocal atherosclerosis

Authors:
I Mykhailichenko1, L Kardashevska1, 1National medical university named after M. Gorky - Donetsk - Ukraine,

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Background/Introduction. In current understanding high activity of tissue renin-angiotensin system (RAS) plays a key role in development of vessel remodeling and atherosclerosis in patients with cardiovascular pathology (CVP). Despite broad applications of angiotensin-converting enzyme (ACE) inhibitors and angiotensin II receptors blockers (ARBs), in a number of cases we don't observe the expected clinico-morphological response to the prescribed therapy, and we quite often observe the «ACE-escape» effect in patients taking ACE inhibitors. We assumed that not all the patients with CVP have high tissue density of angiotensin II receptors type 1 (AT1R) and the «ACE-escape» effect can be related to influence of long-term ACE inhibitors therapy on AT1R receptor density.

Purpose: to study AT1R density in vessel smooth muscle cells (VSMCs) and to estimate its connection with long-term ACE inhibitors treatment in patients with multifocal atherosclerosis.

Methods. We investigated 30 resected arteries of average caliber. The 1st group was formed from 16 arteries affected with atherosclerosis taken during reconstructive surgery on vessels of lower extremities in treatment-naïve patients. 14 internal mammarian arteries taken from patients with significant coronary heart disease during coronary artery bypass grafting taking ACE inhibitors more than 2 years were included in the 2nd group. AT1R localized in the VSMCs were determined immunohistochemically with specific polyclonal AT1R antibodies. In each case Anti-AT1R marker expression in the form of cytoplasmic or membrane brown stain (coloration) was studied in 30 fields of vision at magnification x200. We applied a semi-quantitative method of calculation for assessment of AT1R expression level using the 3rd-level scale based on percent of positively staining cells: "-" negative (lack of positively staining cells); "+", focal or weak expression (<50% of positive cells); "++", diffusive or intensive positive reaction (>50% of positive cells).

Results. In both groups we got the similar results. In the 1st group 8 arteries (47,05%) had weak AT1R expression, in other 8 arteries (47,05%) AT1R expression was strong, in 1 case (5,9%) AT1R expression wasn't defined. In the 2nd group we observed a weak expression in 7 cases (50%) and a strong expression of AT1R in 7 other cases (50%). Differences in AT1R density receptors in treatment-naïve and treatment-experienced patients wasn't statistically significant (P=0,626). Conclusions. Thus, we found out that ACE inhibitors therapy doesn't influence on AT1R receptor density in arterial vessels.The results of our research allow to draw a conclusion that tissue RAS activity is heterogeneous among the patients with multifocal atherosclerosis. In a number of patients with significant atherosclerosis we didn't observe any AT1R expression in VSMCs that calls the leading role of RAS in pathogenesis of vascular remodeling into question in some cases.