PATHOGENETIC CORRECTION OF MICROVASCULAR DYSFUNCTION WITH THE USE OF IMMUNOMODULATING THERAPY IN PATIENTS WITH RESISTANT ANGINA

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Introduction. Resistance to standard antianginal therapy in patients with microvascular angina is primarily due to endothelial dysfunction and inflammatory changes in the microcirculation, necessitating the use of pathogenetically based immunomodulatory therapy. Scientific substantiation and clinical testing of this approach can improve the effectiveness of treatment for resistant forms of angina, improve patients' quality of life, and reduce the risk of cardiovascular complications.
Purpose of the study. To scientifically substantiate approaches to pathogenetic correction of microvascular dysfunction using immunomodulatory therapy and evaluate its clinical effectiveness in patients with resistant forms of angina.
Materials and methods. Patients with resistant microvascular angina (failure of standard antianginal therapy for 3 months) were randomized into two groups: the main group (immunomodulatory therapy + basic treatment, n = 114) and the control group (basic treatment, n = 32). Basic treatment included β-blockers, ACE inhibitors, statins, and antiplatelet agents. Immunomodulatory therapy was administered for 12 weeks. Clinical symptoms (frequency and severity of angina attacks according to the CCS scale), functional tests (bicycle ergometry, exercise echocardiography), and levels of immunological markers (IL-6, TNF-α, sVCAM-1, sICAM-1, endothelin-1, hsCRP) were assessed before and after treatment. Quality of life was assessed using the Seattle Angina Questionnaire (SAQ). Statistical analysis included the t-test, Mann-Whitney test, and repeated measures ANOVA.
Research results. After 12 weeks of therapy, the frequency of angina attacks in the main group significantly decreased from 8.4±2.1 to 3.2±1.4 per week ($p<0.001$), while in the control group the decrease was only from 8.6±2.3 to 6.8±1.9 ($p<0.05$, intergroup difference $p<0.001$). The severity of angina according to the CCS scale significantly decreased in the main group: the proportion of patients with CCS I–II increased from 28% to 76% ($p<0.001$), in the control group — from 26% to 42% ($p<0.01$, intergroup difference $p<0.001$). According to bicycle ergometry data, exercise tolerance in the main group increased from 78±12 W to 124±18 W ($p<0.001$), in the control group —

from 76±14 W to 92±16 W (p<0.01, intergroup difference p<0.001). The time to the appearance of ischemic changes on the ECG increased in the main group from 4.2±0.8 min to 7.8±1.2 min (p<0.001). Exercise echocardiography demonstrated an improvement in regional myocardial contractility in the main group: the number of segments with contractility impairment decreased from 3.8±0.6 to 1.2±0.4 (p<0.001). Immunological markers in the main group significantly decreased: IL-6 - from 18.4±3.2 to 9.8±2.1 pg/ml (p<0.001), TNF-α - from 34.8±5.6 to 18.2±3.4 pg/ml (p<0.001), endothelin-1 - from 4.2±0.8 to 2.4±0.5 fmol/ml (p<0.001), sVCAM-1 - from 985±142 to 524±78 ng/ml (p<0.001), sICAM-1 - from 456±78 to 268±42 ng/ml (p<0.001), hsCRP - from 5.8±1.2 to 2.4±0.6 mg/l (p<0.001). In the control group, the changes in immunological markers were insignificant and did not reach the level of statistical significance. The concentration of circulating endothelial microparticles in the main group decreased from 1248±186 to 486±68 μh/μl (p<0.001), which indicated the restoration of endothelial function. According to the SAQ questionnaire, all components of the quality of life significantly improved in the main group: physical limitation - from 42±8 to 68±10 points (p<0.001), angina stability - from 38±6 to 62±8 (p<0.001), satisfaction with treatment - from 45±7 to 72±9 (p<0.001). In the control group, the improvement in SAQ indicators was less pronounced (p<0.05, intergroup differences p<0.001). After 6 months of observation, the main group showed a 56% decrease in the frequency of visits to emergency medical care compared to the control group (p<0.001).

Conclusion. Immunomodulatory therapy is an effective pathogenetic approach to treating resistant forms of microvascular angina, allowing for a significant reduction in the inflammatory response, correction of endothelial dysfunction, reduction in the frequency and severity of angina attacks, increased exercise tolerance, and significant improvement in patients' quality of life. The obtained results support the inclusion of immunomodulatory therapy in the comprehensive treatment of resistant forms of microvascular angina.

References:

1. Mehta P.K., Wei J. et al. Treatment of angina and microvascular coronary dysfunction. // Curr. Treat. Options Cardiovasc. Med. – 2011. – Vol. 13. – P. 73-83.
2. Pauly D.F., Johnson B.D. et al. In women with microvascular coronary dysfunction angina despite stenosis: a pilot study. // JACC. – 2011. – Vol. 57. – P. 1549-1556.
3. Bairey Merz C.N., Pepine C.J. et al. Ischemia and No Obstructive Coronary Artery Disease (INOCA). // Circulation. – 2017. – Vol. 135. – P. 1070-1078.