REVIEW ARTICLE

CONTENTS

Anti-inflammatory therapy in patients with coronary artery disease: A new era in the treatment of atherosclerosis or false hopes?

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ABSTRACT

Aim: To investigate the potential use of anti-inflammatory drugs in patients with acute myocardial infarction (MI).

Materials and Methods: During December 2025, a comprehensive search was conducted in the scientometric databases PubMed, Scopus, Web of Science and Google Scholar for data from peer-reviewed English-language studies on the use of anti-inflammatory drugs in patients with CAD, published over the past 10 years. The search used the following terms: anti-inflammatory drugs, MI, acute coronary syndrome, chronic coronary syndrome, CVE, CAD, atherosclerosis. Preference was given to the most relevant sources of information, results of randomized placebo-controlled trials, international recommendations, meta-analyses, and more recent literary sources. A total of 94 literary sources were analyzed.

Conclusions: Measuring levels of inflammatory markers and using anti-inflammatory agents, particularly colchicine, in addition to baseline therapy in patients with acute MI to prevent recurrent index events is justified and promising.

KEYWORDS: atherosclerosis, cardiovascular mortality, anti-inflammatory therapy, myocardial infarction, cardiovascular events

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INTRODUCTION

Atherosclerosis is a complex and multifactorial process. In addition to the «classic» factors of its onset and progression, such as dyslipidemia, hypertension, diabetes mellitus, and smoking, the scientific community is actively discussing the importance of inflammation [1].

The basis for this was the results of a 30-year observation of Redker P. and co-authors on 12,530 women. Traditionally, it was believed that patients without "classical" risk factors or after their correction have a relatively low risk of cardiovascular events (CVE). However, it turned out that with high levels of systemic inflammation, in particular highly sensitive C-reactive protein (hsCRP) >3 mg/L, the risk of recurrent CVE remains disproportionately high. Thus, the risk of CAD in this cohort increased by 77%, stroke - by 39%, and major adverse cardiac events (MACE) - by 52%, compared to a group of patients without traditional risk factors and with low hsCRP levels [2].

hsCRP is one of the most indicative pro-inflammatory markers, the increase of which is closely correlated with the risk of MACE. Its level is recommended to be determined in all patients with CAD [3, 4].

In addition to laboratory markers for personalized determination of the degree of inflammation in the coronary arteries and stratification of cardiovascular risks, the Fat Attenuation Index (FAI Score) scale can be used, based on CT coronary angiography data with assessment of perivascular fat. This method has high prognostic value, however, it requires a high-resolution multispiral tomograph and special software [5].

Considering the above, assessing the level of systemic inflammation and correcting it in patients with obstructive forms of coronary artery atherosclerosis is no less important than treating dyslipidemia [4].

AIM

To investigate the potential use of anti-inflammatory drugs in patients with acute myocardial infarction (MI).

MATERIALS AND METHODS

During December 2025, a comprehensive search was conducted in the scientometric databases PubMed, Scopus, Web of Science and Google Scholar for data

from peer-reviewed English-language studies on the use of anti-inflammatory drugs in patients with CAD, published over the past 10 years.

The search used the following terms: anti-inflammatory drugs, MI, acute coronary syndrome, chronic coronary syndrome, CVE, CAD, atherosclerosis.

Preference was given to the most relevant sources of information, results of randomized placebo-controlled trials, international recommendations, meta-analyses, and more recent literary sources. A total of 94 literary sources were analyzed.

ETHICS

All sources used in this literature review are publicly available.

AI STATEMENT

The author states that no AI tools were used in writing this article.

REVIEW AND DISCUSSION

Statins are currently the cornerstone of pathogenetic therapy for atherosclerosis, not only due to their lipid-lowering effect, but also due to the whole spectrum of pleiotropic effects, including anti-inflammatory. Reducing the systemic inflammatory response in the vascular walls makes it possible to stabilize and slow the progression of atherosclerosis [3, 4, 6].

A rather active search for agents with anti-inflammatory effects that could be used to treat atherosclerosis is being carried out among drugs of the rheumatological group, since hyperreactivity and aseptic inflammation also play a key role in the pathogenesis of rheumatic diseases [7].

In particular, the CANTOS trial tested three doses of the monoclonal antibody to interleukin-1β, canakinumab, against placebo in more than 10,000 patients with a history of MI and plasma CRP level ≥2 mg/L. Only the highest dose of the drug (300 mg every 3 months) had a significant positive effect on reducing plasma interleukin-6 and CRP levels, as well as improving the composite endpoint of cardiovascular mortality (CVM), nonfatal MI, and nonfatal stroke. Despite the positive results, further study of the drug in this indication was stopped due to the risk of fatal infections and high cost [8].

The CIRT study focused on the possibility of using low doses of methotrexate (15-20 mg once a week) for secondary prevention of CVE in patients with type 2 diabetes mellitus or metabolic syndrome and a history of MI. The study included nearly 5,000 participants. However, since the announced endpoints (reduction in CVM, risk of non-fatal MI, non-fatal stroke, or need for urgent revascularization due to unstable angina (UA)) were not achieved, it was terminated early [9].

The theory that atherosclerosis is a crystallopathy and that it is the crystallization of free cholesterol in atherosclerotic plaques that causes crystal-induced inflammation, similar to the pathophysiological mechanisms of gout, has proven to be quite promising. It has been suggested that antigout drugs, in particular colchicine, may be used in the treatment of CAD. The mechanism of action of the drug is to block the NLRP3 inflammasome, which interrupts the inflammatory cascade IL-1β→IL-6→CRP, thus inhibiting the key processes underlying atherosclerosis [7].

One of the first scientific tests of this theory was the Australian LoDoCo study (2012). It aimed to evaluate the effect of low-dose colchicine (0.5 mg/day) on the rate of CVE in patients with stable forms of CAD. The result was positive, but the study had a small cohort (only 532 patients) and was not placebo-controlled [10].

The next research that initiated the study of colchicine in patients with obstructive forms of CAD was COLCOT. It suggested that patients with acute forms of CAD have a very high level of systemic inflammation and the use of a drug with anti-inflammatory effect may contribute to the stabilization of the condition and be a means of secondary prevention of recurrent CVE. The study included 4745 patients with a recent MI (less than 30 days) regardless of the level of CRP [10, 11].

During 2.3 years of follow-up, colchicine had a significant positive effect on both the composite primary endpoint (CVM, resuscitated cardiac arrest, nonfatal MI, nonfatal stroke, urgent revascularization due to UA) compared with placebo (5.5 vs. 7.1%, respectively, $p=0.02$), and on each indicator separately. Analysis in subgroups based on the timing of colchicine administration showed that the best results were achieved in patients who received colchicine within 3 days of the index event, compared with groups receiving it between 4 and 7 days and after 8 days [10, 11].

The difference in the frequency of adverse drug reactions, such as diarrhea, between the comparison groups was statistically insignificant (9.7% vs. 8.9%, $p>0.05$). No cases of serious infectious complications or myopathy (although 99% of patients were taking statins) were recorded [10, 11].

The joint Australian-Dutch LoDoCo2 study, which included 5,522 patients with stable forms of CAD, was more thoroughly organized. It should be noted that 84% of the patients included in the study had a history of MI. During 2.4 years of follow-up, the group of

patients who took colchicine at a dose of 0.5 mg/day showed a significantly positive effect on the primary composite endpoint (CVM, spontaneous MI or stroke, urgent revascularization due to ischemia) compared to the control group (6.8% vs. 9.6%, respectively, p<0.001), as well as on secondary endpoints (CVM and non-fatal MI or stroke) (4.2% vs. 5.7%, respectively, p=0.007) [12].

A meta-analysis (12,869 patients) was initiated to summarize the results of studies on the use of colchicine for the prevention of MACE in patients with CAD, which confirmed that low-dose colchicine in this cohort significantly reduced the risk of MI, stroke, and the need for urgent revascularization due to UA. There was no significant difference in the rate of death, death from any cause, or adverse drug reactions from the gastrointestinal tract compared with placebo [13; 14].

The accumulated scientific and clinical data allowed colchicine to be included in the European and American guidelines for the treatment of acute and chronic coronary syndromes as an additional means of secondary prevention of recurrent CVE. And the sufficient safety profile of this agent for use in wide clinical practice is confirmed by the approval of the FDA ((Food and Drug Administration, USA) [3, 4, 6].

However, recent studies have cast doubt on the possibility of using colchicine as a secondary prevention agent for cardiovascular and cerebrovascular events in patients with CAD.

In particular, in the CLEAR SYNERGY study, which included 7062 patients with MI after primary percutaneous coronary intervention, during 3 years of follow-up, a positive effect on the primary composite endpoint (CVM, recurrent IM or stroke, and the need for urgent revascularization due to ischemia) was not achieved with colchicine compared to placebo (9.1% vs. 9.3%, respectively, p=0.93) [15, 16].

The CONVINCE and CHANCE-3 trials did not provide convincing evidence that low-dose colchicine can reduce the risk of recurrent strokes or transient ischemic attacks in patients with acute non-cardioembolic stroke [17, 18].

To resolve the discrepancy between the results of the studies and to make a final assessment of the advisability of using colchicine in patients with CAD as a means of secondary prevention, a new retrospective meta-analysis of existing randomized placebo-controlled studies was initiated, regardless of when they were conducted, the language of publication of the results, and the ethnicity of the patients included in the studies (31,397 cases). The results showed that colchicine at a dose of 0.5 mg/day for a treatment duration of ≥ 6 months significantly reduces the risk of MACE (by 30%) in both acute atherothrombotic and all cardiovascular diseases in representatives of different ethnic groups. There was no increase in all-cause mortality with colchicine treatment, as reported in some studies [19].

Colchicine significantly reduces the risk of CAD destabilization and the need for urgent revascularization, but the reduction in the risk of non-cardioembolic ischemic stroke while taking the drug is borderline statistically significant [19].

Serious adverse drug reactions affecting the gastrointestinal tract, including gastrointestinal bleeding and hospitalization due to these complications, did not differ significantly between the colchicine groups and the comparison group. The incidence of adverse drug reactions not related to the gastrointestinal tract did not differ between the colchicine and control groups [19].

Patients with MI against a background of non-obstructive forms of CAD (MINOCA) are quite difficult to treat. The frequency of these forms can reach 5 to 15% of all cases of acute coronary syndrome. Inflammation also plays an important role in the development of this syndrome [20].

A recent retrospective cohort study involving 42,167 patients with MINOCA showed a positive effect of colchicine on the primary endpoint (recurrent MI, all-cause mortality, CVE, and all-cause hospitalization) compared with placebo (49% vs. 55.1% respectively, p<0.001), and secondary endpoints - recurrent MI and all-cause mortality were significantly lower in the colchicine group (29.6% vs. 33.5% and 1.9% vs. 3.9%, respectively, p<0.001). The incidence of heart failure and hospitalizations for any reason tended to decrease with colchicine, but did not reach statistical significance. No differences in the incidence of cerebrovascular events were observed between the comparison groups [20].

To sum up the above, it should be noted that the assessment of systemic inflammation markers, in particular hsCRP, in patients with CAD is no less important than the assessment of the lipid profile. A comprehensive assessment of clinical status allows for personalised pathogenetic therapy in this category of patients and achieves the most positive impact on prognosis.

The use of anti-inflammatory agents is an important component of prognosis-modifying therapy, especially in clinically complex patients who have recurrent index events on background therapy.

Currently, colchicine appears to be the most promising anti-inflammatory drug for patients with CAD. Its effectiveness in reducing the risk of recurrent CVE in patients with acute and chronic coronary syndromes and its adequate safety profile have been proven in a large number of randomised placebo-controlled studies.

Of course, anti-inflammatory drugs are not an alternative to basic prognosis-modifying therapy. And at present, there are still many unresolved issues regarding the prospects for the use of this group of drugs in broad clinical

practice. In particular, questions remain unanswered regarding the timing of their administration in patients with acute coronary syndrome from the onset of the index event, the duration and long-term effects of such treatment (in existing studies, the observation period for patients did not exceed 3 years), markers for monitoring its efficacy and safety, the advantages of such therapy in patients with multivessel coronary artery disease, high levels of systemic inflammation, and concomitant diseases that are also characterized by general hyperreactivity (diabetes mellitus, gout, and other rheumatic nosologies) as opposed to patients without such clinical characteristics.

It is also unclear whether anti-inflammatory therapy can affect the frequency of cardiovascular events associated with restenosis of implanted stent systems, since there is also an inflammatory component in the pathogenesis of this process.

CONCLUSIONS

1. Measuring levels of inflammatory markers, particularly hsCRP, is an essential component of a comprehensive clinical assessment of patients with CAD and an important predictor of recurrent adverse cardiovascular events.

2. Anti-inflammatory agents, when added to standard CAD therapy, help reduce the risk of recurrent major adverse cardiovascular events.

3. Colchicine is an anti-inflammatory agent with the most well-established prognosis-modifying effect in patients with CAD and a favorable safety profile.

4. Long-term outcomes of anti-inflammatory therapy, the timing of its initiation following an index event, benefits in specific subpopulations of CAD patients, and the impact on stent restenosis remain subjects for further study.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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