Current Vascular Pharmacology, 2023, *Vol. 21, No. 1*

LETTER TO THE EDITOR

Response to Athyros and Colleagues: Inflammation and LDL Reduction

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ARTICLE HISTORY

Received: November 23, 2022
Accepted: December 23, 2022

DOI:
10.2174/1570161121666230118115539

Dear Editor:

First and foremost, we thank Athyros *et al*. [1] for their interest, and we appreciate their knowledgeable comments regarding our recent manuscript *"The Role of Inflammation as a Preponderant Risk Factor in Cardiovascular Diseases"* [2].

Athyros *et al*. [1] discussed the role of statins in different clinical scenarios, doses, and timing of administration. Indeed, statins have changed the natural history of atherosclerotic disease in patients with hyperlipidaemia and inflammation. Even in patients without hyperlipidaemia, and with low-grade systemic inflammation data, studies such as Justification for the Use of Statins in Primary Prevention: an Intervention Trial Evaluating Rosuvastatin (JUPITER) [3] demonstrated that statins reduce the risk of major cardiovascular events. In recent years, the use of these lipid-lowering drugs has been extended to patients whose cardiovascular risk is determined by increased inflammation, such as patients with human immunodeficiency virus disease [4, 5], rheumatoid arthritis [6], systemic lupus erythematosus [7] or heart transplant recipients [8].

As mentioned in our review [2], innate immunity represents an interesting field of study in the diagnosis and treatment of cardiovascular disease. In fact, innate immunity mechanisms, such as the activation of monocytes, T-lymphocytes and platelets, strengthen the local inflammatory response, which contributes to the rupture of the atherosclerotic plaque [9]. These physiopathological events finally lead to acute thrombus formation, the major cause of acute coronary syndromes [10, 11]. The stability of atherosclerotic plaque mainly depends on immune and anti-inflammatory pathways [12]. Contemporary studies in stable and unstable coronary artery disease, such as the Canakinumab Anti-Inflammatory Thrombosis Outcomes Study (CANTOS) [13], Colchicine Cardiovascular Outcomes Trial (COLCOT) [14], Low-Dose Colchicine *vs*. Placebo in Patients with Chronic Coronary Disease (LODOCO2) [15], and Hydroxychloroquine for the prevention of cardiovascular events in myocardial infarction patients - a Safety Pilot Trial (OXI trial) [16], have supported the inflammatory hypothesis of atherosclerosis. The majority of these studies have demonstrated that the coronary residual inflammatory risk, a crucial prognostic factor of cardiovascular events, could be successfully decreased by the inhibition of different proinflammatory interleukins [17]. However, none of these drugs is free from the adverse side-effects. To begin with, the JUPITER study using rosuvastatin, reported more frequently diabetes and changes in glycosylated haemoglobin [3]; on the other hand, CANTOS using monoclonal antibodies reported an increase in leukopenia, risk of infections and thrombocytopenia without major bleeding events, probably related to the immunomodulatory nature of canakinumab [13]; then COLCOT and LODOCO2, using colchicine found an increase in gastrointestinal discomfort [14, 15]; and finally, OXI trial reported an increase in the cases of arrhythmias among the participants enrolled for the study [16].

In conclusion, another objective in the treatment of atherosclerosis is the prevention of cardiovascular events by targeting the systemic low-grade inflammation and the innate immune response.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

ACKNOWLEDGEMENTS

Declared none.

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