ejpmr, 2020,7(6), 265-269

SJIF Impact Factor 6.222

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Review Article

ISSN 2394-3211

EJPMR

ROLE OF INFLAMMATION IN ACUTE MYOCARDIAL INFARCTION

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Article Received on 27/03/2020 **Article Revised on 16/04/2020** **Article Accepted on 06/05/2020**

ABSTRACT

The important therapeutic goals of current cardiology are to project approaches to reduce myocardial necrosis and improving cardiac restoration following myocardial infarction. Myocardial infarction (MI) refers to partial (regional) myocardial necrosis, typically endocardium-based, inferior to occlusion of an epicardial artery. In dissimilarity, concentric subendocardial necrosis may affect from global ischemia and reperfusion in cases of long cardiac arrest with resuscitation. Zones of myocardial infarction may be subepicardial if there is occlusion of slighter vessels by thromboemboli creating from coronary thrombi. Myocardial necrosis encourages match initiation and free radical group, generating a cytokine cascade initiated by Tumour Necrosis Factor (TNF)-α release. Despite this potential damage, substantial evidence proposes that reperfusion improves cardiac repair cultivating patient survival; this outcome may be in part associated to the inflammatory response.

KEYWORDS: Acute Myocardial Infarction, Atherosclerosis, Inflammation, Inflammatory Markers, Reactive Oxygen Species.

INTRODUCTION

Acute myocardial infraction, also known as acute heart attack. It is induced by sudden blockade or occlusion in the coronary artery leading to ischemia. Myocardial infarction is a major public health concern and is one of the primary causes of mortality worldwide.[1] Myocardial Ischemia Reperfusion MI/R induced-inflammatory reaction is one of the most important elements in myocardia injury.[2] The main pathological process consists of the release of inflammatory cytokines and the aggregation and infiltration of inflammatory cells upon the inflammatory response.[3] During the process of inflammation, inflammatory cells are stimulated, and various cytokines are released, including tumour necrosis factor α (TNF-α), interleukin (IL)-6 and IL-8.[4] In addition, myocardial apoptosis is also associated with MI/R injury and is considered to be one of the key pathological processes in MI/R injury, and may be associated with heart failure, the amount of which is determined by the severity of MI/R injury.[5] During MI/R injury, myocardial apoptosis leads to myocardial contractile dysfunction, compensatory hypertrophy and reparative fibrosis, further increasing myocardial injury, which ultimately develops into cardiac dysfunction and failure.[6]

INFLAMATION IN ACUTE MYOCARDIAL INFARCTION

Inflammation is a physiological process by which the body responds to external insults and stress conditions, and it is characterized by the production of pro-inflammatory mediators such as cytokines. The acute inflammatory response is solved by removing the threat. Conversely, a chronic inflammatory state is established due to a prolonged inflammatory response and may lead to tissue damage.

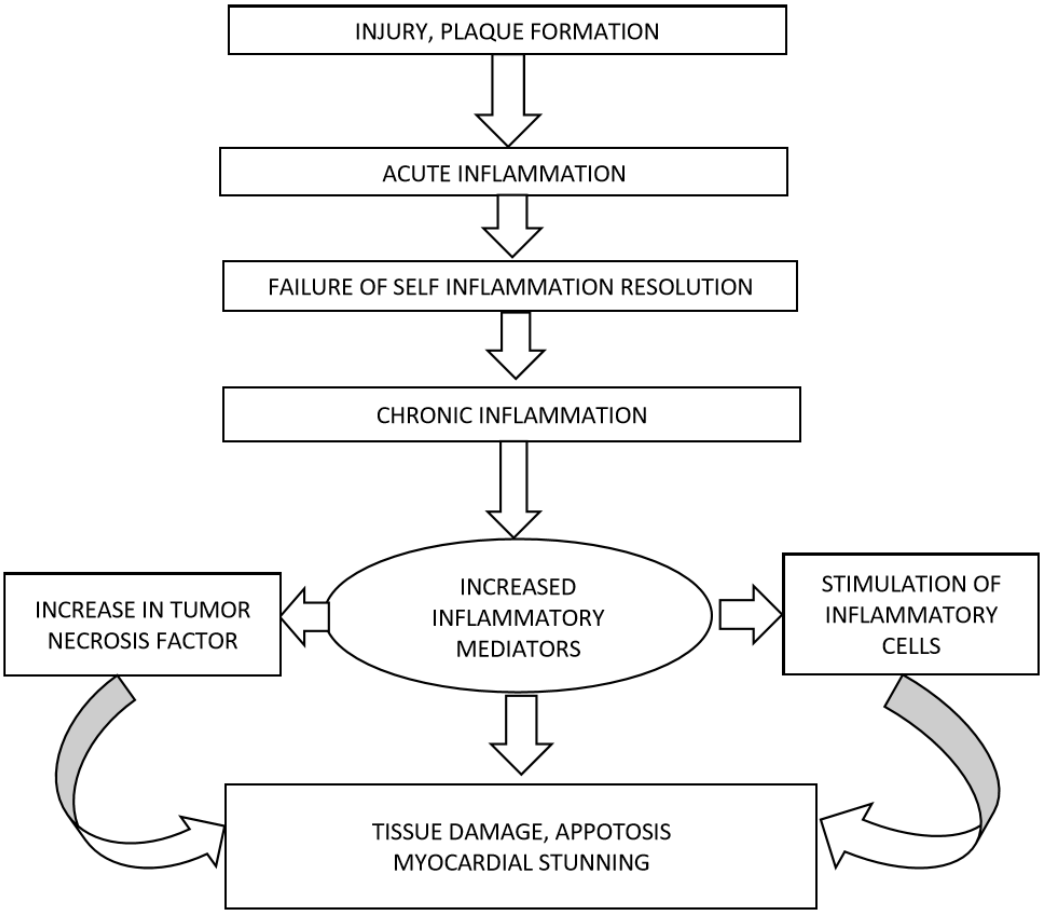

Figure 1: A detailed overview of various causes resulting in inflammation. Both environmental and endogenous factors are equally associated with the generation of inflammatory mediators. The mechanism of plaque formation and injury which leads to acute and chronic inflammation. This chronic inflammation will lead to an increase in inflammatory mediators, stimulation of inflammatory cells and increase in tumour necrosis factor which will further causing tissue damage, apoptosis and myocardial stunning.

INFLAMMATION IN MYOCARDIAL DAMAGE

Inflammation is a natural and essential immune response that occurs when organism experience infections, stress, or tissue damage to fight the impertinent agent. Although essential for body protection against pathogens, unnecessary inflammation can provoke by-Sander's injury and cause organ failure.[7] Inflammation is a complex process ensuring leukocyte infiltration at the site of tissue injury, and it is finely tuned by a large panel of molecules, tissue resident immune cells, and stromal cells. The production and secretion of pro-inflammatory cytokine, such as interleukin (IL)-1, tumor necrosis factor (TNF)-α, IL-6, colony stimulating factor (CSF), interferon's, transforming growth factor β (TGF-β), and chemokines, which contribute to the inflammatory response.[8]

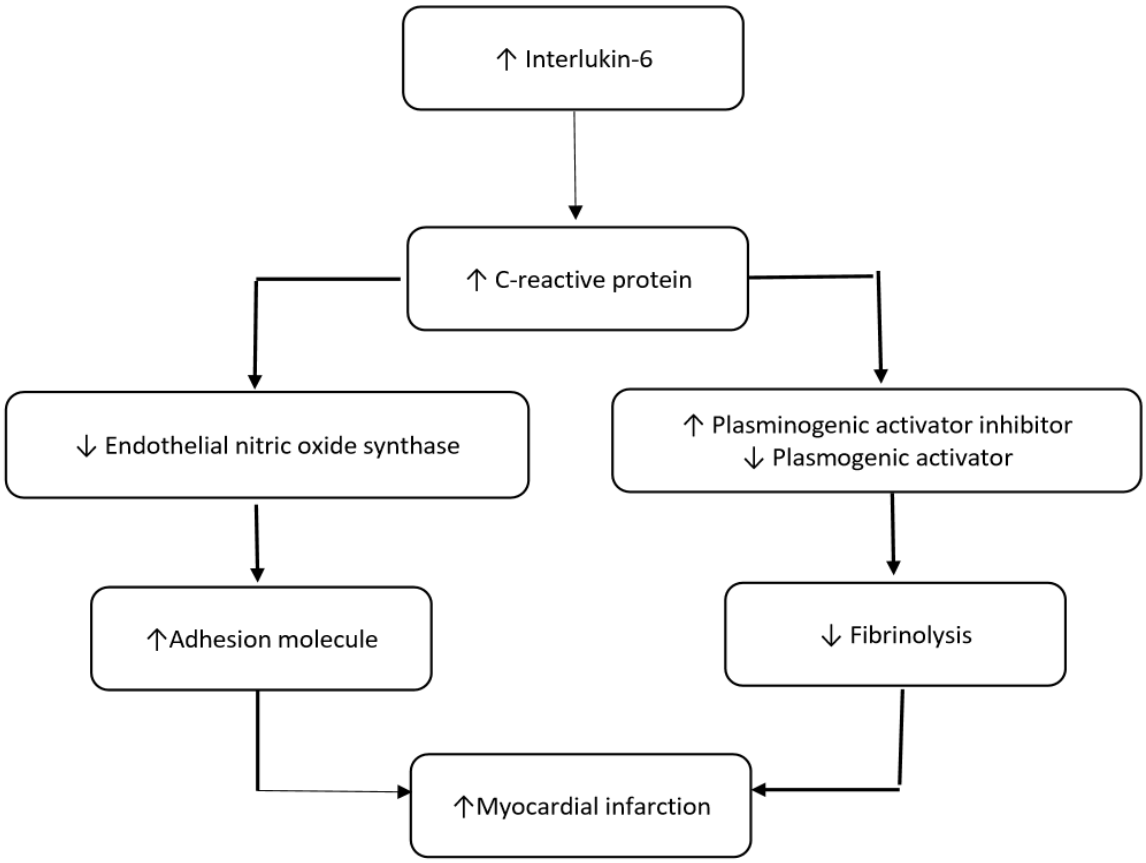

Figure 2: This schematic diagram demonstrates that the increase in levels of interlukin-6 causing myocardial infarction. C-reactive proteins mediates and having the contribution of forming lesion and rupture of plaques and increase in adhesion molecules and decreasing in process of fibrinolysis and therefore leading to myocardial infarction.

Typically, the inflammatory reaction is composed of four constituents: inducers of inflammation; sensors on the cell surface that detect them; mediators, produced when prompted by the sensors; and the target tissues that respond specifically to the inflammatory mediators. Different forms exist for each constituent, and their combinations compose distinct inflammatory pathways. The type of pathway induced depends on the nature of the trigger. Pathogens are recognized by several major classes of pattern recognition receptors (PRRs), expressed both in immune and non-immune sentinel cells, which are activated by pathogen-associated molecular patterns (PAMPs).[9]

Chronic inflammatory process plays a crucial role in the progression of heart diseases and exerts a deleterious role on cardiac function. Heart specific cytokines, neurohormones and pro-inflammatory molecules, which can be referred to as cardiokines, actively drive the progression of cardiac dysfunction in heart failure.[10] The cells composing the heart, such as cardiomyocytes, fibroblasts, vascular cells, and progenitor cells, can secrete several cardiokines following different environmental stimuli, realizing a specialized network that is critical for heart homeostasis. These proteins, including cytokines, such as TNF-α and TGF-β or different interleukins, are able to control the balance between normal cardiac function and pathological myocardial remodelling based on their ability to influence cardiomyocyte apoptosis, fibroblast activation, and vascular cell proliferation. Low concentrations of TNF-α produces a cardio protective effect, while increased levels of TNF-α have been associated to heart failure and diastolic dysfunction and is positively correlated to the severity of the diseases.

Cardiac-specific TNF-α overexpression display heart failure, cardiac dilatation, fibrosis, altered contractile function, Ca^{2+} handling defects, and premature death.[11] The progression of TNF-α-induced cardiac remodeling is associated to the activation of cardiomyocyte apoptosis and proteasome dysfunction.[12,13] In addition, TGF-β, another cardiokine that also has a physiological cardioprotective effect, if deregulated, actively participates in the pathological cardiac remodelling mediating the tissue fibrosis that follows the tissue-injury-derived inflammation acting on fibroblast activation, differentiation, and extracellular matrix

protein secretion.[14, 15] TGF-β1 and collagen levels are up-regulated in cardiomyocytes subjected to mechanical stress, but this event is reverted in RyR2 knockdown cardiomyocytes.[16] Up-regulation of peroxisome proliferator activated receptor alpha and results in the down - regulation of collagen gene expression in the hypertrophy-model of cardiac fibroblasts.[17] An emerging role for the IL-33/ST2 pathway in the inflammation that occurs during the cardiac stress condition has been described. The IL-33/ST2 interaction results in an anti-hypertrophic effect by blocking NF-κB activation. Mice lacking ST2 have worsened hypertrophy, cardiac dilation, ventricular fractional shortening, increase fibrosis, and reduced survival in a pressure overload condition.[18]

INFLAMMATORY RESPONSE IN THE TREATMENT OF MYOCARDIAL INFARCTION

Targeting specific inflammatory mediators may not rescue a significant number of cardiomyocytes in reperfused infarcts but may protect from chamber dilation and adverse remodelling and postinfarction heart failure. Infiltrating mononuclear cells and mast cells appear to orchestrate the cardiac repair process through a complex cascade involving cytokines and growth factors. Inflammation-induced adverse remodelling of the infarcted heart may be due to activation of matrix metalloproteinases and subsequent matrix loss, resulting in reduced tensile strength of the infarct, cardiomyocyte slippage and loss of essential matrix-derived homeostatic signals that may support cardiomyocyte survival and function.[19] The molecular signals induced following myocardial infarction may mediate suppression of tissue injury and regulate scar formation. Interleukin-10 (IL-10), a cytokine initially described as cytokine synthesis inhibitory factor (CSIF) is primarily a product of activated Th2 cells and endotoxin-stimulated monocyte.[20]

TGF-β may have an important indirect role in promoting angiogenesis following experimental myocardial infarction by suppressing expression of IP-10. IL-10 inhibits the production of IL-1a, IL-1b, TNF-a, IL-6 and IL-8 by LPS-activated monocytes, sup- pressing the inflammatory response. Inflammatory mediators (such as MCP-1) may have worse prognosis due to the development of dilative remodelling and may benefit from targeted inhibition of inflammation. Thus, personalised, biomarker-based approaches may be needed to effectively target cardiac remodelling following myocardial infarction. The role of inflammatory markers in predicting CHD risk is still evolving. While CRP was the first to be studied in this field there is a need to focus on other plaque-specific inflammatory markers.[21]

The effects of most inflammatory markers found to date are generally modest, and we need to identify new inflammatory markers with more robust predictive power independent of conventional risk factors. We also need to evaluate each of their potential roles in contributing to inflammation and atherogenesis in preclinical and clinical studies. Specific inhibitors of inflammatory markers can be tested for preventing CV events. Currently, there is a relative paucity of medications that can be used safely and effectively as primarily anti-inflammatory agents in CHD. The discovery of such medications and their administration orally, intravenously or perhaps directly into vulnerable atherosclerotic plaques, is an area of great importance in potentially preventing myocardial infarctions and their complications.[22]

CONCLUSION

It is believed that inflammation plays an important role in the pathophysiology of numerous human diseases. The imbalance in the metabolic activity and antioxidant activity in acute myocardial infarction replicates the importance of measuring the level of inflammatory markers and biomarkers as a diagnostic and predictive tool for medical treatment of AMI. Estimation of inflammatory marker compounds will help to improve defense system which may help in the treatment, prognosis, and prevention of AMI. The review reflects the ability of inflammatory markers are tool for integrate in the development of acute myocardial infarction. Therefore, measuring of inflammatory markers and biomarkers in AMI is necessary for the effective management of the disease which may help in the treatment.

ACKNOWLEDGMENTS

The authors would like to acknowledge and thank the Department of Science and Technology – Fund for Improvement of Science and Technology Infrastructure in Universities and Higher Educational Institutions [DST-FIST], Govt. of India, New Delhi for their infrastructure support to Department of Pharmacology. The authors acknowledge and sincerely thank the Principal and Management, JSS College of Pharmacy, Ooty, for providing all the needed support and encouragements to do this work.

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