The inflammatory phases of atherosclerosis

People

Abstract

Aim– This review describes recent investigations in to the impact of atherosclerosis on the vessel using four inflammatory stages eventually leading to cardiovascular complication.

Research in to atherosclerosis has intensified globally as it has become one of the main reasons for increased mortality among individuals particularly within western societies. Inflammation has been established as the principal concept due to it stimulating progressive lesion development. As a result it is known as a chronic inflammatory disorder. Numerous cellular and molecular inflammatory mediators participate in the formation, development and rupture of the atherosclerotic plaque. Several experimental studies have demonstrated that monocyte- derived macrophages as well as T-lymphocytes are the most distinctive cells to accumulate within progressive plaques and induce the production of pro-inflammatory components, more recently, potential anti-inflammatory mediators have been identified in the inflammatory response. The rate of progressive plaque development varies in different types of people. Risk factors increase the development of this condition and promote the occurrence of physical symptoms on the patient.

Conclusions– (1) Inflammation attacks arteries systematically within phases and (2) the significance of the role of inflammatory molecules, linking inflammation to atherosclerosis.

Introduction

The management of cardiovascular diseases has significantly improved, however it is still not clearly understood as to why atherosclerosis remains

the leading pathological cause of both morbidity and mortality in developed countries. Atherosclerosis is known to be a type of arteriosclerosis, but in addition to the hardening and narrowing of the arteries, cholesterol begins to deposit within their walls. It is a multifactorial disease which includes build up of atheromatous plaque and accumulation of more complex lesions within the arterial walls specifically in the intimal layer leading to the rupture of these vulnerable atherosclerotic plaques (Skjot-Arkil et al, 2010).

This process is initiated inchildhoodand according to the results of PDAY (pathobiological determinants of atherosclerosis in youth study), visible symptoms of atherosclerosis will occur between ages of 15-54 years (McGill et al. 2007). Furthermore this disease can occur in both medium and large sized arteries including the aorta, carotid artery and even the smaller coronary arteries. Due to the fact that it affects multiple arterial locations, it can then lead to clinical diseases such as coronary artery disease, cerebrovascular disease, myocardial infarction.

Jongstra et al. (2006) demonstrated that within the intima of VCAM-1 positive mice, local chronic inflammation predisposed to atherosclerosis. This provided further evidence to support previous studies that inflammation participates in the atherosclerotic process. Consequently, inflammation is progressively involved in the plaque formation, resulting in an inevitable stenosis (Vidal-Vanaclocha, 2009).

Numerous epidemiological studies have revealed many risk factors that accelerate atherosclerosis development including age, male gender, obesity, smoking, hypertension anddiabetesmellitus. Moreover, a recent study

(Holvoet et al, 2007) found that a positive correlation exists between an increased amount of oxidised LDL and the quantity of calcium built up in the coronary artery. Therefore showing that increased amount of oxidised LDL is a unique risk factor for the development of atherosclerosis. The factors that facilitate this plaque formation are inflammatory mediators. As the endothelial cell is activated, this results in expression of many cell surface adhesion molecules including cytokines, chemokines, monocytes, immunoglobulins. These promote endothelial dysfunction in atherosclerosis as well as inducing foam cell formation with the assistance of macrophages. However, the functional mechanisms of cytokines in initiating and prolonging atherosclerosis are still not clearly understood.

Aims

To explore the role of inflammation in atherosclerosis

To explore the mechanisms of inflammatory cell recruitment and accumulation within the plaque.

To explore the function of various different mediators in this process, including both pro and anti-inflammatory mediators.

Rationale of the aims

To investigate the effects of the inflammatory cycle on arteries using atherosclerosis as the central condition.

Hence, following the aims and objectives of the literature review, an overview of numerous meta-analyses of mediator involvement in this process is provided. This would be performed by reviewing the most relevant

literature for the past five years using Pubmed, Sciencedirect andGoogleScholar.

Table 1 Methodical reviews on the involvement of inflammatory components within the development of atherosclerosis.

Type of componentMediatorExperimental sourceInflammatory effectEffect on AtherosclerosisAuthor, year

ImmunoglobulinICAM-1Human plasma

Human aortic SMC

Human aortic endothelial cells^

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Bielinski et al, 2008

Burton et al, 2009

Roth et al, 2007

ImmunoglobulinVCAM-1Human plasma

Human aortic endothelial cells^

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Bielinski et al, 2008

Roth et al, 2007

CytokineTNF-alphaAPoE-/- micev

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Bhaskar et el, 2011

CytokineIFN-gammaHuman RNA^

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Niedzielska and Cierpka, 2010

CytokineM-CSFHuman platelets^

Siezer et al, 2010

CytokineIL-6Human aortic endothelial cells

Human Plasma

APoE-/- mice^

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Roth et al, 2007

Hoshi et al, 2008

Bhaskar et al, 2011

CytokineIL-1 (beta)Human aortic SMC

APoE-/- mice

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Burton et al, 2009

Bhaskar et al, 2011

ChemokineCXCL16Human and murine macrophages

APoE-/-^

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Lehrke et al, 2007

Wen-Yi et al, 2011

ChemokineCXCR6Human and murine macrophages^

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Lehrke et al, 2007

LigandCD40 LHuman umbilical vein endothelial cells^

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Chakrabarti et al, 2010

Monocyte ProteinMCP-1Human aortic endothelial cellsAPoE-/- mice^

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Roth et al, 2007

Bhaskar et al, 2011

Toll-like receptorTLR-2^

Doherty et al, 2006