Letter to the Editor

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Inflammation as a Therapeutic Target of Betablockers in Ischemic Heart Disease

To the editors:

Experimental evidence suggests a crucial role of inflammation in the pathophysiology of atherosclerosis and acute myocardial infarction.

In myocardial ischemia, a pleiotropic proinflammatory imbalance with damaging effects in terms of left ventricular performance and patient outcome is the result of uncontrolled immune response. Cardiac injury activates specific immune mechanisms initiating an inflammatory reaction. Immunological receptor-mediated pathways, the complement cascade, and reactive oxygen generation induce nuclear factor (NF) kappa B activation and up-regulation of chemokine and cytokine syntheses are just some of them. In the infarcted tissue, chemokines stimulate the chemotactic attraction of inflammatory leukocytes into infarcted areas, while cytokines promote adhesion between leukocytes and endothelial cells. The latter elicit invasion of inflammatory cells into the site of injury and thus promote cell damage.

The complexity of the inflammatory cascade involved in the development of atherosclerosis makes it difficult to develop single-target drugs in order to slow down or affect the process. Drug developers have always been in search for new approaches to speed up single-target drugs in order to slow down or affect the development of atherosclerosis makes it difficult to decrease inflammation in vulnerable plaques [9]. However, a more complex, likely favourable regulation has also been seen in several aspects of early inflammatory response: neoendothelial inflammatory and endothelial functions have been indicated as crucial not only in the development of atherosclerosis [5] but also for heart failure (HF) patients.

The effect of carvedilol on cytokines and asymmetric dimethylarginine (ADMA) and left ventricular ejection fraction (LVEF) at baseline and after long-term administration of carvedilol has been studied and carvedilol reduced symptoms as well as parameters of inflammation, regardless of the left ventricular functional response [10]. Carvedilol has also been shown to attenuate inflammation, oxidative response, myocardial fibrosis, and apoptosis, as well as in preserving energy transcription factors and LV function in DCM [11]. It is often cardiac injury itself which propagates immune mechanisms leading to an inflammatory reaction [12]: on the one hand, immunological receptor-mediated pathways and the complement cascade lead to activation of nuclear factor (NF) kappa B and increase chemokine and cytokine syntheses in the ischemic tissue, thus attracting inflammatory leukocytes into the ischemic area. On the other hand, cytokines promote adhesive interactions between leukocytes and the endothelial layer enabling transmigration of inflammatory cells into the site of injury. Inflammatory cytokines stimulate apoptosis through a TNF-α receptor/caspase pathway [13]. Inflammatory mechanisms thus play a role in both the development of atherosclerosis and the effect on coronary artery disease.
In summary, there is a complex relationship between α-adrenergic blockade, sympathetic activity, and inflammation [14]. The next decade will certainly be marked by the investigation of pleiotropic drug effects upon inflammatory processes searching for further and more specific applications of drugs in primary prevention.

References:

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