Review

Angiotensin converting enzyme (ACE) and HydroxyMethylGlutaryl-CoA (HMG-CoA) reductase inhibitors in the forefront of pharmacology of endothelium

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Abstract

Healthy endothelium is essential for undisturbed functioning of the cardiovascular system, while endothelial dysfunction leads to its various pathologies. For example endothelial dysfunction precedes clinical symptoms of atherothrombosis, such as acute coronary syndrome, ischemic stroke, peripheral arterial disease or diabetic microangiopathies e.g. retinopathy and nephropathy. Accordingly, pharmacological reversal of endothelial dysfunction may represent a new approach in preventing the aforementioned vasculopathies.

In modern cardiovascular pharmacology, inhibitors of angiotensin converting enzyme (ACE-I) or inhibitors of HydroxyMethylGlutaryl-CoA (HMG-CoA) reductase (statins) are among the most widely used cardiovascular drugs. Originally, ACE-I and statins were introduced to clinical medicine to lower arterial blood pressure or to lower blood LDL cholesterol levels, respectively. They were respectively targeted to inhibit ACE in blood or to inhibit HMG-CoA reductase in the liver. Surprisingly, these two classes of drugs apart from their classic mechanisms of action exert pleiotropic endothelial actions, which involve the inhibition of ACE or HMG-CoA reductase within the endothelium, as well as other less understood endothelial mechanisms. Typically, therapeutic effectiveness of ACE-I by far exceeds the benefits expected from their hypotensive effect or as the matter of fact of other hypotensive drugs. Similarly, statins offer cardiovascular protection irrespective of initial LDL cholesterol levels in patients. In our view, it is the endothelial action of ACE-I or statins that contributes significantly to their anti-inflammatory, anti-thrombotic, and vasculoprotective actions. Importantly, actions of ACE-I or statins are not limited to the correction of functioning of a single endothelial mediator, but they do possess a broader spectrum of endotheliotropic properties that proved efficient in preventing atherothrombosis and other vasculopathies.

Quite surprisingly, the history of ACE-I and statins has a major impact for the future development in pharmacology of endothelium.

Key words:
endothelium, atherothrombosis, ACE, ACE-I, HMG-CoA reductase, statins, pleiotropic drug action