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Invited Commentary

Commentary on 'Simvastatin Decreases Free Radicals Formation in the Human Abdominal Aortic Aneurysm Wall via NF-κB'

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The complex biological processes associated with abdominal aortic aneurysm (AAA) include oxidative stress and proteolysis in relation to both leukocyte recruitment and platelet activation, leading to immuno-inflammatory response, cell death and extracellular matrix breakdown. A key player in regulating immune-inflammatory processes is nuclear factor-κB (NF-κB), a redox-sensitive transcription factor involved in the transmission of various signals from the cytoplasm to the nucleus of numerous cell types, activating genes which codify products such as adhesion molecules, chemoattractants, proinflammatory enzymes and procoagulant proteins. Piechota's paper confirms that NF-κB could be involved in the pathogenesis of AAA, as suggested by previous data.[1]

Statins have proved the greatest impact on cardiovascular disease since aspirin. Their pleiotropic effects beyond lipid lowering are still being researched. Recent findings suggest that the clinical benefit of these drugs could be related to a reduction in oxidative stress, blood thrombogenicity and to anti-inflammatory and immunomodulatory properties. Piechota et al offer new interesting data on the effect of simvastatin on inflammation and free radicals generation within the aortic wall. The current results are somewhat baffling, as the authors have obtained an increase in catalase activity, and a decrease in TNFα concentration and NF-kB expression in the AAA wall samples treated with simvastatin, but not superoxide dismutase (SOD) activity or H_2O_2. This is not the first study to show a significant inhibition of statins on both NF-kB activity[2] and oxidant enzymes such as NADPH oxidase and myeloperoxidase,[3] as well as an up-regulation of the activity of anti-oxidant enzymes such as catalase.[4] However, none have obtained an absolute reduction in the tissue's oxidative end-products, such as H_2O_2. These are indeed difficult to quantify and often the net effect must be extrapolated indirectly, through the evaluation of the activity of oxidant or antioxidant enzymes. Still, the exact mechanism remains unclear.

The reduction in the incidence of cardiovascular events and death associated with statins has been sufficiently proved and current guidelines recommend that all vascular patients, unless specifically contraindicated, should receive the drug. But the evidence of its impact on AAA growth and rupture risk is still weak, level B and C at best, with contradictory published results. Studies aiming to better understand the therapeutical effects of statins are timely and welcome.

References

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