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Symposion I: „Endothel – Funktion und Dysfunktion“

1 Endothelfunktion und -dysfunktion

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2 Endothelial dysfunction – the target for pharmacological intervention

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Healthy endothelium is essential for undisturbed functioning of the cardiovascular system, while endothelial dysfunction leads to its various pathologies. Indeed, endothelial dysfunction precedes clinical symptoms of atherothrombosis, and has diagnostic and prognostic significance in atherothrombosis. Accordingly, pharmacological reversal of endothelial dysfunction represents a new approach to prevent atherothrombosis. Phenotype of endothelial dysfunction involves: impairment of vasculoprotective mediators (NO and PGI2), robust activation of pro-inflammatory phenotype (expression of various cytokines, chemokines, adhesion molecules) as well as activation of pro-thrombotic endothelial mechanisms. Pharmacotherapy of endothelium should aim to reverse all these alterations in endothelial function.

There are number of drugs that modulate endothelial phenotype: inhibitors of angiotensin converting enzyme (ACE-I), inhibitors of HydroxyMethylGlutaryl-CoA reductase (statins), β-adrenolytics, angiotensin receptors antagonists, endothelin receptor antagonists, antiplatelet drugs, aldosteron antagonists, xantine oxidase inhibitors and many others. Surprisingly, ACE-I and statins constitute the forefront of pharmacology of endothelium. Therapeutic effectiveness of ACE-I by far exceeds the benefits expected from their hypotensive effect. Similarly, statins offer cardiovascular protection irrespective of initial LDL cholesterol. These two classes of drugs – apart from their classic mechanisms of action – exert pleiotropic endothelial actions that contributes significantly to their anti-inflammatory, anti-thrombotic, and vasculoprotective actions. In a search of a new candidates for endotheliotropic drug we studied several nicotinamide analogues. We found that 1-N-