INHIBITION OF PHOSPHODIESTERASES IN AIRWAYS

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Phosphodiestrases (PDEs) represent a superfamily of 11 different types of hydrolases responsible for degradation of cyclic AMP and cyclic GMP. A tissue variability in PDE families expression influences significantly functions of respective tissues and organs. Their inhibition may lead to specific symptoms, with possible pharmacological use in various diseases. In the respiratory system, PDE3 and PDE4 are expressed in airway smooth muscle, PDE1 and PDE5 are expressed in vessels smooth muscle, and PDE3, PDE4 and PDE7 are found in inflammatory cells. While cGMP is a preferred substrate of PDE1 and PDE5, other isoforms (i.e. PDE3, PDE4 and PDE7) are predominantly involved in degradation of cAMP. Therefore, a selective inhibition of different PDE isoforms may lead to various pharmacological effects, including bronchodilation, vasodilation, suppression of inflammation or antitussive action. In this presentation the roles of the most important PDE isoforms will be described and documented by recent results from in vivo and in vitro testing the contractility of smooth muscle, hematological, immunological and biochemical screening of markers characteristic for allergic inflammation. Furthermore, therapeutic use of selective PDE inhibitors will be suggested, including their use in combinations.

Grant support: APVV-0305-12, CEKR 2, VEGA 1/0260/14, BioMed Martin ITMS 26220220187