Cyclic AMP generating system in human microvascular endothelium is highly responsive to adrenaline

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Abstract:
We have tested cultured human microvascular endothelial cells (HMEC-1) for their ability to synthesize cyclic adenosine 3',5'-monophosphate (cAMP) in the absence or presence of various drugs. The accumulation of cAMP was only slightly affected by the addition of a phosphodiesterase inhibitor 3-isobutyl-1-methylxanthine (IBMX) to the incubation medium. A direct stimulator of adenylyl cyclase forskolin and adrenergic drugs, such as adrenaline and noradrenaline, strongly increased cAMP accumulation in IBMX-treated HMEC-1 cells, whereas some other drugs known to stimulate the nucleotide synthesis in different cell/tissues were inactive (dopamine, histamine). Adrenaline was significantly more potent than noradrenaline. The effect of adrenaline on cyclic AMP production was reproduced by a selective β-adrenoceptor agonist isoprenaline, antagonized by β-blocker propranolol, and was not influenced by both α₁- and α₂-selective antagonists, prazosin and yohimbine, respectively. Adrenaline did not significantly affect the ability of HMEC-1 cells to produce vascular endothelial growth factor (VEGF) or interleukin-8 (IL-8), the major angiogenic mediators. The results indicate that under basal (non-stimulated) conditions, the cAMP generating system of HMEC-1 cells maintained in culture remains rather quiescent, yet it can strongly respond to the hormone adrenaline acting on β-adrenergic receptors.

Key words:
human microvascular endothelium, HMEC-1, cyclic AMP, isoprenaline, adrenaline, noradrenaline, forskolin, β-adrenergic receptor, VEGF, IL-8