ΕΠΙΘΕΩΡΗΣΗ ΚΛΙΝΙΚΗΣ ΦΑΡΜΑΚΟΛΟΓΙΑΣ
ΚΑΙ ΦΑΡΜΑΚΟΚΙΝΗΤΙΚΗΣ 27: 40-41 (2009)

The Effect of Corticosteroids and beta 2-Adrenergic Agonists on Hyaluronic Acid Homeostasis by Human Airway Smooth Muscle Cells

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Hyaluronic acid (HA), is an essential extracellular matrix molecule which regulates tissue flexibility, a parameter that is reduced in airways of patients with asthma. First-line therapy of persistent asthma involves the combination of inhaled corticosteroids and beta 2-adrenergic agonists. The aim of our study was to investigate the effect of corticosteroids, beta 2-agonists, and their combination on HA homeostasis by human airway smooth muscle cells (ASMC). For this purpose, we established primary cultures of ASMC from dissected airway muscle bundles obtained from lung resections. Cells were incubated for 48 h in the presence of therapeutic doses of budesonide, formoterol or their combination. HA secretion was measured by ELISA and gene expression of hyaluronic acid synthases (HAS), hyaluronidases (HYAL) and the HA receptors CD44 and RHAMM (receptor for HA-mediated motility) was assessed by RT-PCR.

We found that budesonide had no effect on the secretion of HA by ASMC, while formoterol significantly stimulated HA secretion, an effect that was further induced by the combination of the drugs. RT-PCR analysis revealed that the combination of formoterol and budesonide significantly induced gene expression of HAS-1, inhibited gene expression of HYAL-1 and induced gene expression of CD44 and RHAMM.

Our results indicate that treatment of asthma with corticosteroids and beta 2-adrenergic agonists is associated with increased production and secretion of HA by ASMC, an effect which is beneficial since HA plays a protective role in the human airways.