Long-acting muscarinic antagonists and small airways: which link?

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Abstract

Involvement of small airways, those of less than 2 mm in internal diameter, is present in all stages of asthma and contributes substantially to the pathophysiologic expression of asthma. Therefore, small airways are increasingly viewed as a potential target in optimal asthma control. Airway tone, which is increased in asthma, is mainly controlled by the vagus nerve that releases acetylcholine (ACh) and activates muscarinic ACh receptors (mAChRs) post-synaptically on airway smooth muscle (ASM). In small airways, M3 mAChRs are expressed, but there is no vagal innervation. Non-neuronal ACh released from the epithelial cells that may express choline acetyltransferase (ChAT) in response to inflammatory stimuli, as well as from other structural cells in the airways, including fibroblasts and mast cells, can activate these receptors. By antagonizing M3 mAChR, the contraction of the ASM is prevented and, potentially, local inflammation can be reduced and the progression of remodeling may be affected. In fact, ACh also contributes to inflammation and remodeling of the airways and regulates the growth of ASM. Several experimental studies have demonstrated the potential benefit derived from the use of mAChR antagonists, mainly long-acting mAChR antagonists (LAMAs), on small airways in asthma. However, there are several confounding factors that may cause a wrong estimation of the relationship between LAMAs and small airways in asthma.

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