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Budesonide/Formoterol

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Corticosteroids combined with long-acting β_2-agonists, for example budesonide/formoterol, have been suggested for the treatment of inflammatory lung diseases, including asthma and chronic obstructive pulmonary disease (COPD). The incidence of both diseases is increasing worldwide, but there is no effective therapy available. With regard to COPD, cessation of smoking or corticosteroid or β_2-agonist therapy can only slow down the progression of the disease, but can neither stop nor revert it.

Corticosteroids and long-acting β_2-agonists have been used to treat inflammatory lung diseases for a long time and the combination of both classes of drugs is advised in severe forms of these diseases. Budesonide/formoterol has been shown to yield much better control of symptoms, with fewer exacerbations and improved lung function and quality of life compared with one or both drugs used alone.

Formoterol acts via a cell membrane receptor that activates cyclic adenosine monophosphate (cyclic AMP) and protein kinase A, and then diverts into several subsequent signalling pathways. The immediate action of β_2-agonists as a bronchodilator is mediated via cyclic AMP, resulting in relaxation of the constricted bronchial musculature. The anti-inflammatory potential of β_2-agonists is controversial.

Corticosteroids bind to their cytosolic glucocorticoid receptor; the complex migrates into the nucleus where it binds to a specific DNA sequence to modulate gene activity, or interacts with other transcription factors, including signal transducers and activators of transcription, activator protein 1, CCAAT/enhancer binding protein (C/EBP) or inhibitor of κB, and modulates their function. Both actions can reduce the synthesis and release of various pro-inflammatory or mitogenic proteins.

Budesonide/formoterol exerts a synergistic, or at least additive, effect on several cellular processes linked to COPD, and is more effective than either drug alone in reducing cytokine release by lymphocytes, macrophages and eosinophils, and slowing down proliferation of several pulmonary cell types, including fibroblasts. The latter effect may be explained by the synchronised activation of the glucocorticoid receptor and C/EBP-α, which, after activation form a complex that induces the anti-proliferative protein, $p21^{(Waf1/Cip1)}$. In cell cultures, an optimal effect was only achieved when both drugs were applied together, as would be the case when using an inhalation device.

The recently published data on the favourable effect of budesonide/formoterol on COPD symptoms and progress seem to support further long-term efficacy investigations. ▲