Title: Formoterol and fluticasone reduce the deposition of pro-inflammatory collagens

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Body: Background: Increased deposition pro-inflammatory collagen I and III has been shown in the sub-epithelial airways in asthma. Formoterol has been reported to reduce collagen deposition, while steroid action depends on the presence of inflammation. Under inflammatory condition, steroids increased collagen deposition. Objective: We investigated the effect of three steroids on the inhibitory effect of formoterol on collagen deposition in TGF-β1 and serum stimulated human airway smooth muscle (ASM) cells. Methods: ASM cells were incubated for 3 days with serum (5%) or TGF-β1 (1ng/ml) in the presence or absence of formoterol, dexamethasone, budesonide or fluticasone (1nM – 1microM). Collagen deposition was determined by an in house ELISA. Results: Serum and TGF-β1 significantly increased the deposition of collagen I and III, while they did not affect the collagen IV content. In non-stimulated cells, all 3 steroids reduced the deposition of collagen I and III dose dependently, while they increased collagen IV. In stimulated cells (TGF-β1, serum) collagen I and III deposition were further increased. Formoterol dose dependently reduced the deposition of all three collagens in non-stimulated and stimulated cells. When combined with steroids the inhibitory of formoterol on collagen I and III deposition was dose dependently increased, but had no effect on collagen IV. The combination with fluticasone achieved more often a stronger inhibitory effect than the other 2 steroids. Conclusion: Our data suggests that formoterol has the potential to reduce airway wall remodelling in asthma and in combination with fluticasone, it is more effective than with other steroids.