ABSTRACT

Effect of Caffeic Acid on Myofibroblast Differentiation and Collagen Production in Nasal Polyp-Derived Fibroblasts

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ABSTRACT

Effect of CAPE on Nox4 expression

The pathophysiology of nasal polyp formation is still poorly understood. Previous experimental studies suggested that the proliferation of fibroblasts and differentiation into myofibroblasts have a role in formation of nasal polyps. The myofibroblasts produce extracellular matrix (ECM) such as collagen. Transforming growth factor-β (TGF-β) is a cytokine that stimulates proliferation of fibroblasts and their differentiation into myofibroblasts. Therefore, TGF-β has been implicated in the pathogenesis of nasal polyps as well as by-products in aerobic metabolism, but is also produced by specialized enzymes, such as NADPH oxidases (Noxs).

Objectives: Caffeic acids are known to have antioxidant, anti-inflammatory, immunomodulatory, and tissue reparative effects. The purpose of this study was to determine the effect of caffeic acid on transforming growth factor-β (TGF-β)-induced myofibroblast differentiation and collagen production, and to determine whether or not caffeic acid is involved in the antioxidant effect.

Methods: Nasal polyps myofibroblasts (NPDFs) pre-treated with caffeic acid (5-25 µM) and stimulated with TGF-β (5 ng/ml) for 24h. The expression of α-SMA, collagen types I and III, and Nox4 mRNA was determined by a reverse transcription-polymerase chain reaction, and the level of total soluble collagen production was analyzed with the Sircol assay for the proper regulation of cell function such as intracellular signaling, transcription activation, cell proliferation, inflammation, and apoptosis. ROS has been implicated in the pathogenesis of a large number of diseases, including bronchial asthma. ROS is not only generated by by-products in aerobic metabolism, but is also produced by specialized enzymes, such as NADPH oxidases (Noxs).

It has been reported that caffeic acid was a superior antioxidant compared with p-coumaric and ferulic acids, in inhibiting low density lipoprotein oxidation, but also quenching radicals and singlet oxygen. Caffeic acid acts as potent antioxidants. However, the effects of caffeic acid on nasal polyp myofibroblasts were used to determine the effect of Nox4.

Results: The expression of α-SMA and production of collagen were significantly increased following TGF-β treatment. In contrast, the level of expression of α-SMA was prevented by pre-treatment with caffeic acid. The expression of Nox4 and the subsequent production of ROS were also reduced by pre-treatment with caffeic acid.

Conclusion: Caffeic acid may inhibit TGF-β-induced myofibroblast differentiation; the effects of CAPE on TGF-β-induced myofibroblast differentiation, collagen production and to determine whether the effects of caffeic acid on Nox4 and ROS are involved in the process.