Exogenous nitric oxide stimulated collagen type I expression and TGF-beta1 production in keloid fibroblasts by a cGMP-dependent manner

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摘要

Abstract

Keloids arise from the aberrant wound healing process and nitric oxide (NO) plays an important role in the inflammation stage of wound healing. In order to better define the potential effect of NO/cGMP signal pathway in the keloid pathogenesis, the enhancing effect of exogenous NO (released from NO donor) on collagen expression in the keloid fibroblast (KF) as well as on the induction of collagen type I protein and TGF-beta1 expression in the KF were studied in this investigation. The DETA NONOate, an NO donor, was added to the KF, as the exogenous NO, to release NO in the culture medium. The expression of collagens was then determined by assaying the total soluble collagens and collagen type I in the KF. The cellular concentration of cGMP was measured by EIA in the KF. Exogenous NO was found to enhance the expression of collagens and elevate the cellular levels of cGMP. Moreover, to evaluate the effect of the elevated cellular cGMP levels on the expression of collagen and TGF-beta1, both cGMP and TGF-beta1 were measured by ELISA. The inhibitors for phosphodiesterase (PDE), such as IBMX (3-isobutyl-1-methylxanthine), Vinpocetine, EHNA, Milrinone and Zapriast, which have been reported to reduce the ability of PDE and subsequently produce an increase of cellular cGMP, induce the production of autocrine TGF-beta1 as well as the synthesis of collagen in the KF. In this investigation, the inhibition of the PDE enzyme activity was observed to enhance the effect on the collagen synthesis, and was induced by exogenous NO. Taken together, these results have suggested that the NO/cGMP pathway could positively influence the progression of keloid formation, via the TGF-beta1 expression in

the KF.